



# PAEDIATRIC PROTOCOLS

For Malaysian Hospitals

2nd Edition

Hussain Imam Hj Muhammad Ismail  
Ng Hoong Phak  
Terrence Thomas



Kementerian Kesihatan Malaysia

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## FOREWORD

Malaysia is a relatively young country with a young population. Realizing this, the government have always given priority to maternal and child health services. The progress made in all indices of Maternal and Child Health since Independence is indeed praiseworthy. However, while we have made much progress in primary health care, we still lag behind in some aspects of secondary and tertiary care.

The maldistribution of doctors and specialists between urban and rural areas leaves many children out of reach of specialist care during their first contact with the health services. There are still parts of the country, especially in Sabah and Sarawak, where emergency health care services are heavily dependent on Medical Assistants (now called Assistant Medical Officers).

Meanwhile, our population is getting more educated and aware of their health needs. This results in greater expectations of the health services and decreasing tolerance of mistakes and shortcomings on the part of health professionals.

One way of overcoming this disparity between expectations and the availability of specialist's services is the production of clinical practice guidelines, clinical pathways and protocols which are evidenced-based and simplified. This will help junior doctors to confidently manage ill patients. The first few hours of the patient's presentation to hospital are often the most important and if things are done right from the very beginning, the eventual outcome would certainly be more favourable.

The Ministry of Health has produced CPGs in many areas. However the pediatric services are the first to produce a comprehensive book covering all major pediatric conditions. I would like to congratulate the paediatricians in the Ministry of Health for successfully updating their protocol book and coming up with a second edition within 4 years.



**Tan Sri Dato' Seri Dr. Hj. Mohd Ismail Merican**  
Director General of Health, Malaysia.

## FOREWORD TO SECOND EDITION

In 2005, we managed to produce the first edition of a national protocol book for paediatric services in Malaysia. There were many teething problems and the final product had to be temporarily withdrawn due to errors in tables and flow charts. In addition there were mistakes in drug dosing and grammar due to translational errors when symbols were used. Fortunately we managed to create an erratum section at no extra cost and the mistakes were corrected in the soft copies before the CDs were produced.

Despite these initial setbacks the protocol book has gained wide acceptance within the paediatric fraternity locally and in neighbouring countries. The positive feedback we received has spurred us on to produce a new edition. However this time we have recruited new blood into the editorial board to make the presentation more attractive while avoiding the mistakes of the past.

The number of contributors has increased as has the number of chapters. We have incorporated adolescent and end of life issues and merged some chapters. However we have managed to create a smaller book which can fit into the laboratory coats of doctors and medical students.

Prof Frank Shann has once again provided us a copy of the latest edition of his world famous drug dosages book for free and this will definitely add utility to the final product.

This new edition like its predecessor is the result of team work involving many busy individuals who have none the less found time to meet our printing dateline. The Ministry of Health has again provided the funding for production making free distribution possible. We would like to record our gratitude to all concerned.

Once again we dedicate this book to the children of Malaysia.

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# GENERAL PAEDIATRICS

- 1 Normal Values in Paediatrics
- 2 Immunisation
- 3 Developmental Milestones Table
- 4 Developmental Assessment
- 5 H.E.A.D.S.S- A Psychosocial Interview For Adolescents
- 6 End of Life Care



## NORMAL VALUES IN CHILDREN

### Vital Signs

Table 1. Respiratory rate

Infant	30 - 40 / min
Toddler	24 - 40 / min
School age	18 - 30 / min
Adolescent	12 - 16 / min

Table 3. Tachypnoea in children

Age	Breaths/minute
< 2 mths	> 60
2 mths - 1 yr	> 50
1 yr - 5 yrs	> 40

Table 4. Normal range of Blood pressure

	Systolic (mmHg)	Diastolic (mmHg)
Day 1 (< 1000g)	39 - 59	16 - 36
Day 1 (> 3000g)	50 - 70	25 - 45
Neonate	60 - 90	20 - 60
Infant	87 - 105	53 - 66
Toddler	95 - 105	53 - 66
> 7 years	97 - 122	57 - 71
> 15 years	112 - 128	66 - 80

*from Hazinski 1992*

Table 6. Blood pressure in hypertension

Age	Significant Hypertension	Severe Hypertension
1 week	Systolic $\geq 96$	Systolic $\geq 106$
7d - 1 mo	Systolic $\geq 104$	Systolic $\geq 110$
Infant	Systolic $\geq 112$ Diastolic $\geq 74$	Systolic $\geq 118$ Diastolic $\geq 82$
3 - 5 years	Systolic $\geq 116$ Diastolic $\geq 76$	Systolic $\geq 124$ Diastolic $\geq 86$
6 - 9 years	Systolic $\geq 122$ Diastolic $\geq 78$	Systolic $\geq 130$ Diastolic $\geq 86$
10 - 12 years	Systolic $\geq 126$ Diastolic $\geq 82$	Systolic $\geq 134$ Diastolic $\geq 90$
13 - 15 years	Systolic $\geq 136$ Diastolic $\geq 86$	Systolic $\geq 144$ Diastolic $\geq 92$
16 - 18 years	Systolic $\geq 142$ Diastolic $\geq 92$	Systolic $\geq 150$ Diastolic $\geq 98$

### Anthropometric Measurements

#### Head Circumference

- rate of growth in preterm infants approximates that of term infant when chronological age reaches term
- the head circumference increases by 12 cm in the 1st year of life ( 6 cm in first 3 months, then 3 cm in second 3 months, and 3 cm in last 6 months) and only 2 cm in the 2nd year of life
- the rate of cerebrospinal production is 0.35 ml/min or 500 ml/day (total CSF volume is 50 mls in newborns, increasing to 150 mls in adulthood)

Table 2. Normal range for Heart rate

Age	Awake	Mean	Sleeping
< 3 mth	85 - 205	140	80 - 160
3 mth - 2 yr	100 - 190	130	75 - 160
2 yr - 10 yr	60 - 140	80	60 - 90
> 10 yr	60 - 100	75	50 - 90

*from Gillette 1989*

**Note: Any age HR > 220 consider  
Supraventricular tachycardia !**

Table 5. Blood pressure in hypotension

Age	Minimum systolic blood pressure <sup>1</sup>
< 1 mth	60 mm Hg
1 mth - 1 yr	70 mm Hg
1 - 10 yrs	70 mm Hg + (2 x age in yrs)
> 10 yrs	90 mm Hg

<sup>1</sup> 5th percentile. BP below this is hypotension

Table 7. Rate of head growth

Age	Rate of increase
30-33 wks	1.1 cm / wk
34-37 wks	0.8 cm / wk
< 3 mth	2.0 cm / mth
4 - 6 mth	1.0 cm / mth
6 - 12 mth	0.5 cm / mth
1 - 2 yr	2.0 cm / yr
2 - 7 yr	0.5 cm / yr
7 - 12 yr	0.33 cm / yr

## Weight

- in the first 7 - 10 days of life, babies lose 10 - 15% of their birth weight
- in the first 3 months of life, the rate of weight gain is 25 gm / day
- Babies usually *regain* their birth weight by the 7 - 10th day, *double* this by 5 months age, and *triple* the birth weight by 1 year of age
- formula to calculate weight for age:

$$1 - 9 \text{ yrs : } Wt \text{ (kg)} = (Age \text{ in yrs} + 4) \times 2$$

$$7 - 12 \text{ yrs : } Wt \text{ (kg)} = Age \text{ in yrs} \times 3$$

Table 8. Weight for age (rough guide)

Age	Weight (kg)
birth	3.5
1 year	10
2 year	20
3 year	30

## Length and height

Table 9. Length and height for age

Age	Length / height
birth	50 cm
6 mths	68 cm
1 yr	75 cm
2 yr	85 cm
3 yr	95 cm
4 yr	100 cm
5-12 yr	5 cm / yr

## Haematology

### Routine Haematological Values

Table 10. Normal values for haematological parameters

Age	Hb (g/dL)	PCV (%)	Retics	MCV (fL) Lowest	MCH (pg) Lowest	TWBC (x1000)	Neutrophil (Mean)	Lymphocytes (Mean)
Cord Blood	13.7–20.1	45–65	5.0	110	-	9–30	61	31
2 wk	13.0–20.0	42–66	1.0	-	29	5–21	40	63
3 mo	9.5–14.5	31–41	1.0	-	27	6–18	30	48
6 mo – 6 yr	10.5–14.0	33–42	1.0	70–74	25–31	6–15	45	48
7–12 yr	11.0–16.0	34–40	1.0	76–80	26–32	4.5–13.5	55	38
Adult Male	14.0–18.0	42–52	1.6	80	27–32	5–10	55	35
Adult Female	12.0–16.0	37–47	1.6	80	26–34	5–10	55	35

### Differential WBC

- eosinophils: 2–3%; monocytes: 6–9 %

### Platelets

- platelets are mildly decreased in first few months of age; but by 6 months have reached  $250 - 300 \times 10^9$

### Erythrocyte sedimentation rate (ESR)

- should be < 16 mm/hour in children, provided the PCV is at least 35%.

Table 11. Differential counts and

< 7 days	neutrophils > lymphocytes
1 w - 4 yr	lymphocytes > neutrophils
4 - 7 yr	neutrophils = lymphocytes
> 7 yr	neutrophils > lymphocytes

**Other normal values are found in the relevant chapters of the protocol.**

Nelson Textbook of Pediatric 15th Edition  
Pediatric Advanced Life Support Textbook 1994.

## IMMUNISATIONS

Table 1. The Extended Programme for Immunisation (EPI) Schedule. Ministry of Health,

Immunisation	Age (months)						Age (years)			
	0	1	2	3	5	6	12	18	6	12
BCG	1								if no scar	
Hep B	1	2				3			2	
DTaP <sup>1</sup>			1 <sup>1</sup>	2 <sup>1</sup>	3 <sup>1</sup>			4 <sup>1</sup>	DTaP <sup>2</sup>	DTaP <sup>2</sup>
IPV <sup>1</sup>			1 <sup>1</sup>	2 <sup>1</sup>	3 <sup>1</sup>			4 <sup>1</sup>	IPV	
Hib <sup>1</sup>			1 <sup>1</sup>	2 <sup>1</sup>	3 <sup>1</sup>			4 <sup>1</sup>		
Measles	Sabah									
MMR							1		2	

footnote:

1. The combination vaccine used in the primary immunisation schedule is a 5-in-1 DTaP-IPV/Hib.

2. DTaP after primary immunization: for those who had not received primary DTaP in their childhood, replace the booster with Td (adult tetanus-diphtheria) vaccine if they received their last dose of Td > 10 years earlier.

Also:

A child who has been started on DTaP must complete his immunisation with DTaP; it cannot be inter-change with DTP. However a child started on DTP can use DTaP for subsequent doses.

Abbreviations. BCG, Bacille-Calmette-Guerin vaccine; Hep B, Hepatitis B vaccine; DTaP, Diphtheria, tetanus, acellular pertussis vaccine; IPV, inactivated polio vaccine; Hib, Haemophilus influenzae b vaccine; MMR, measles, mumps, rubella vaccine.

### Other vaccines available in Ministry of Health formulary (Blue Book)

- **Pneumococcal polysaccharide vaccine**
  - single dose IM/SC. Booster 3 - 5 years only for high risk persons.
  - protective efficacy 56 - 81%. Immunogenic in children ≥ 2 years.
  - recommended for children with: immunosuppression (including asymptomatic HIV), asplenia, nephrotic syndrome and chronic lung disease
  - for infant < 2 years old, need to consider conjugate vaccine (not in MOH list).
  - category A (specialist prescription)
- **Cholera**
  - oral inactivated vaccine
  - children 2-6 years: 3 doses at 1-6 week interval. Children > 6 years: 2 doses at 1-6 week interval. Booster dose after 2 years.
  - protective efficacy 80-90% after 6 months waning to 60% after 3 years
  - category B (MO prescription)
- **Meningococcal A, C, Y & W-135 vaccine (does not cover B)**
  - single dose IM
  - polysaccharide vaccine. Immunogenic in children ≥ 2 years. Immunity up to 3 years
  - protective efficacy 90-95%
  - conjugate vaccine is not currently available in Malaysia
  - category C (MO prescription)
- **Japanese Encephalitis vaccine**
  - 3 doses SC. Dose 1 and 2 at 2 - 4 weeks interval then dose 3 after 1 year
  - inactivated vaccine. Protective efficacy > 95%.
  - given in Sarawak as part of the EPI at age 9, 10 and 18 months. Booster at 4 years.
  - category B (MO prescription)



- *Rabies vaccine*
  - IM dose
  - pre-exposure immunisation: 3 doses at Day 0, 7 and 28. Boosters every 2-3 years.
  - post-exposure treatment:
    - fully immunised: 2 doses at Day 0, 3. Rabies Immune Globulin (RIG) unnecessary.
    - unimmunised: 5 doses at Day 0, 3, 7, 14 and 28. RIG (20 IU/kg given half around the wound and the rest IM).
  - inactivated vaccine. Available in Malaysia as Purified Vero Cell Rabies Vaccine (PVRV)
  - category B (MO prescription)
- *Typhoid*

Two vaccines available:

  1. Vi polysaccharide vaccine
    - single dose IM. Boosters every 3 years
    - seroconversion in 85-95%; confers 60 – 80% protection 2 weeks after vaccination
    - immunogenicity < 2 years of age has not been established.
  2. Oral typhoid vaccine (Ty21a vaccine)
    - 3 doses 2 days apart. Effective 7 days after last dose. Booster every 3 years.
    - live attenuated vaccine
    - category B (MO prescription)
- *Varicella zoster*
  - Live attenuated vaccine. 70 – 90 % effectiveness.
  - SC dose: 12 months - 12 years age: single dose; > 12 years: 2 doses at least 28 days apart.
  - 2 vaccines available: Okavax (Sanofi Pasteur) and Varilrix (GSK)
  - recommended for:
    - non-immune susceptible health care workers who regularly come in contact with patients with VZV infection
    - asymptomatic or mildly symptomatic HIV infected children (with CD4% > 15%); 2 doses at 3 months interval
    - children with leukaemia and in remission for at least 1 year, have > 700/ml circulating lymphocytes may receive vaccination under supervision of the attending paediatrician (2 doses)
  - category A\* (Specialist prescription – special indication)
- *Hepatitis A*
  - 2 doses via IM injection. Dose 1 and 2 at 6-12 months apart.
  - protective efficacy 94%
  - inactivated vaccine. Approved for children age > 1 year.
  - category A (Specialist prescription)

#### Other Vaccines available in Malaysia but not in MOH list:

- *Influenza vaccine*
  - single dose IM. Minimum age is 6 months. Unprimed individuals require a 2nd dose 4 - 6 weeks after the first dose. Yearly re-vaccination for continuing protection
  - protective efficacy 70-90%
  - recommended for children with:
    - chronic decompensated disorders of respiratory or cardiovascular systems: e.g. cyanotic heart diseases, chronic lung diseases
    - HIV infection. In advanced disease, vaccination may not be effective.

- *Pneumococcal conjugate vaccine (PCV)*
  - 3 dose schedule via IM injection. 4-8 weeks apart. Earliest age is 6 weeks.
  - conjugation to carrier protein enables vaccine to be immunogenic in children < 2 years
  - inactivated vaccine. Protective efficacy against invasive disease 97% for vaccine strains and 89% for all pneumococcal strains.
  - only 1 currently available vaccine: Prevenar (Wyeth) (7-valent vaccine).
  - 10-valent and 13-valent vaccines may be introduced in the near future
- Rotavirus:
  - given orally. 2 vaccines available:
    1. Rotarix (GSK) (monovalent) - 2 dose schedule 4-8 weeks apart
    2. RotaTeq (MSD) (pentavalent) - 3 dose schedule 4-8 weeks apart between doses
  - live-attenuated vaccine.
  - protective efficacy 88-91% for any rotavirus gastroenteritis episode; 63-79% for all causes of gastroenteritis. For both vaccines, the earliest age to vaccinate is 6 weeks.
- Human Papilloma Virus (HPV)
  - 2 vaccines available: Cervarix (GSK): bivalent. Gardasil (MSD): quadrivalent.
  - 3 dose schedule IM (0, 1-2month, 6 month). Requirement for booster uncertain.
  - indicated in females aged 9-45 years.
  - recombinant vaccine. Protective efficacy almost 100% in preventing vaccine type cervical cancer in first 5 years. The vaccine prevents HPV infection and disease but not protective on existing or past HPV infection.

### General Notes

- many vaccines (inactivated or live) can be given together simultaneously (does not impair antibody response or increase adverse effect). But they are to be given at different sites unless given in combined preparations. Many vaccines are now packaged in combinations so that the child is not subjected to multiple injections.
- sites of administration
  - oral – OPV, rotavirus, live typhoid vaccines
  - intradermal (ID) - BCG. Left deltoid area (proximal to insertion deltoid muscle)
  - deep SC, IM injections. (ALL vaccines *except* the above)
    - anterolateral aspect of thigh – preferred site in children
    - upper arm – preferred site in adults
    - upper outer quadrant of buttock - associated with reduced antibody level production
- a person who has been immunised using OPV can subsequently use IPV for booster and vice versa (interchangeable)
- repeat dose of OPV if child vomits soon after administration
- PRP-T (Act Hib) and PRP-OMP (Pedvax) (H. influenzae b vaccines) used in the primary series are interchangeable. Children partially immunized in the private sector with one particular type may be immunized with another type in the MOH schedule.
- MMR can be given despite of previous history of measles, mumps or rubella infection.

### Immunisation : Contraindications

- absolute contraindication for any vaccine: severe anaphylaxis reactions to previous dose of the vaccine or to a component of the vaccine.
- postponement during acute febrile illness. Minor infection without fever or systemic upset is NOT a contraindication.
- relative contraindication: do not give a vaccine within 2 weeks of an elective surgery.

- live vaccines: *Absolute* contraindications
  - immunosuppression - malignancy; irradiation, leukaemia, lymphoma, primary immunodeficiency syndromes (but *not* asymptomatic HIV).
  - on chemotherapy or < 6 months after last dose.
  - high dose steroid: Prednisolone  $\geq 2$  mg/kg/day for > 7 days or low dose systemic > 2 weeks; (delay vaccination for 3 months).
  - if topical or inhaled steroids or low dose systemic < 2 weeks or EOD for > 2 weeks can give live vaccine
  - if another *live vaccine* including BCG had been given < 4 weeks ago. (Either give live vaccines simultaneously or if cannot then separately with a 4 week interval)
  - within 3 months following IV Immunoglobulin (11 months if given high dose IVIG e.g. in Kawasaki disease) (except yellow fever or oral polio)
  - pregnancy (live vaccine theoretical risk to foetus) unless there is significant exposure to serious conditions like polio or yellow fever in which case the importance of vaccination may outweigh the possible risk to the foetus.
- killed vaccines are generally safe. The only absolute contraindications are *severe* local (induration > 2/3 of limb) or severe generalised reactions in the previous dose
- Specific Contraindications
  - BCG - Not to be given to symptomatic HIV infected children. Can be given to newborns of HIV infected mother as the infant is usually asymptomatic at birth.
  - Hep B vaccine – Severe hypersensitivity to aluminium. The vaccine is also not indicated for HBV carrier or immuned patient (i.e. HBsAg or Ab positive).
  - Pertussis
    - absolute contraindications: anaphylaxis to previous dose; encephalopathy develops within 7 days of vaccination.
    - precautions: severe reactions to previous dose (fever > 40.5 °C, fits within 72 hours, persistent inconsolable crying, hyporesponsive state, severe local reaction involving 2/3 of limbs) and progressive neurological diseases like infantile spasm, tuberous sclerosis.
    - static neurological diseases, developmental delay, personal or family history of fits are *not* contraindications.
- Diphtheria and Tetanus: Severe hypersensitivity to aluminium and thiomersal
- Oral Polio (OPV)
  - diarrhoea and vomiting (can give the dose but must repeat the dose 1 month later)
  - hypersensitivity to neomycin, streptomycin or polymyxin.
  - within 3 weeks from a tonsillectomy (remote risk of vaccine induced bulbar polio)
- Rubella - contraindicated in pregnancy (even though no reported cases of congenital rubella syndrome due to vaccine).
- Measles - if < 9 months old presence of maternal Ab may decrease immunogenicity. Avoid in persons hypersensitive to neomycin, polymyxin or anaphylaxis to egg ingestion.
- MMR and Influenza – severe reaction to hen's eggs or neomycin
- Pneumococcal – children < 2 years age (polysaccharide vaccine); revaccination within 3 years has high risk of adverse reaction; avoid during chemotherapy or radiotherapy and < 10 days prior to starting such therapy – antibody response is poor. Pregnancy.
- Hepatitis A: Severe hypersensitivity to aluminium hydroxide, phenoxyethanol, neomycin
- Japanese B: contraindicated in immunodeficiency and malignancy, diabetes, acute exacerbation of cardiac, hepatic and renal conditions

### The following are *not* contraindications to vaccination

- mild illness without fever e.g. mild diarrhoea, cough, runny nose.
- asthma, eczema, hay fever, impetigo, heat rash (avoid injection in area of skin lesion)
- treatment with antibiotics or locally acting steroids
- child's mother is pregnant
- breastfed child (does not affect polio uptake)
- neonatal jaundice
- underweight or malnourished
- over the recommended age
- past history of pertussis, measles or rubella (unless confirmed medically)
- non progressive, stable neurological conditions like cerebral palsy, Down's syndrome, simple febrile convulsions, controlled epilepsy, mental retardation.
- family history of convulsions
- history of heart disease, acquired or congenital
- prematurity (give immunisation according to schedule irrespective of gestational age)

### Vaccination: Possible Side Effects

- Diphtheria and Tetanus vaccine
  - swelling, redness and pain
  - a small painless nodule may develop at injection site – harmless.
  - transient fever, headaches, malaise, rarely anaphylactic reaction.
  - neurological reactions rare
- DPT
  - local swelling and redness within 24 – 72 hours lasting 1 – 2 weeks.
  - acute encephalopathy (0 – 10.5 per million doses)
  - shock and 'unusual shock-like state' (3.5 to 250 cases per 100 000 doses)
  - anaphylaxis (2 per 100 000 doses)
  - protracted crying (0.1 to 6%)
- OPV
 

Vaccine associated paralytic polio (VAPP):

  - risk at 1 case/ 5.3 million doses
  - highest risk after 1st dose estimated at 1 per 1 million contacts of first dose recipients.
  - risk for subsequent doses is greatly reduced. It is important that contacts of children receiving OPV are themselves fully immunized.
- IPV
  - no serious side effects have been documented, apart from local reaction.
- HiB (*Haemophilus influenzae b*) vaccine
  - local swelling, redness and pain soon after vaccination and last up to 24 hours in 10% of vaccinees
  - malaise, headaches, fever, irritability, inconsolable crying. Very rarely seizures.
- Measles:
  - transient rash in 5% of cases; URTI symptoms.
  - fever between D5 - D12 post vaccination, for 1-3 days (5 -15% of doses of vaccines).
  - febrile convulsions (D6 - D14) in 1: 1000 - 9000 doses of vaccine. (Natural infection 1:200)
  - encephalopathy within 30 days in 1 : 1,000,000 doses of vaccines. (Natural infection 1:1000 - 5000)
  - long term prospective studies have found no association between measles or MMR vaccine and inflammatory bowel diseases, autism or SSPE.

- Mumps
  - rarely transient rash, pruritis and purpura.
  - parotitis in 1% of vaccinees, 3 or more weeks after vaccination
  - orchitis and retro bulbar neuritis very rare
  - meningoencephalitis is mild (rare) in 1: 800,000 doses. natural infection 1: 400)
- Rubella
  - may have rash, fever, lymphadenopathy, thrombocytopenia, transient peripheral neuritis
  - arthritis and arthralgia occurs in 3% of children and 20% of adults
  - rarely polyneuropathy (e.g. Guillain-Barre syndrome)
- BCG
  - local reaction: a papule at site of vaccination occurs within 2 to 6 weeks. This grows and flattens with scaling and crusting. Occasionally a discharging ulcer may occur. This heals leaving a BCG scar of at least 4 mm in successful vaccination.
  - BCG adenitis may occur.
- Influenza and Rabies
  - transient swelling, redness, pain and induration locally; myalgia, malaise and fever for 1 – 2 days starting within a few hours post vaccination
  - rare: neurological or anaphylactic reaction, Guillain-Barre syndrome, glomerulonephritis, ITP or anaphylaxis.
- Hepatitis A
  - local reactions. Flu-like symptoms lasting 2 days in 10% of recipients.
- Hepatitis B
  - local reactions; fever, flu-like symptoms in 1st 48 hours; Rarely, erythema multiforme or urticaria.
- Typhoid (Typhim Vi):
  - local reactions. Myalgia, malaise, nausea, headaches and fever in 3% of recipients.
- Cholera
  - gastrointestinal upset
- Meningococcus A, C, Y & W-135
  - local reactions. Irritability, fever and rigors for 1 – 2 days. Very rarely, anaphylaxis.

### Vaccination: Special Circumstances

- what to do if a measles case is admitted to the Paediatric Ward?
  - protect all immunocompromised children with immunoglobulin (HNIG) 0.25-0.5 mls/kg (Measles is a major cause of mortality in leukaemia in remission.)
  - check status of other children with regards to measles immunisation. If not immunised then give measles monocomponent vaccine within 24 hours of exposure. Vaccination within 72 hours can abort clinical measles in 75% of contacts.
  - discharge children with uncomplicated measles
  - notify the Public Health Office
- immunisation in HIV infected children (*see Chapter on Paediatric HIV*)
- in patients with past history or family history of fits, neurological or developmental abnormalities that would predispose to febrile fits:-
  - febrile fits can occur 5 – 10 days after measles (or MMR) vaccination or within the first 72 hours following pertussis immunisation.
  - Paracetamol (120 mg, ¼ tablet) prophylaxis after immunisation (esp. DPT) 4-6 hourly for 48 hours regardless of whether the child is febrile or not. This reduces incidence of high fever, febrile convulsions, fretfulness, crying, anorexia, local inflammation
  - rectal Diazepam may need to be considered

- maternal Chicken Pox during perinatal period (*see chapter on Perinatally acquired varicella section*)
- close contacts of immuno-deficient children and adults must be immunized, particularly against measles and polio (use IPV)
- in cases of contact with a patient with invasive *Haemophilus influenzae* B disease:
  - close contacts in household, nursery, kindergarden < age 4 years should be immunised
  - rifampicin prophylaxis (20 mg/kg once daily (maximum 600 mg) for 4 days) is given to all household contacts at (except pregnant women - one IM dose of ceftriaxone)
  - index case should be immunised irrespective of age
- asplenia (Elective or emergency splenectomy; asplenic syndromes; sickle cell anaemia) – susceptible to encapsulated bacteria and malaria :
  - give Pneumococcal, Meningococcal A, C, Y & W-135, *Haemophilus influenza* b vaccines
  - for elective splenectomy (also chemotherapy or radiotherapy): give vaccines preferably  $\geq 2$  weeks before procedure. However, they can be given even after the procedure.
  - Penicillin prophylaxis should continue even after vaccination. Ideally for life. If not until 16 years old for children or 5 years post splenectomy in adults.
- babies born to mothers who are HbeAg or HbsAg positive should be given Hepatitis B immunoglobulin (200 IU) and vaccinated with the Hepatitis B vaccine within 12 hours and not later than 48 hours. Given in different syringes and at different sites.
- premature babies may be immunised at the same chronological age as term infants. (*also see Chapter on The Premature Infant for more discussion*)

Table 2. Recommended Immunisation Schedule for Infants and Children with missed immunisations











Time of Immunisation	Age at first visit	
	Between 6 weeks - 12 months	12 months and older
1st visit	BCG, DPT/DTaP, Hib1, Polio1, HBV1	BCG, DPT/DTaP, Hib1, Polio1, HBV1, measles ( <i>see footnote 2</i> ) 6 or 9 mths MMR at 12 months of age
2nd visit (1 mth later)	DPT/DTaP2, Hib2, Polio2, HBV2	DPT/DTaP2, Polio2, HBV2, Hib2
3rd visit (1 mth later)	DPT/DTaP3, Hib3, Polio3,	DPT/DTaP3, Polio3,
4th visit (4 mths after 3rd visit)	HBV3	HBV3, DPT/DTaP4, Polio4,
2-8 mths later	DTaP4, Hib4 & Polio4 (booster) measles in Sabah at 9 months of age	Polio, DT/DTaP, MMR (at school entry)

**Notes:**

1. For infants aged less than 6 weeks, use "Recommended Immunisation Schedule for Infants & Children".
2. measles vaccine should be given only after 9 months. (exception - given at 6 months in Sabah)
3. For special groups of children with no regular contact with Health Services and with no immunisation records, BCG, HBV, DTaP- Hib-IPV and MMR can be given simultaneously at different sites at first contact.
4. It is not necessary to restart a primary course of immunisation regardless of the period that has elapsed since the last dose was given. Only the subsequent course that has been missed need be given. (Example. An infant who has been given IPV1 and then 9 months later comes for follow-up, the IPV1 need not be repeated. Go on to IPV2.). Only exception is Hepatitis A vaccine.

## CHILDHOOD DEVELOPMENTAL MILESTONES

AGE	GROSS MOTOR	FINE MOTOR	SPEECH/LANGUAGE	SOCIAL
6 weeks	Pull to sit: Head lag, rounded back. Ventral Suspension: Head momentarily in same plane as body. Prone: Pelvis high, knees no longer under abdomen. Chin raised occasionally.	Fixates and follows to 90 degrees	Vocalising by 8/52 Quiets to sound. Startles to sound.	Smiles Responsively.
3 mths	Pull to sit: Only slight head lag. Head occasionally bobs forward. Ventral Suspension: Head above plane of body. Prone: Pelvis flat. Lifts head up 45° - 90°.	Hand regard. Follows object from side to side (180°). Hands held loosely. Grasps object placed in hand. Not reaching out.	Squeals with delight. Turns head to sound.	Laughs.
5 mths	Pull to sit: No head lag and sits with straight back. Lying supine: Feet to mouth.	Reaches for objects. Plays with toes.		Mouthing.
6 mths	Pulls to sit: Lifts head off couch in anticipation. Sits with support. Bears weight on legs. Prone: Supports weight on hands; chest, upper abdomen off couch. Rolls prone to supine.	Palmar grasp of cube, ulnar approach. Moves head, eyes in all directions. No squint (after 4 months).		
7 mths	Sits with hands on couch for support. Rolls from supine to prone.	Feeds self with biscuits. Transfers objects - hand to hand. Rakes at pea.	Babbling in single syllables. (combined syllables at 8 months). Distraction Test.	Stranger anxiety.
9 mths	Sits steadily. Leans forward but cannot pivot. Stands holding on. Pulls self to stand.	Inferior pincer grasp (Scissors grasp)	Localises sound at 3 feet, above and below the ear level.	Feeds with spoon occasionally. Looks for fallen toys. Understands "NO!"
10 mths	Crawls on abdomen. Pull self to sit.	Index approach. Uses index finger to poke at pea. Able to let go of cube in hand.	Waves "Bye bye" Plays "pat-a-Cake"	
11 mths	Creeping on all FOURS Pivoting. Cruising. Walks with 2 hands held.		ONE word with meaning.	Plays "peek-a-boo"
1 year	Gets from lying to sitting to crawling to standing. Walks like a bear. Walks with ONE hand held. Walks well (13 months). Stands alone	Neat pincer grasp. Bangs 2 cubes. Sees and picks up hundreds and thousands.	Understands phrases; 2 - 3 words with meaning. Localising sound above head.	Casting (13 months) Less mouthing. Shy.
15 mths	Creeps upstairs. Stoops for toy and stands up without support. (best at 18 months)	Tower of 2 cubes. Scribbles spontaneously (15-18 months)	More words. Points to objects he wants. Continual jabber and jargon.	Takes off shoe. Feeds self with cup and spoon (but spills). Mouthing stops

AGE	GROSS MOTOR	FINE MOTOR	SPEECH/LANGUAGE	SOCIAL
18 months	Gets up and down stairs holding on to rail or with one hand held. Pulls toy or carries doll. Throws ball without falling. Sits on a chair.	Tower of 3 cubes. Scribbles spontaneously. Visual test: Picture charts. Handedness	Points to 2 - 3 body parts. Picture Cards - identify one.	Imitates housework. Toilet trained. Uses spoon well. Cashing stops.
2 years	Goes up and down stairs alone, 2 feet per step. Walks backwards (21 months) Runs. Picks up toy without falling. Able to throw and kick ball without falling.	Tower of 6 cubes.  Imitates cubes of train with no chimney. Imitates straight line. Visual test: Snel-len's chart.	2-3 word sentences. Uses 'you' 'me' 'I'. Names 3 objects. Obeys 4 simple commands. Points to 4 body parts.	Puts on shoes, socks, pants. Dry by day. Play near other children but not with them.
2.5 years	Jumps on both feet. Walks on tip toes.	Tower of 8.  Imitates train with chimney. Holds pencil well. Imitates — and —	Knows FULL name and gender. Names one colour.	
3 years	Goes up stairs one foot per step. Down stairs 2 feet per step. Jumps off bottom step. Stands on 1 foot for seconds. Rides tricycle.	Tower of 9.  Imitates bridge with cubes:  Copies  Imitates Draw a man test. (3 - 10y)	Can count to 10. Names 2 colours. Nursery rhymes. Understands "on", "in", "under".	Dresses, undresses with help. Dry by night. Plays with others.
4 years	Goes up and down stairs one foot per step. Skips on one foot. Hops on one foot.	Imitates gate with cubes.  Copies  Goodenough test 4.	Names 3 colours. Fluent conversation. Understands "in front of", "between", "behind".	Buttons clothes fully. Attends to own toilet needs.
4.5 years		Copies gate with cubes.		
5 years	Skips on both feet. Runs on toes.	Copies square. Draws recognisable man and house. Copies 'X' (5 years)  Copies (5½ years) triangle. Goodenough test 8.	Knows AGE. Names 4 colours. Triple order preposition. Tell's the time.	Ties shoelaces. Dresses and undresses alone.
6 years	Walks heel to toe Kicking, throwing, climbing.	Goodenough test 12.  Imitates or copies steps with 10 cubes 		

Note: Goodenough test: 3 + a/4 years (a = each feature recorded in his picture).



## DEVELOPMENTAL ASSESSMENT

Development is the progressive, orderly, acquisition of skills and abilities as a child grows. It is influenced by genetic, neurological, physical, environmental and emotional factors.

### Key Development Warning Signs

1. discrepant head size or crossing centile lines (too large or too small).
  2. persistence of primitive reflexes > 6 months of age
  3. no response to environment or parent by 12 months
  4. not walking by 18 months
  5. no clear spoken words by 18 months
  6. no two word sentences by 2 years
  7. problems with social interaction at 3 years
  8. congenital anomalies, odd facies
  9. any delay or failure to reach normal milestones
- parental concerns must always be taken seriously*

### Important points to note:-

- child must be co-operative, not tired, fretful, hungry nor sick. Remember that a child may behave differently in an unfamiliar environment
- allowance must be made for prematurity up to two years.
- take note of parental account of what child can/cannot do. Note comments on abnormal gait, speech defects, etc.
- normal development is dependent on integrity of child's hearing and vision.
- normal pattern of speech and language development is essential for a normal social, intellectual and emotional development.
- delay in development may be global i.e. affecting all areas equally, or specific areas only e.g. oro-motor dysfunction causing speech delay.

## ASSESSMENT OF CHILDREN WITH GLOBAL DEVELOPMENTAL DELAY

### History

- consanguinity
- family history of developmental delay
- maternal drugs, alcohol, illness and infection in pregnancy
- prematurity, perinatal asphyxia
- severe neonatal jaundice, hypoglycaemia or seizures
- serious childhood infections, hospital admissions or trauma
- home environment conditions (environmental deprivation)

### Investigations

(individualised according to findings)

- visual and auditory testing
- T4, TSH
- Chromosomal Analysis
- consider
  - creatine kinase in boys
  - MRI Brain
  - metabolic screen
  - specific genetic studies (Prader Willi/Angelman syndrome, Fragile X PCR, subtelomeric rearrangements) or refer for genetic consultation.
  - EEG if history of seizures

### Examination

- head circumference
- neurocutaneous markers
- dysmorphic features
- neurological abnormalities
- full developmental assessment

### Consider

- structural brain disorder
- chromosomal anomaly e.g. Down or Fragile X
- cerebral palsy
- congenital infection
- hypothyroidism & metabolic disorders
- autism & hyperactivity
- previous head injury, intracranial bleed, CNS infections.
- syndromes, e.g. tuberous sclerosis
- muscular dystrophies

## ASSESSMENT OF CHILDREN WITH HEARING IMPAIRMENT / SPEECH DELAY

### History

- congenital infection, perinatal drugs
- severe neonatal jaundice
- family history of deafness / speech delay
- chronic ear infections
- quality, quantity of speech

### Examination

- check ears, dysmorphic features
- Distraction Test
- assess expressive, receptive speech
- neurological / development assessment

### Management

- formal hearing test
- speech-language therapy

### Warning signs for hearing impairment

- child appears not to hear or has no attempt to listen.
- no respond to name, "No" or to clue words e.g. "Shoe", by 12 mths age
- speech / language delay

### Consider

- congenital sensorineural deafness
- familial, genetic causes
- congenital rubella
- oro-motor dysfunction

Table 1. Hearing tests at different ages

age	type of test	comments
newborn screening	Automated Otoacoustic Emission (AOAE) test	determines cochlear function. Negative test in conductive hearing loss, middle ear infections, or with moderate - severe sensorineural hearing loss.
any age	Brainstem Auditory Evoked Response (BAER)	measures brainstem responses to sound. Negative test in sensorineural hearing loss
7 - 9 months	Infant Distraction Test (IDT)	determines response to sound whilst presented during a visual distraction.
infants	Behavioural observation assessment (BOA) test	audiologist identifies bodily reactions to sound i.e. cessation of activity, body movement, eye widening / opening
> 2.5 years age	Conditioned play audiometry	earphones placed on child and various games are done when test tone is heard.
older children	Pure tone audiometry (Traditional hearing test)	patient presses a response button or raises a hand when the test tone is heard

## ASSESSMENT OF CHILDREN WITH VISUAL IMPAIRMENT

### At risk

- prematurity.
- Intrauterine Infection (TORCHES)
- family history of cataract, retinoblastoma, squint.
- previous meningitis, asphyxia
- dysmorphic babies

### Warning signs for poor vision

- does not fix on mother's face by 6 wks
- wandering / roving eyes after 6 wks or has abnormal head postures.
- leukocoria (white eye reflex)
- holds objects very close to eye.
- squint after 6 months of age.

## ASSESSMENT OF CHILDREN WITH LEARNING DIFFICULTIES

### History

- perinatal or childhood problems
- developmental delay
- family history of developmental delay or learning difficulty
- areas of learning difficulties – specific or general

### Examination/Assessment

- past, current education performance
- neurological, development assessment

### Consider

- autism & ADHD
- specific learning difficulty (e.g. dyslexia)
- mild intellectual impairment
- limited environmental stimulation

### Plan of management

- specific learning disorder tests e.g. Dyslexia screening test, DSM IV, Conners' Rating Scales-Revised, etc
- referral to a developmental paediatrician or clinical / educational psychologist

# H.E.A.D.S.S - A PSYCHOSOCIAL INTERVIEW FOR ADOLESCENTS

## Introduction

Adolescence is the developmental phase between childhood and adulthood and is marked by rapid changes in physical, psychosocial, sexual, moral and cognitive growth. Dr. Cohen refined a system for organizing the developmentally-appropriate psychosocial history that was developed in 1972 by Dr. Harvey Berman. The approach is known as the acronym **HEADSS** (**H**ome, **E**ducation /employment, **A**ctivities, **D**rugs, **S**exuality, and **S**uicide/depression). It was subsequently expanded to **HEEADSSS** by adding **E**ating and **S**afety.

## Preparing for the Interview

Parents, family members, or other adults should not be present during the HEADSS assessment unless the adolescent specifically gives permission, or asks for it.

## Starting the interview

- 1. Introduction**  
Set the stage by introducing yourself to the adolescent and parents. If the parents are present before the interview, always introduce yourself to the adolescent first.
- 2. Understanding of Confidentiality**  
Ask the adolescent to explain their understanding of confidentiality.
- 3. Confidentiality Statement**  
After the adolescent has given you his/her views, acknowledge his/her response and add your views accordingly (confidentiality statement), based on the particular situation.

Table 1. Questions for the HEADSS interview

Item	Examples of Questions
<b>H:</b> <i>Home</i>	<ul style="list-style-type: none"> <li>• who lives at home with you? Where do you live? Do you have your own room?</li> <li>• how many brothers and sisters do you have and what are their ages?</li> <li>• are your brothers and sisters healthy?</li> <li>• are your parents healthy? What do your parents do for a living?</li> <li>• how do you get along with your parents, your siblings?</li> <li>• is there anything you would like to change about your family?</li> </ul>
<b>E:</b> <i>Education</i>	<ul style="list-style-type: none"> <li>• which school do you go to? What grade are you in? Any recent changes in schools?</li> <li>• what do you like best and least about school? Favourite subjects? Worst subjects?</li> <li>• what were your most recent grades? Are these the same or different from the past?</li> <li>• how much school did you miss last/this year? Do you skip classes? Have you ever been suspended?</li> <li>• what do you want to do when you finish school?</li> <li>• how do you get along with teachers? How do you get along with your peers?</li> <li>• inquire about “bullying”.</li> </ul>
<i>Employment</i>	<ul style="list-style-type: none"> <li>• are you doing any full time or part time job?</li> </ul>
<i>Eating</i>	<ul style="list-style-type: none"> <li>• what do you like and not like about your body?</li> <li>• has there been any recent change in your weight?</li> <li>• have you dieted in the last one year? How? How often?</li> <li>• how much exercise do you get on an average day ?Week?</li> <li>• do you worry about your weight? How often?</li> <li>• does it ever seem as though your eating is out of control?</li> <li>• have you ever made yourself throw up on purpose to control your weight?</li> </ul>

Table 1. Questions for the HEADSS interview (continued)

Item	Examples of Questions
<b>A:</b> <i>Activities</i>	<ul style="list-style-type: none"> <li>• are most of your friends from school or somewhere else? Are they the same age as you?</li> <li>• do you hang out with mainly people of your same sex or a mixed crowd?</li> <li>• do you have a lot of friends?</li> <li>• do you see your friends at school and on weekends, too?</li> <li>• do you do any regular sport or exercise? Hobbies or interests?</li> <li>• how much TV do you watch? What are your favourite shows?</li> <li>• have you ever been involved with the police? Do you belong to a group/gang?</li> </ul>
<b>D:</b> <i>Drugs</i>	<ul style="list-style-type: none"> <li>• when you go out with your friends, do most of the people that you hang out with drink or smoke? Do you? How much and how often?</li> <li>• have you or your friends ever tried any other drugs? Specifically, what?</li> <li>• do you regularly use other drugs? How much and how often?</li> </ul>
<b>S:</b> <i>Sexuality</i>	<ul style="list-style-type: none"> <li>• have you ever been in a relationship? When?</li> <li>• have you had sex? Number of partners? Using contraception?</li> <li>• have you ever been pregnant or had an abortion?</li> <li>• have you ever been checked for a sexually transmitted infection (STI)? Knowledge about STIs and prevention?</li> <li>• for females: Ask about menarche, last menstrual period (LMP), and menstrual cycles. Also inquire about breast self examination (BSE) practices.</li> <li>• for males: Ask about testicular self-examination (TSE) practices.</li> </ul>
<b>S:</b> <i>Suicide, Depression</i>	<ul style="list-style-type: none"> <li>• do you have difficulties to sleep? Has there been any change in your appetite recently?</li> <li>• do you mix around well others? Do you have hopeless/helpless feelings?</li> <li>• have you ever attempted suicide?</li> </ul>
<b>S:</b> <i>Safety</i>	<ul style="list-style-type: none"> <li>• have you ever been seriously injured? Do you always wear a seatbelt in the car?</li> <li>• do you use safety equipment for sports and or other physical activities (for example, helmets for biking)?</li> <li>• is there any violence in your home? Does the violence ever get physical?</li> <li>• Have you ever been physically or sexually abused?</li> <li>• have you ever been bullied? Is that still a problem?</li> <li>• have you gotten into physical fights in school or your neighborhood? Are you still getting into fights?</li> </ul>

### Suggestions for ending interviews with adolescents

- give them an opportunity to express any concerns you have not covered, and ask for feedback about the interview.
- ask if there is any information you can provide on any of the topics you have discussed. Try to provide whatever educational materials young people are interested in.

## END OF LIFE CARE

### Introduction

Paediatric palliative care is defined as an active and total approach to care embracing physical, emotional and spiritual elements. It focuses on quality of life for the child and support for the family and includes management of distressing symptoms, provision of respite and care through death and bereavement'.

### Causes of Paediatric Mortality (Malaysian State Hospitals)

- Approximately 70% of deaths are in the neonate group; 30% in older children. A small proportion deaths are due to acute illnesses where death is sudden; the rest are lethal congenital malformations or one of the following broad groups of life limiting conditions (i.e. where there is no reasonable hope of cure, from which children will die):
  - conditions where potentially curative treatment has failed. (e.g. malignancy)  
Note: excludes children in long term remission, or following successful treatment
  - conditions where intensive treatment may prolong life but premature death occurs. (e.g. cystic fibrosis)
  - progressive conditions where treatment is exclusively palliative (e.g. Duchenne's muscular dystrophy )
  - non progressive neurological conditions which result in an increased susceptibility to complications and premature death (e.g. cerebral palsy).

There is a perception that most deaths are due to malignancy but < 50% of paediatric deaths are due to malignancy. Congenital abnormalities, chromosomal disorders and neurodegenerative disorders are common causes.

### Impact of the lost of a child

- one of the differences highlighted by Papadatou between the care of dying adults and dying children is that the dying process of a child affects many individuals with grief over the loss that is more intense, long lasting and complicated. This is because children are generally expected to outlive their parents. Parental grief is the most severe form of grief; with an associated increase in morbidity and mortality. It often intensifies in 2nd or 3rd year (when friends and relatives expect them to be 'over it').
- for parents who have lost a child , there is an increased risk of first psychiatric hospitalisation for any disorder compared with parents who did not lose a child. This risk is higher in bereaved mothers than bereaved fathers, the risk being highest during the 1st year following their child's death, and remains elevated for  $\geq 5$  years
- care related factors may influence parents' psychological outcomes. Among factors that continued to affect parents 4-9 years following their child's death were the child having had unrelieved pain and experienced a 'difficult moment of death'. Parental interviews suggest that the child's physical pain and circumstances at the moment of death contributed to parents' long term distress.

### Quality of End of life care

Parents associate the quality of end of life care with physicians:

- giving clear information about what to expect in the end of life period
- communicating with care and sensitivity
- communicating directly with child where appropriate
- preparing the parent for circumstances surrounding the child's death

As healthcare providers we have the unique opportunity to proactively provide good symptom control and supporting the child through a "good death".

## End of life Care for Paediatric Patients .

When the disease trajectory of a patient has reached the final days, and the family or caregivers understand the situation, the following are steps that can be taken to help the patient/family. Medical management in such instances needs a review of existing orders and management strategies with the goal of enhancing comfort and decreasing noxious and invasive interventions.

### *Aspects of care that should be addressed are*

- discontinuation of parenteral nutrition. Enteral feeding reduced, discontinued or offered as comfort measure; breastfeeding may be offered if desired by mother and baby; a lactation referral for breastfeeding mothers to stop milk production
- tests and treatments usually discontinued to minimize noxious or painful procedures
- intravenous access maintained for medications to decrease pain, anxiety or seizures. Alternatives to IV access are the use of oral, sublingual or rectal medications.
- antibiotics may be discontinued.
- cardiac medications e.g. dopamine, adrenaline may be discontinued.
- ventilator support: parents must be included in the decision to stop ventilator support and should be provided with information about the expected sequence of events surrounding removal from the ventilator as well as the infant's physical response, including the possibility that the infant may not die immediately.
- moral/ethical issues e.g. do not resuscitate status; Do not resuscitate ( DNR) orders should be explicit and developed collaboratively with the family.
- pain management; comfort measures e.g. discontinuing non essential investigations, observations for pain, agitation, nausea and vomiting; appropriate management to improve the quality of life; give additional morphine for breakthrough pain.
- communication with care givers ; their understanding of what to expect, choice of place where they prefer the child to die; how the rest of the family is coping or understands; patient's desire/wish list ; organ donation
- religious /spiritual needs
- for the child dying in hospital, whether the family wants to take the body home, how will the body be transported; are there any specific religious requirements, and does the family want symbolic memorials (e.g. handprints, hair lock).
- transitional care ,family support, sibling support, staff support, organ donation, follow up support for family

## End of life care for infants with lethal anomalies

The goal of palliative care is the best quality of life for patients and their families.

The following is a list of lethal congenital anomalies:

- *Genetic*  
Trisomy 13 or 18, triploidy, thanatophoric dwarfism or lethal forms of osteogenesis imperfecta; inborn errors of metabolism that are lethal even with available therapy
- *Renal* (with oligo/anhydramnios and pulmonary hypoplasia)  
Potter's syndrome / renal agenesis, multicystic / dysplastic kidneys, polycystic kidney disease, renal failure that requires dialysis
- *Central nervous system*  
Anencephaly, holoprosencephaly, complex, severe meningomyelocele, large encephaloceles, hydranencephaly. Congenital severe hydrocephalus with absent or minimal brain growth; neurodegenerative diseases, e.g. spinal muscular atrophy

- *Cardiac*  
Acardia, Inoperable heart anomalies, hypoplastic left heart syndrome, pentalogy of Cantrell (ectopia cordis)
- *Other structural anomalies*  
certain cases of giant omphalocele, severe congenital diaphragmatic hernia with hypoplastic lungs; inoperable conjoined twins

Some of these conditions may be prenatally diagnosed – thus allowing the paediatric palliative care team to be activated immediately. Others may need further evaluation to ensure certainty – in these cases it is advisable to do what is medically necessary to support the baby. The life sustaining medical support can be withdrawn once a definitive diagnosis or prognosis is established.

In the event of child's survival to homegoing, Hospice services should be offered. Hospice admission must occur on the day of discharge to coordinate for continuity of care from hospital to home.

## NEONATAL PALLIATIVE CARE PLAN: INFANT WITH LETHAL ANOMALIES

Mother's name: \_\_\_\_\_

Father's name: \_\_\_\_\_

Infant's name: \_\_\_\_\_

Date, time of birth: \_\_\_\_\_

Discussion for palliative care done by: \_\_\_\_\_

in the presence of \_\_\_\_\_

### Comfort measures for babies

- dry and warm baby, provide warm blankets
- provide hat
- allow mothers to room in
- minimize disruptions within medically safe practice for mother
- lower lights if desired
- allow presence of parents and extended family as much as possible without disruption to work flow in the unit
- make siblings comfortable; they may wish to write letters or draw for the baby
- begin bereavement preparation and memory building, if indicated, to include hand and footprints, pictures, videos, locks of hair.
- encourage parent/child bonding and interaction: bathe, dress baby; feeds, diaper change

### Selected medical interventions

- humidified oxygen ( \_\_\_\_\_ % )
- nasal cannula oxygen ( \_\_\_\_\_ L/min)
- suction
- morphine sublingual 0.15 mg/kg or iv 0.05 mg/kg as needed
- buccal midazolam or oral clonazepam as needed
- artificial hydration or nutrition : \_\_\_\_\_
- natural hydration or nutrition : \_\_\_\_\_

*Avoid distressing delays in treating symptoms by making medications available in all available concentrations and doses.*

### Spiritual care:

- religious preference: \_\_\_\_\_
- identified religious leader: \_\_\_\_\_
- religious ritual desired at or near time of death: \_\_\_\_\_

### In the event of child's death in hospital

- diagnostic procedures: \_\_\_\_\_
- autopsy preference: \_\_\_\_\_
- tissue/organ procurement preferences: \_\_\_\_\_

Funeral home chosen by family: \_\_\_\_\_

Rituals required for body care: \_\_\_\_\_

Please notify: \_\_\_\_\_



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# NEONATOLOGY

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## PRINCIPLES OF TRANSPORT OF A SICK NEONATE

### Introduction

- the transport of sick neonates involve pre-transport intensive care level resuscitation, stabilisation and continuing intra-transport care to ensure that the child arrives in a stable state.
- organised neonatal transport teams bring the intensive care environment to critically ill infants before and during inter-hospital or intra-hospital transport.
- the basis of a safe and timely transport is good communication and coordination between the referring and receiving hospital to ensure adequate stabilisation pre-transport and continuing intra-transport care.
- there is a rare need for haste.
- there must be a balance between anticipated clinical complications that may arise due to delay in definitive care and the benefits of further stabilisation.

### Special considerations in neonates

- *apnoea*: premature and septic babies are especially prone to apnoea
- *bradycardia*: hypoxia causes bradycardia, heart block and asystole in newborns
- *oxygen toxicity*: to lungs and retina - especially important in the premature baby
- *reversal to fetal circulation (Persistent pulmonary hypertension of the newborn PPHN)*: can be precipitated by hypoxia, hypercarbia, acidosis and sepsis
- *hypothermia*: mechanisms of thermoregulation are less developed; neonates have a larger body surface area: mass ratio. Non shivering thermogenesis is induced by the oxidation of brown fat. If the bowels are exposed, the heat and fluid loss are compounded by evaporation. The effects of hypothermia are acidosis and subsequent PPHN, impaired immune function and delayed wound healing.
- *hypoglycaemia* – neonates lack glycogen stores in liver, and fat deposits
- *jaundice* – worsen in the baby with sepsis or intestinal obstruction.

### Mode of transport

Careful consideration must be made as to the mode of transport.

- the best mode of transfer is “in utero” as far as possible, e.g. a mother in premature labour should be managed in a centre with NICU facilities or if a surgical anomaly has been detected antenatally, the mother should be advised to deliver at a centre with paediatric surgical facilities.
- for post natal transfers, the advantages and disadvantages of road, air (helicopter or commercial airlines) and riverine transport must be considered in each child. If air transport is chosen, then the effects of decreased atmospheric pressure on closed cavities and the lack of working space must be taken into account. Transport incubators with monitors, ventilators and suction equipment are ideal.

### Air Transport

A number of patients are transported by commercial airlines with pressurised cabins flying at higher altitudes or by helicopters flying at lower altitudes but without pressurised cabins. There are special problems associated with air transport:

- *changes in altitude* – physiologic changes associated with altitude are due to the decreased atmospheric pressure causing a decreased oxygen concentration and expansion of gases. This becomes especially important in children with air trapped in closed cavities e.g. pneumothorax, pneumoperitoneum, volvulus and intestinal obstruction. These cavities must be drained before setting off as the gases will

expand and cause respiratory distress. Children requiring oxygen may have an increased requirement and become more tachypnoeic at the higher altitude. Assessment of hypoxia can be difficult due to poor lighting.

- **noise and vibration:** in addition to causing stress to the baby and the transport team, there is usually interference with the monitors especially pulse oximeters. It is also impossible to perform any procedures.
- **limited cabin space:** prevents easy access to the baby especially in the helicopters. The commercial aircraft and current helicopters also are not able to accommodate the transport incubators. The baby is thus held in the arms of a team member.
- **weather conditions, availability of aircraft:** speed of transfer may be compromised “waiting” for the availability of aircraft/flight or for the weather to change. Stress and safety to the baby and team during poor weather conditions needs to be considered.
- **take off and landing areas:** special areas are required and there will be multiple transfers, e.g. hospital – ambulance – helicopter – ambulance - hospital
- **finances:** air transport is costly

### Pre-transport stabilisation

Transport of the neonate is a significant stress on the child - they can easily deteriorate during the journey. The presence of hypothermia, hypotension and metabolic acidosis has a significant negative impact on the eventual patient outcome. It is also almost impossible to do any significant procedures well during the actual transport. Therefore, stabilisation pre-transport is critical to ensure a good patient outcome.

The principles of initial stabilisation follow the widely recognised ABC's of resuscitation:

**Airway**

**Breathing**

**Circulation/ {Communication}**

**Drugs/ {Documentation}**

**Environment/ {Equipment}**

**Fluids – Electrolytes/ Glucose**

**Gastric decompression**

#### *Airway management*

- establish a patent airway
- evaluate the need for oxygen, frequent suction (Oesophageal atresia) or an artificial airway (potential splinting of diaphragm).
- security of the airway – The endotracheal tubes (ETT) must be secure to prevent intra-transport dislodgement
- chest X-ray – to check position of the ETT

#### *Breathing*

The need for intra-transport ventilation has to be assessed:

- requires FiO<sub>2</sub> 60% to maintain adequate oxygenation
- ABG – PaCO<sub>2</sub> >60mmHg
- tachypnoea and expected respiratory fatigue
- recurrent apnoeic episodes
- expected increased abdominal/bowel distension during air transport

***If there is a possibility that the child may require to be ventilated during the transfer, it is safer to electively intubate and ventilate before setting off.***

However, there may be certain conditions where it may be preferable not to ventilate if possible, e.g. tracheo-oesophageal fistula. If in doubt, consult the receiving surgeon or paediatrician. If manual ventilation is to be performed throughout the journey, due consideration must be taken about fatigue and possible erratic nature of ventilation.

### *Circulation*

- heart rate and perfusion (capillary refill) are good indicators of hydration status
- blood pressure in a neonate drops just before the baby decompensates.
- minimum urine output should be 1-2 mls/kg /hr. The baby can be catheterised or the nappies weighed (1g = 1 ml urine)
- ensure a reliable intravenous access (at least 2 cannulae) before setting off.
- if the child is dehydrated, the child must be rehydrated before leaving.

### *Fluid therapy*

#### Resuscitation fluid:

- rate – 10 – 20 mls/kg aliquots given as boluses over up to 2 hours according to the clinical status
- type – Normal Saline or Hartmann's solution
- If blood loss then whole blood or pack cells may be needed when ready.
- this fluid is also used to correct ongoing measured (e.g. orogastric) or 3rd space losses. The perfusion and heart rates are reliable indicators of the hydration.

#### Maintenance fluid:

- rate :   Day 1 (age):       60 mls/kg  
              Day 2:         90 mls/kg  
              Day 3:        120 mls/kg  
              Day 4 onwards: 150 mls/kg
- type: If there are ongoing or anticipated losses in the surgical neonate, e.g. intestinal obstruction, gastroschisis, the recommended solution is ½ Saline + 10% D/W. Watch out for hyponatraemia and hypoglycemia.

### *Communication*

Good communication between the referring doctor, transport team and the neonatologist / paediatric surgeon will help better coordination of the transfer, stabilisation of the baby before transfer, timing of the transfer, and preparedness of the receiving hospital.

- inform the receiving specialist and emergency department of the receiving hospital
- name and telephone contact of the referring doctor and hospital
- patient details
- history/ physical findings/provisional diagnosis/investigations
- current management and status of the baby
- mode of transport/ Expected Times of Departure and Arrival at referral centre
- destination of the patient (e.g. A&E, NICU, Ward)

### *Drugs as required*

- antibiotics: most sick neonates will require antibiotics
- analgesia/ sedation: especially if the baby has peritonitis or is intubated
- inotropes
- vitamin K
- sodium bicarbonate

### Documentation

- history including antenatal and birth history/ Physical Findings/ Diagnosis
- previous and current management
- previous operative and histopathology notes, if any
- input/output charts
- investigation results/ X-rays
- consent - informed and signed by parents especially if high risk, parents not escorting
- parents' contact address and telephone numbers, if not escorting
- mother's blood - 5-10 mls for cross match, if the mother cannot escort the child

### Environment

- Neutral Thermal Environment – environmental temperature at which an infant can sustain a normal temperature with minimal metabolic activity and oxygen consumption
- optimal temperature for the neonate (axilla) – 36.5 – 37.0 C

- prevention of heat loss

As the mechanisms of heat loss are radiation, conduction, convection and evaporation, prevention of heat loss involves maintaining an optimal ambient temperature as well as covering the exposed surfaces:

- transport incubator – would be ideal
- wrap the limbs of the baby with cotton, metal foil or plastic.
- do not forget a cotton-lined cap for the head.
- care of the exposed membranes (See section on Abdominal wall Defects)
- warm the intravenous fluids

### Equipment

(Please see table at the end of chapter)

Check all equipment - their completeness and function before leaving the hospital

- monitors: cardiorespiratory monitor/ pulse oximeter for transport would be ideal. However, if unavailable or if affected by vibration, perfusion, a praecordial stethoscope and a finger on the pulse will be adequate.
- syringe and/or infusion pumps with adequately charged batteries
- intubation and ventilation equipment and endotracheal tubes of varying sizes
- oxygen tanks – ensure adequacy for the whole journey
- suction apparatus and catheters and tubings
- anticipated medication and water for dilution and injection
- IV fluids, tubings. Pre-draw fluids or medication into syringes if required during journey

### Gastric decompression

- an orogastric tube will be required in nearly all surgical neonates especially if the baby has intestinal obstruction, congenital diaphragmatic hernia or abdominal wall defects.
- the oral route is preferred as a larger bore tube can be inserted without compromising the nasal passages (neonates are obligatory nasal breathers). However, the orogastric tube can easily dislodge and the position needs to be checked regularly. 4 hourly aspiration and free flow of the gastric contents is recommended.

### Immediately before departure

- check vital signs and condition of the baby
- check and secure all tubes
- check the completeness and function of equipment
- re-communicate with receiving doctor about current status and expected time of arrival

## Intra-transport Care

- **Staff** - Ideally, there should be a specialised neonatal transport team. If not, the medical escort should be a neonatal trained doctor with/without a neonatal trained staff nurse. A minimum of 2 escorts will be required for the ventilated/critically ill baby. The team should be familiar with resuscitation and care of a neonate. They should also be able to handle critical incidents. The team members should preferably not be prone to travel sickness!
- **Safety of the Team** must be a priority. Insurance, life jackets and survival equipment should be made available for the escort team and parents.
- **Monitoring**: regular monitoring of the vital signs, oxygenation and perfusion of the should be performed
- **Fluids** : intravenous fluids must be given to the ill child to prevent dehydration and acidosis during the transport. Boluses need to be given as necessary depending on the assessment of the perfusion and heart rate of the child. If catheterised, the urine output can be monitored. The orogastric tube should be aspirated as required.
- **Temperature Regulation**: a check on the baby's temperature should be made. Wet clothes should be changed if required especially in the child with abdominal wall defects. Disposable diapers and one way nappy liners can be very useful here.
- **Critical Incidents** – preoperative preparation is to minimise the critical incidents as these can cause loss of life and stress to the transport team.

## Arrival at the Receiving Hospital

- reassessment of the baby
- handover to the resident team

## Special Surgical Conditions

### *Oesophageal Atresia with /without Tracheo-oesophageal fistula*

(These babies have a risk of aspiration of saliva as well as reflux of the gastric contents through the distal fistula)

- evaluation for other anomalies e.g. cardiac, pneumonia, intestinal atresias
- suction of the upper oesophageal pouch – A Replogle (sump suction) tube inserted and continuous low pressure done if possible. Otherwise, provide frequent intermittent (every 10-15 mins) suction of the oropharynx throughout the journey.
- ventilation only if absolutely necessary if there is a tracheo-oesophageal fistula as it may lead to intubation of the fistula, insufflation of the GI tract, and possible perforation if there is a distal atresia of the bowel.
- warmth
- fluids - Maintenance fluids and resuscitation fluids as required
- positioning - Lie the baby lateral or prone to minimise aspiration of saliva and reflux
- monitoring – Pulse oximetry and cardiorespiratory monitoring



### *Congenital Diaphragmatic Hernia*

- evaluate for associated anomalies and persistent pulmonary hypertension of the newborn (PPHN)
- ventilation - Intubation and ventilation may be required pre-transport. Avoid ventilation with a bag and mask; low ventilatory pressures used. A contralateral pneumothorax or PPHN need to be considered if the child deteriorates. If the baby is unstable or on high ventilatory settings, the baby should not be transported. Frequent consultation with a Paediatric Surgeon will be helpful to decide when to transport the baby. If a chest tube has been inserted, it should not be clamped during the journey.
- orogastric tube — gastric decompression is essential here and a size 6 or 8 Fr tube is inserted, aspirated 4 hourly aspiration and placed on free drainage.
- fluids — caution required as dehydration and overload can precipitate PPHN
- monitoring
- warmth
- consent - high risk
- positioning — lie baby lateral with the affected side down to optimise ventilation
- air transport considerations

### *Abdominal Wall Defects*

Exomphalos and Gastroschisis are the more common abdominal wall defects. Fluid loss and hypothermia are important considerations in these babies.

*Gastroschisis* - defect in the anterior abdominal wall about 2-3 cm diameter to the right of the umbilicus with loops of small and large bowel prolapsing freely without a covering membrane.

*Exomphalos* - Defect of anterior abdominal wall of variable size (diameter of base) It has a membranous covering (amnion, Wharton's jelly, peritoneum) and the umbilical cord is usually attached to the apex of the defect. The content of the large defect is usually liver and bowel but in the small defect the content is just bowel loops.

- evaluation: for associated syndromes and cardiac anomalies (more commonly in babies with exomphalos).
- fluids: IV fluids are essential as the losses are tremendous especially from exposed bowel. Boluses (10-20 mls/kg) of normal saline/ Hartmann's solution must be given frequently to keep up with the ongoing losses. A maintenance drip of ½ N/S + 10% D/W at 60 – 90 mls/kg (Day 1 of life) should also be given. Hypoglycemia can occur in about 50% of babies with Beckwith-Wiedemann's Syndrome (exomphalos, macroglossia, gigantism).
- orogastric tube — gastric decompression is essential here and a Size 6 or 8 Fr tube is inserted, aspirated 4 hourly and placed on free drainage.
- warmth — pay particular attention to temperature control because of the increased exposed surface area and the fluid exudation causing evaporation and the baby to be wet and cold. Wrapping the baby's limbs with cotton and plastic will help.
- care of the exposed membranes — The bowel/membranes should be wrapped with a clean plastic film (*Clingwrap/Gladwrap*) without compressing, twisting and kinking the bowel. Please do not use a "warm, saline soaked gauze" directly on the bowel as the gauze will get cold and stick to the bowel/membranes. Disposable diapers or cloth nappies changed frequently will help the keep the child dry. The baby may need to be catheterised to monitor urine output.
- positioning — place baby in a lateral position to prevent tension and kinking of bowel

### Intestinal Obstruction

May be functional e.g. Hirschsprung's disease or mechanical e.g. atresias, volvulus. Fluid loss with dehydration and diaphragm splinting needs to be assessed for.

- evaluation – for associated syndromes and cardiac anomalies.
- fluids – Intravenous fluids here are essential, too.
  - boluses - 10-20 mls/kg Hartmann's solution/normal saline to correct dehydration and replace the measured orogastric losses.
  - maintenance -  $\frac{1}{2}$  N/S + 10% D/W.
- orogastric tube – gastric decompression is essential here and a size 6 or 8 Fr tube is inserted, aspirated 4 hourly and placed on free drainage.
- warmth
- monitoring – vital signs and urine output
- air transport considerations

**Table 1. Pre-departure checklist**

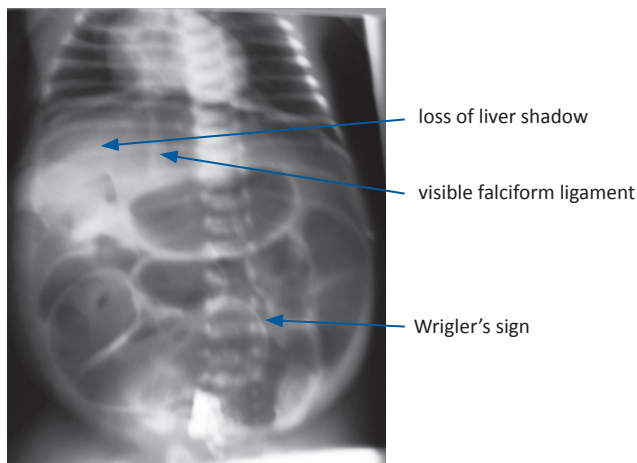
Equipment	Medication
<ul style="list-style-type: none"> <li>• transport incubator ( if available )</li> <li>• airway and intubation equipment all available and working (ET tubes of appropriate size, laryngoscope, Magill forceps)</li> <li>• batteries with spares</li> <li>• manual resuscitation (Ambu) bags and masks of appropriate size are available and in working order</li> <li>• suction device functions properly</li> <li>• oxygen cylinders are full</li> <li>• a spare oxygen cylinder is available</li> <li>• oxygen tubing</li> <li>• infusion pumps are functioning properly</li> <li>• intravenous cannulae of various sizes</li> <li>• needles of different sizes</li> <li>• syringes and tubings</li> <li>• suture material</li> <li>• adhesive tape, scissors</li> <li>• gloves, gauze, swabs (alcohol and dry)</li> <li>• stethoscope, thermometer</li> <li>• nasogastric tube</li> <li>• pulse oximeter (if available) - working order, set alarm limits</li> <li>• cardiac monitor if indicated</li> <li>• chest clamps (if an underwater chest drain is present)</li> </ul>	<ul style="list-style-type: none"> <li>• intravenous fluids               <ul style="list-style-type: none"> <li>- normal saline</li> <li>- Hartmann's solution</li> <li>- 5% albumin</li> <li>- 1/5 N/S + 10% D/W</li> <li>- dextrose 10%</li> </ul> </li> <li>• ionotropes               <ul style="list-style-type: none"> <li>- dopamine</li> <li>- dobutamine</li> <li>- adrenaline</li> </ul> </li> <li>• sedative               <ul style="list-style-type: none"> <li>- morphine</li> <li>- midazolam</li> </ul> </li> <li>• blood products if indicated</li> <li>• others               <ul style="list-style-type: none"> <li>- atropine</li> <li>- sodium bicarbonate</li> <li>- sterile water for injection</li> <li>- normal saline for injection</li> </ul> </li> </ul>
Patient status	Documents
<ul style="list-style-type: none"> <li>• airway is secured and patent (do a post-intubation chest X-ray before departure to make sure ET tube is at correct position )</li> <li>• venous access is adequate and patent ( at least 2 IV lines )</li> <li>• intravenous drip is running well</li> <li>• patient is safely secured in transport incubator or trolley</li> <li>• vital signs are charted</li> <li>• all drains ( if present ) are functioning and secured</li> </ul>	<ul style="list-style-type: none"> <li>• patient notes, referral letter</li> <li>• X-rays</li> <li>• consent form</li> <li>• vital signs chart</li> <li>• input/output charts</li> <li>• maternal blood (for infant)</li> </ul>

### *Necrotising Enterocolitis*

- evaluation – these babies are usually premature and septic with severe metabolic acidosis, coagulopathy and thrombocytopenia. There may be an associated perforation of the bowel or gangrenous bowel, initiating the referral to the surgeon.
- ventilation – most of the babies may require intubation and ventilation before setting out especially if are acidotic.
- fluids – aggressive correction of the dehydration, acidosis and coagulopathy should be done before transporting the baby. May require replacement of gastric aspirates during the journey if significant
- orogastric tube with free flow and 4 hourly aspirates– essential
- drugs – will require antibiotics and possibly inotropic support that needs to be continued during the journey
- peritoneal drain – If there is a perforation of the bowel, insertion of a peritoneal drain with/without lavage with normal saline or dialysate solution should be considered. This can help to improve the ventilation as well as the acidosis.

### **Intrahospital Transport**

- use transport incubator if available
- ensure all parties concerned are ready before transfer
- send team member ahead to commandeer lifts, clear corridors
- ensure patient is stable before transport
- skilled medical and nursing staff should accompany patient
- ensure adequate supply of oxygen
- prepare essential equipment and monitors for transport
- ensure venous lines are patent, well secured
- infusion pumps should have charged batteries. To decrease bulk of equipment,



*Figure 1: Supine abdominal X-ray showing free intraperitoneal gas – loss of liver shadow, visible falciform ligament and Wrigler's sign*

## THE PREMATURE INFANT

### Introduction

- the *Premature* infant: < 37 weeks gestation
- *Low Birth Weight* (LBW): < 2500 g
- *Very Low Birth Weight* (VLBW): < 1500 g
- *Extremely Low Birth Weight* (ELBW): < 1000 g
- *Small for Gestational Age*: < 10th centile of birth weight for age.

### Management

#### *Before and During Labour*

- prewarmed incubator and appropriate equipment for neonatal intensive care should always be kept ready in the neonatal unit (NNU).

#### *Adequate Resuscitation*

#### *Transfer from Labour Room (LR) to NNU (Neonatal Unit)*

- use prewarmed transport incubator if available. If not the baby must be wiped dry and wrapped in dry linen before transfer.
- if the infant's respiration is inadequate, keep the infant INTUBATED and AMBU BAGGED with oxygen during the transfer. For those with mild respiratory distress, preferably initiate CPAP in labour room, and if tolerated CPAP during transport.

#### *Admission Routine*

- ensure thermoneutral temperature for infant. An incubator or radiant warmer is necessary for more premature and ill babies.
- ventilation is often necessary if ventilated during transfer.
- if oxygen saturation is < 90%, oxygen therapy should be given.
- head circumference (OFC), length measurements and bathing can be omitted.
- quickly and accurately examine and weigh the infant.
- assess the gestational age with Dubowitz or Ballard score when stable (see end of this section for score).
- monitor temp, HR, RR, BP and SaO<sub>2</sub>.

#### *Immediate Care for Symptomatic babies*

- investigations are necessary as indicated and include:
  - Blood gases.
  - Blood glucose (dextrostix)
  - Full blood count with differential WBC and IT ratio (if possible)
  - Blood culture.
  - CXR (if respiratory signs and symptoms are present)
- start on 10% dextrose drip.
- correct anaemia.
- correct hypotension (keep mean arterial pressure (MAP) > gestational age (GA) in weeks). Ensure hyperventilation is not present (a cause of hypotension). If the baby has good tone and is active, observe first as the BP often rises after the first few hours of life towards a MAP approximating GA in weeks.
- correct hypovolaemia: Give 10 ml/kg over 20-30 minutes of normal saline, or packed cells if anaemic. Avoid repeated boluses of fluid unless there is volume loss.
- start inotrope infusion if hypotension persists after volume correction.

- start antibiotics after taking cultures e.g. Penicillin and Gentamycin
- start iv aminophylline in premature babies < 34 weeks.
- maintain SaO<sub>2</sub> at 89-92% and PaO<sub>2</sub> at 50–80 mmHg

#### *General Measures for Premature infants*

- monitor vital signs (colour, temperature, apex beat, respiratory rate). Look for signs of respiratory distress (cyanosis, grunting, tachypnoea, nasal flaring, chest recessions, apnoea). VLBW, ill babies pulse oximetry and blood pressure monitoring are necessary.
- check Dextrostix (see Hypoglycaemia protocol).
- keep warm in incubator at thermoneutral temperature for age and birth weight, ELBW may need humidified environment.
- ensure adequate nutrition
- provide parental counselling and allow free parental access.
- infection control : observe strict hand washing practices
- immunisation:
  - Hep B vaccine at birth if infant stable and BW is >1.8 kg. Otherwise give before discharge.
  - ensure BCG is given on discharge
  - for long stayers other immunisation should generally follow the schedule according to chronological rather than corrected age.
  - in the presence of acute illnesses immunisation is usually deferred.
- supplements:
  - at birth : Vitamin K IM (0.5 mg for BW<2.5 kg and 1 mg for BW= 2.5 kg and above)
  - once on full feeding, give Infant Multivitamin drops 1 mls OD ( to be continued till \ fully established weaning diet) For preterm infants, choose the formulation with 400 IU Vit D, and Folic acid 1 mg OD.
  - starting at about 4 weeks of life: Elemental Iron 2-3 mg/kg/day – to be continued for 3-4 months

#### *ICU care and Criteria for Replacement Transfusion in Neonates*

See relevant chapter.

#### *Discharge*

- cranial Ultrasound for premature babies < 32 weeks recommended at:
  - within first week of life to look for intraventricular haemorrhage (IVH)
  - around day 28 to look for periventricular leucomalacia (PVL)
  - as clinically indicated
- screening for Retinopathy of Prematurity (ROP) at 34 - 36 weeks' gestation or at 4-6 weeks of age is recommended for
  - all babies < 32 weeks gestation at birth or birth weight <1500 g.
  - all preterms <36 weeks who received oxygen therapy depending on individual risk as assessed by the clinician
- the infants are discharged once they are well, showing good weight gain, established oral feeding and gestational age of at least 34 weeks.

#### **Prognosis**

- mortality and morbidity are inversely related to gestation and birth weight.
- complications include retinopathy of prematurity, chronic lung disease, neurodevelopmental delay, growth failure, cerebral palsy, mental retardation, epilepsy, blindness and deafness.

## ENTERAL FEEDING IN NEONATES

### Introduction

- the goal of nutrition is to achieve as near to normal weight gain and growth as possible
- enteral feeding should be introduced as soon as possible. This means starting in the labour room itself for the well infant
- breast milk is the milk of choice. All mothers should be encouraged to give breast milk to their newborn babies
- the calorie requirement : Term infants: 110 kcal/kg/day  
Preterm infants : 120 – 140 kcal/kg/day

### Type of milk for Newborn feeding

There are three choices:

- expressed breast milk
- normal infant formula
- preterm infant formula

#### *Breast Milk*

Breast milk is preferred as studies have shown that breast fed babies had low risk for necrotising enterocolitis and had better development quotients. However, expressed breast milk (EBM) alone is not adequate for the nutritional needs of the very preterm infant as it:

- has insufficient calories and protein to ensure optimal early growth at 20 kcal/30mls
- has insufficient sodium to compensate for high renal sodium losses
- has insufficient calcium or phosphate - predisposes to osteopenia of prematurity.
- is deficient in vitamins and iron relative to the needs of a preterm infant

#### *Human Milk Fortifier (HMF)*

- It is recommended to add HMF to EBM in babies < than 32 weeks or < 1500 grams.
- HMF will give extra calories, vitamins, calcium and phosphate.
- HMF should be added to EBM when the baby is feeding at 75 mls/kg/day.
- VLBW infants on exclusive breastmilk may require sodium supplementation until 32-34 weeks corrected age.

### Infant Formula

Infant formula should only be given if there is no supply of EBM. There are 2 types of infant formula: Preterm formula and Normal Term Formula.

- preterm formula : for babies born < 32 weeks or < 1500 grams.
- normal infant formula : for babies born > 31 weeks or > 1500 grams.

### Strategies of administering enteral feeding

#### *Orogastric Route*

Neonates are obligate nose breathers thus nasogastric tubes can obstruct the nasal passage and compromise breathing. Thus the orogastric route is preferable.

#### *Continuous vs. intermittent bolus feeding*

Bolus fed babies tolerate feeds better and gain weight faster. Babies on continuous feeding have been shown to take longer to reach full feeding but there is no difference in days to discharge, somatic growth and incidence of necrotising enterocolitis (NEC).

#### *Cup feeding*

If baby is able to suckle and mother is not with the baby, cup feeding is preferable to bottle feeding to prevent nipple confusion.

Table 1. Composition of various milk

component		cow's milk	standard formula	preterm formula	mature breastmilk
carbohydrate	g/100ml	4.6	7.5	8.6	7.4
fat	g/100ml	3.9	3.6	4.4	4.2
protein	g/100ml	3.4	1.5	2.0	1.1
casein/lactalbumin ratio		4:1	2:3	2:3	2:3
calories	/100ml	67	67	80	70
sodium	mmol/L	23	16	33	15
potassium	mmol/L	40	65	33	64
calcium	mg%	124	46	77	35
phosphate	mg %	98	33	41	15
iron	mg%	0.05	0.8	0.67	0.08

### When to start milk?

- as soon as possible for the well term babies
- however in the very preterm infant there is a concern of increase risk of NEC if feeding is started too early/advanced too rapidly, although early feeding with EBM is to be encouraged. Studies have suggested that rapid increment in feeding has a higher risk for NEC than the time at which feeding was started.
- minimal enteral feeding (MEF) is recommended in very preterm infants. The principle is to commence very low volume enteral feeds on day 1 - 3 of life (i.e. 5 - 25 mls/kg/day) for both EBM and formula milk. MEF enhances gut DNA synthesis hence promotes gastrointestinal growth. This approach allows earlier establishment of full enteral feeds and shorter hospital stays, *without any concomitant increase in NEC.*

### How much to increase?

- generally the rate of increment is about 20 to 30 mls/kg/day.
- well term babies should be given breast feed on demand.
- milk requirements for babies on full enteral feed from birth:
 

Day 1	60 mls/kg/day
Day 2 – 3	90 mls/kg/day
Day 4 – 6	120 mls/kg/day
Day 7 onwards	150 mls/kg/day

*Add 15% if the babies is under phototherapy*

- in babies requiring IV fluids at birth: The rate of increment need to be individualized to that baby. Babies should be observed for feeding intolerance (vomit or large aspirate) and observe for any abdominal distention before increasing the feed. to feed intolerance or fluid overload.
- infants that require high calories due to increase energy expenditure e.g. chronic lung disease, should consider adding polyose and MCT.

### What is the maximum volume?

- the target weight gain should be around 15g/kg/day (range 10-25g/kg/day). Less than this suggests calories need increasing. More than this should raise the possibility of fluid overload particularly in babies with chronic lung disease.
- preterm infants
  - increase feed accordingly to 180 to 200 mls/kg/day.
  - if on EBM, when at 75 mls/kg/day: add HMF
- term infant
  - allow demand feeding

#### Notes:

- in a randomised trial in babies < 30 weeks comparing remaining at a final feed volume of 150 ml/kg/day (120 cal/kg/day) to advancing to 200 mls/kg/day, it was noted that half the 200 mls/kg/day group had to be cut back (to a mean of 180 mls/kg/day) due

### When to stop HMF or Preterm Formula?

Consider changing preterm to standard formula and stop adding HMF to EBM when babies are breastfeeding on demand or have reached their expected growth curve.

### Vitamin and mineral supplementation.

- *Vitamins*: a premature infant's daily breast milk/ breast milk substitute intake will not supply the daily vitamin requirement. Multivitamin can be given after day 14 of life when on feeding of 150 ml/s kg/day.  
Vitamin supplements at 0.5 mls daily to be continued for 3-4 months post discharge.
- *Iron*: Premature infants have reduced intra uterine iron accumulation and can become rapidly depleted of iron when active erythropoiesis resumes. Therefore babies of birth weight < 2000g should receive iron supplements.  
Iron is given at a dose of 3 mg/kg elemental iron per day.
  - Ferric Ammonium Citrate (400mg/5mls) contains 86 mg/5 mls of elemental iron.
  - start on day 42, continue until 3-4 months post discharge or until review by doctor
  - Babies who have received multiple blood transfusions may not require as much iron supplementation.

### Special Cases

- IUGR babies with reversed end-diastolic flow on antenatal Doppler: Studies have shown that these babies are at risk of NEC. Thus feeds should be introduced slowly and initially use only EBM.



## TOTAL PARENTERAL NUTRITION FOR NEONATES

### Introduction

- total parenteral nutrition (TPN) is the intravenous infusion of all nutrients necessary for metabolic requirements and growth
- earlier introduction and more aggressive advancement of TPN is shown to be safe and effective, even in the smallest and most immature infants
- premature infants tolerate TPN from day 1 of post-natal life

### *The goal of TPN is to*

- provide sufficient nutrients to prevent negative energy and nitrogen balance and essential fatty acid deficiency
- support normal rates growth without increased significant morbidity.

### Indication for TPN

- gastrointestinal tract abnormalities (tracheo-esophageal fistula, omphalocele, gastroschisis, malrotation with volvulus, etc)
- necrotizing enterocolitis (NEC)
- respiratory distress syndrome / BPD patients who are unable to tolerate feeding
- extreme prematurity
- sepsis
- malabsorption

### Components of TPN

The essential components of parenteral nutrition are:

- |                  |                |
|------------------|----------------|
| • fluids         | • protein      |
| • electrolytes   | • carbohydrate |
| • vitamins       | • lipids       |
| • trace minerals |                |

Goal is to provide at least 100-110 cal/kg/day. This will be achieved if we can deliver (for example) 150 mls/kg/day of 12.5% dextrose, 2.5 g/kg/day of synthetic amino acids, and 3.0 g/kg/day of intravenous lipids.

### *Fluid*

- fluid is an essential component.
- usually started at 80-100 ml/kg/day (if newborn), or at whatever stable fluid intake the baby is already receiving.
- volumes are increased over the first 7 days in line with the fluids and electrolytes protocol with the aim to deliver 150 ml/kg/day by day 7.

### *Amino acids*

- amino acids prevents catabolism; prompt introduction via TPN achieves an early positive nitrogen balance.
- decreases frequency and severity of neonatal hyperglycaemia by stimulating endogenous insulin secretion and stimulates growth by enhancing insulin and insulin-like growth factor release
- start protein at 1g/kg/day of crystalline amino acids; advanced by day 3-4 age to 3.0 g/kg/day of protein (term infants) and 3.7 - 4.0 g/kg/day (extremely low birth weight infants , ELBW)
- reduction in dosage may be needed in critically ill, significant hypoxaemia, suspected or proven infection and high dose steroids.

- adverse effects of excess protein include a rise in urea and ammonia and high levels of potentially toxic amino acids such as phenylalanine.

### Glucose

- there is a relatively high energy requirement in the ELBW and continuous source of glucose is required for energy metabolism.
- in the ELBW minimum supply rate is 6 mg/kg/min to maintain adequate energy for cerebral function; additional 2-3 mg/kg/min (25 cal/kg) of glucose per gram of protein intake is needed to support protein deposition. Maximum rate: 12 - 13 mg/kg/min (lower if lipid also administered) but in practice often limited by hyperglycaemia (20 - 80% of ELBW) from decreased insulin secretion and insulin resistance (presumably due to glucagon, catecholamine and cortisol release).
- hyperglycaemia in the ELBW managed by decreasing glucose administration, administering intravenous amino acids and/or infusing exogenous insulin.
- glucose administration is initiated at 6 mg/kg/min, advancing to 10-12 mg/kg/min.
- if hyperglycaemia then infusion rate decreased; if hyperglycaemia on infusion rate of 3 - 4 mg/kg/min then give insulin.

### Lipid

- lipids prevent essential fatty acid deficiency, provide energy substrates and improve delivery of fat soluble vitamins.
- LBW infants may have immature mechanisms for fat metabolism. A number of clinical conditions inhibit lipid clearance e.g. infection, stress and malnutrition.
- start lipids at 1g/kg/day, at the same time as amino acids prevent essential fatty acid deficiency; dose gradually increased up to 3 g/kg/day (3.5g/kg/day in ELBW infants). Use smaller doses in sepsis, compromised pulmonary function, hyperbilirubinaemia.
- it is infused continuously over as much of the 24 hour period as practical.
- avoid concentrations >2g/kg/day if infant has jaundice requiring phototherapy
- preparation of 20% emulsion is better than 10% as 20% solutions require less fluid volume with a lower phospholipid-to-triglyceride ratio and 10% interferes with triglyceride (TG) clearance leading to higher TG and cholesterol values
- the use of heparin at 0.5 to 1 units/mL of TPN solutions (max 137 units/day) can facilitate lipoprotein lipase activity to help stabilize serum triglyceride values.
- lipid clearance monitored by plasma triglyceride levels (maximum triglyceride concentration ranges from 150 mg/dl to 200 mg/dl).
- exogenous lipids may interfere with respiratory function. Suggested mechanisms include impaired gas exchange from pulmonary intravascular accumulation or impaired lymph drainage resulting in oedema. Lipids may also aggravate pulmonary hypertension in susceptible individuals.

### Electrolytes

- sodium requirement: 2-3 mEq /kg/day (term infants); 4-5 mEq/kg/day (preterm)
- potassium requirement: 2-3 mEq/kg/day in both term and preterm infants.

### Minerals, Calcium (Ca), Phosphorus (P) And Magnesium

- the premature infant is unable to maintain the intrauterine accretion rate of Ca and P when parenterally fed; the optimal retention of Ca and P is half the intrauterine accretion
- monitoring for osteopaenia of prematurity is important especially if prolonged PN
- a normal magnesium level is a prerequisite for a normal calcaemia. In well balanced formulations, however, magnesium does not give rise to major problems.

### Trace Elements

- indicated if PN is administered for  $\geq 1$  week. Commercial preparations are available

### Vitamins

- both fat and water soluble vitamins are essential. It should be added to the to fat infusion instead of amino-acid glucose mixture to reduce loss during administration

### Administration

- TPN should be delivered where possible through central lines
- peripheral lines only if TPN  $\leq 3$  days duration and dextrose concentration  $\leq 12.5\%$
- peripheral lines also limited by osmolality ( $<600$  mOsm/L) to prevent phlebitis
- percutaneous central line: confirm position of catheter tip with X-ray prior to use.
- strict aseptic technique in preparation and administration of the TPN is essential
- avoid breakage of the central line through which the TPN is infused, though compatible drugs may be administered if necessary.
- heparin is added to all TPN solutions; omitted on specialist orders if contraindicated

### Caution

- *Hyperkalaemia*. Rarely required in first 3 days unless serum potassium  $< 4$  mmol/l. Caution in renal impairment.
- *Hypocalcaemia*. May result from inadvertent use of excess phosphate. Corrects with reduction of phosphate.
- *never* add bicarbonate, as it precipitates calcium carbonate
- *never* add extra calcium to the burette, as it will precipitate the phosphates.

### Complications

#### Delivery

The line delivering the TPN may be compromised by;

- sepsis - minimized by maintaining strict sterility during and after insertion
- malposition. X-ray mandatory before infusion commences
- thrombophlebitis - with peripheral lines; require close observation of infusion sites
- extravasation into the soft tissue, with resulting tissue necrosis

#### Metabolic complications

- hyperglycaemia
- hyperlipidaemia
- cholestasis

### Monitoring

*Before starting* an infant on parenteral nutrition, investigation required:

- full blood count /haematocrit
- renal profile
- liver function test, bilirubin
- random blood sugar/dextrostix

*While on TPN*, monitoring required :

#### Laboratory

- full blood count, renal profile. Daily for 1 week then 3 times a week
- plasma calcium, magnesium, phosphate. Twice a week until stable then weekly
- triglyceride levels. After dose changes then weekly
- liver function test: If long term TPN ( $> 2$  weeks duration)

#### Clinical

- blood sugar / dextrostix, 4-6 hrly first 3 days, twice a day once stable.
- daily weight
- meticulous care of the catheter site and monitoring of infection.

## NICU: GENERAL POINTERS FOR CARE AND REVIEW

### Checklist for Review of an infant in Intensive Care

- **Age of infant**

If <72 hours state in exact hours of age. Beyond this state in completed days.

- **Weight**

Note birth weight and current weight. An initial drop in weight is to be expected:

- term infants up to 10% BW in the first 3-5 days; preterm up to 15% in the first week.

Abnormal weight gain or losses in the first days often implicate suboptimal fluid therapy.

Less weight loss is expected with the use of humidified incubators.

- **General condition**

e.g. ill, unstable, handles poorly e.g. desaturates on handling, stable, active, responsive to handling, improving, or good is to be noted

- **Cardiopulmonary system**

Check for:

a) signs of poor perfusion (with poor peripheral pulses, rapid pulse, poor capillary refilling and cold peripheries).

If perfusion is poor infuse a fluid bolus of 10 ml/kg of Normal Saline.

This may be repeated if there is no improvement. After the 2nd dose of normal saline 5% albumin can be considered for volume expansion.

*Caution: repeat doses may be required for volume loss or reduced vascular volume due to extravascular fluid losses (e.g. sepsis, intestinal obstruction)*

b) adequacy of the blood pressure

Consider inotropic agents like adrenaline, dobutamine, dopamine or amrinone.

c) examine for presence of a patent ductus arteriosus (PDA) in preterm infants

- **Fluids and Electrolytes**

- is the volume and type of fluid given to the child appropriate?

- empiric fluid therapy for newborns:

0-24 hours : 60 ml/kg/day

24-48 hours : 90 ml/kg/day

48-72 hours : 120 ml/kg/day

> 72 hours : 150 ml/kg/day

- slower rates of increment in preterm infants

- generally a 10% dextrose is started on the 1st day; sodium and potassium added on the second/third day. Empirically:

- preterm infants need 4-5 mmol/kg/day of sodium; 2-3 mmol/kg/day of potassium

- term infants require 2-3 mmol/kg/day of both sodium and potassium

- fluid and electrolyte therapy are influenced by underlying illness and complications: adjustments based on these conditions, intake/output, weight, blood urea and electrolytes

- monitor BUSE; correct any imbalances after considering the underlying cause.

- ensure the urine output is > 1 ml/kg/hr.

- **Infection**

- is there a possibility of infection? Is the child on antibiotics? Consider fungal infection if infant has been given multiple courses of antibiotics, is very premature or on central venous catheters and parenteral nutrition.

- **Feeding**
  - parenteral nutrition should be started in VLBW infants as soon as possible
  - bigger babies may be started on parenteral nutrition unable to feed enterally for  $\geq 5$  days. Enteral feeds can be given via oro- or nasogastric tube.
  - encourage expressed breast milk
- **Temperature Control**
  - ensure thermoneutral environment. Covering the open area of open hoods with *cling wrap* and increasing water content with a humidifier will help in temperature control and fluid regulation of the ELBW infant.
- **Skin care**
  - a vital component of care especially for the premature infants.
  - avoid direct plastering onto skin and excessive punctures for blood taking and setting up of infusion lines. Meticulous attention must be given to avoid extravasation of infusion fluid and medication which can lead to phlebitis, ulceration and septicaemia.
- **Central nervous system**
  - check fontanelle tension and size, condition of sutures i.e. overriding or separated, head circumference (when indicated e.g. in a case of subaponeurotic haemorrhage)
  - sensorium, tone, movement, responses to procedures e.g. suctioning of pharynx, and presence or absence of seizure should be assessed.
- **Ventilation**
  - check if the ventilation is adequate. Is the child maintaining the optimum blood gases? Can we start weaning the child off the ventilator?

### Endotracheal tube (ETT) Care

Table 1. Guidelines for Endotracheal tube (ETT) placement

infant weight	ETT size	ETT position (oral) <sup>1,2,3</sup>
<1000g	2.5	
1000g-2000g	3	7 cm
2000g-3000g	3.5	8 cm
>3000g	3.5-4.0	9 cm

footnote:

1. oral ETT "tip-to-lip" distance

2. or weight in kg + 6

3. for nasal ETT: add 2 cm respectively.

Note:

- check X-ray after intubation: ensure the tip of the ETT

- shorten ETT if more than 4 cm extends from the lips

### Suction of ETT

- Should be done as needed, as it is associated with desaturation and bradycardia
- delivered  $\text{FiO}_2$  may need to be increased, as guided by the  $\text{SaO}_2$  monitor, during suctioning (keep  $\text{SaO}_2$  89-95%).

### Umbilical Arterial Catheter (UAC) and Umbilical Venous Catheter (UVC) care

- **UAC position**
  - length to be inserted measured from the abdominal wall is  $3 \times \text{BW}(\text{kg}) + 9 \text{ cm}$ . This usually puts the tip above the diaphragm. Confirm with X-ray: UAC tip should be above T12 or below L4.
  - wash hands before taking blood from the UAC. Sterile handling of the hub or 3 way tap of the line.

- the UAC is kept patent with a heparin infusion (1U/ml) at 1 ml/hr; intra-arterial blood pressure monitoring transducers and tubings can be connected.

- *UVC position*

- ½ UAC +1 cm

## Ventilation

- initial ventilator setting (in most situations):

Total Flow:	8 - 10 litres/min
Peak Inspiratory Pressure (PIP):	20-25 mmHg (lower in ELBW infants)
Positive End Expiratory Pressure (PEEP):	4 - 5 mmHg
Inspiration Time:	0.3- 0.35 sec
Ventilation rate:	40- 60 / min
FiO <sub>2</sub> :	60 to 70%

- the ventilator setting is then adjusted according to the clinical picture, pulse oximetry reading and ABG which is usually done within the 1st hour.

- Note:

- the I:E ratio should not be inverted (i.e. > 1) unless requested specifically by a specialist.
- tailor the ventilation settings to the baby's ABG.

Keep:	pH	7.35 - 7.45
	PaO <sub>2</sub>	50 - 70 mmHg for premature infants 60 - 100 mm Hg for term babies
	PaCO <sub>2</sub>	40 - 60
	SaO <sub>2</sub>	89 - 92% for preterm babies

- changing of ventilator settings:

- to produce an increase in PaO<sub>2</sub> either: -
  - increase FiO<sub>2</sub> concentration.
  - increase PEEP.
  - increase PIP (increases minute volume).
  - *rarely*, increase I/E ratio (prolong inspiration)
- to produce a decrease in PaCO<sub>2</sub> either: -
  - increase Rate (increases minute volume)
  - decrease I/E ratio (prolong expiration)
  - increase PEEP in worsening lung disease.
  - decrease PEEP in recovery phase.

**Table 2. Complications of ventilation**

*consider the following if the child deteriorates on ventilation:*

- dislodged endotracheal tube
- obstructed endotracheal tube
- displaced or deep endotracheal tube
- pneumothorax
- disconnected ventilator tubes
- ventilator malfunction
- intraventricular haemorrhage
- worsening of the primary condition

*Note: do not 'chase' the PaCO<sub>2</sub> by increasing ventilator settings unless there is respiratory acidosis*

- do the opposite to decrease PaO<sub>2</sub> or to increase PaCO<sub>2</sub>.
- minute volume = tidal volume (volume per breath) x rate per minute
- with volume-limited ventilators, minute volume can be calculated (use tidal volume = 4-6 ml/kg)
- with pressure-limited respirators - increasing peak inspiratory pressure results in increased minute volume.

## Sedation and Ventilation

- avoid paralysing the child as far as possible. Paralysis has been shown to result in poorer lung function and other complications.
- use morphine infusion as an analgesia and sedative, if required.

## High Frequency Oscillatory Ventilation (HFOV)

### Indications

- when conventional ventilation fails HFOV should be considered. This is to be discussed with the specialist.

### Practical management

- switching from conventional ventilation to HFOV :
  - initial setting
    - leave  $\text{FiO}_2$  level at the same as that on conventional ventilation
    - MAP - For RDS, start at 2 cm H<sub>2</sub>O above the MAP of conventional ventilation
    - amplitude - 50-100%; adjust until chest vibrates but not whole abdomen
    - frequency - 10Hz
    - tidal volume - about 2 to 2.5ml/kg
  - continuation of HFOV
    - chest X-ray after 30-60 minutes, aim for lung expansion to 8-9th rib level
    - hypoxia - increase MAP
    - hyperoxia - reduce  $\text{FiO}_2$  or decrease MAP
    - hypercapnia
      - increase amplitude
      - decrease frequency
      - increase MAP
    - hypocapnia
      - decrease amplitude
      - increase frequency
      - decrease MAP
    - overinflation
      - reduce MAP
      - consider discontinuing HFOV
  - weaning
    - reduce  $\text{FiO}_2$  to 0.3-0.5
    - reduce MAP by 1 to 2 mbar per hour until 8 to 9 mbar
    - reduce amplitude
    - extubate to head box/CPAP or change to conventional ventilation

## VASCULAR SPASM AND THROMBOSIS

Thromboembolism (TE) is being increasingly recognised as a significant complication of intravascular catheters in sick newborn infants.

### Definitions

- *Vascular spasm* – transient, reversible arterial constriction, triggered by intravascular catheterisation or arterial blood sampling. The clinical effects of vascular spasm usually last < 4 hours from onset, but the condition may be difficult to differentiate from the more serious TE. The diagnosis of vascular spasm may thus only be made retrospectively on documenting the transient nature of the ischaemic changes and complete recovery of the circulation.
- *Thrombosis* – complete or partial occlusion of arteries or veins by blood clot(s)

### Assessment

#### *Clinical diagnosis*

- peripheral arterial thrombosis/ vasospasm – pallor or cyanosis of the involved extremity with diminished pulses or perfusion.
- central venous line (CVL) associated venous thrombosis – CVL malfunction, superior vena cava (SVC) syndrome, chylothorax, swelling and livid discolouration of extremity
- aortic or renal artery thrombosis – systemic hypertension, haematuria, oliguria.

#### *Diagnostic imaging*

- contrast angiography is the “gold standard”, but difficult to perform in critically ill neonates and requires infusion of radiocontrast material that may be hypertonic or cause undesired increase in vascular volume.
- Doppler ultrasonography – portable, non-invasive, useful to monitor progress over time. False positive and false negative results occur, as compared to contrast angiography.

#### *Additional diagnostic tests*

- obtain detailed family history in all cases of unusual or extensive TE.
- in the absence of predisposing risk factors for TE, consider investigations for thrombophilic disorders: anticardiolipin, antithrombin III, protein C, protein S deficiency

### Management of vascular spasm

- immediate measures to be taken:
  - lie the affected limb in horizontal position
  - if only one limb is affected, warm (using towel) opposite unaffected leg to induce reflex vasodilatation of the affected leg.
  - maintain neutral thermal environment for the affected extremity, i.e. keep heat lamps away from the area.
- inform the paediatrician immediately.
- consider removing the catheter. If mild cyanosis of the fingers or toes is noted after insertion of an arterial catheter, but peripheral pulses are still palpable, a trial of reflex vasodilatation with close observation is reasonable – check continuously to see that the cyanosis is improving within a few minutes. A white or “blanched” appearing extremity is an indication for **immediate** removal of the catheter.
- other risk factors contributing to thrombosis includes dehydration, sepsis, and polycythaemia. These factors may need to be corrected immediately.
- maintain good circulatory volume. If there is no immediate improvement with removal of catheter, try volume expansion 10 mls/kg of normal saline.



- topical nitroglycerine – using patch or topical 2% ointment at a dose of 4mm/kg body weight, applied as a thin film over the affected body area; may be repeated after 8 hours. Monitor for hypotension and be prepared to treat immediately.
- if the limb ischaemia persists for > 1 hour without any improvement, refer urgently to the radiologist if available. A doppler ultrasound needs to be done urgently to ascertain whether the limb ischaemia is caused by vasospasm or thrombosis.

### Management of catheter-related thromboembolism

- management of vascular TE may involve one or more of the following: supportive care, anticoagulation, fibrinolytic therapy, surgical intervention
- treatment for neonates is highly individualised and is determined by the extent of thrombosis and the degree to which diminished perfusion to the affected extremity or organ affects function
- consultation with paediatric haematology, orthopaedic or vascular surgeon may be required
- initial management
  - as for vascular spasm for peripheral arterial ischaemia
  - removal of catheter as soon as blanching is seen
  - supportive care – correct volume depletion, electrolyte abnormalities, anaemia and thrombocytopaenia; treat sepsis
- anticoagulant/ thrombolytic therapy
  - the risk of serious bleeding associated with antithrombotic therapy in neonates must be balanced against the possibility of organ or limb loss or death without appropriate treatment. Adequate randomised trials to guide therapy in neonates are not available.
  - contraindications:
    - major surgery within the preceding 10 days
    - major bleeding: intracranial, pulmonary, gastrointestinal
    - pre-existing cerebral ischaemic lesions
  - relative contraindications –
    - platelet count  $< 100,000 \times 10^9 /L$
    - fibrinogen levels  $< 100\text{mg/dL}$
    - severe coagulation factor deficiency,
    - hypertension

*Note: anticoagulation/thrombolytic therapy can be given after correcting these abnormalities.*

- precautions:
  - no arterial punctures
  - no subcutaneous or IM injections
  - no urinary catheterisations
  - avoid aspirin or other antiplatelet drugs
  - monitor serial ultrasound scans for intracranial haemorrhage
- anticoagulants
  - standard or unfractionated heparin (UFH)
    - anticoagulant, antithrombotic effect limited by low plasma levels of antithrombin in neonates. For dosage see Table 1 below.
    - the optimal duration is unknown but therapy is usually continued for 5-14 days
    - monitor thrombus closely during and following treatment.
    - complications: bleeding, heparin-induced thrombocytopaenia
    - antidote: Protamine sulphate – see Table 2 for dosage

Table 1. Recommended dosing of unfractionated heparin

Stage	Description	aPTT(s)	Bolus (U/kg)	Hold (min)	Rate change (%)	Repeat aPTT
I	Loading dose		75 IV over 10 mins			
II	Initial maintenance dose		28/h			
III	Adjustment	<50	50	0	+10	4 hours
		50-59		0	+10	4 hours
		60-85		0	0	next day
		85-95		0	-10	4 hours
		96-120		30	-10	4 hours
		>120		60	-15	4 hours

A loading dose of 75 U/kg over 10 min followed by a maintenance dose of 28 units/kg (infants < 1 year) is recommended. An aPTT should be checked 4h after the heparin loading dose and 4h after every change in infusion rate. Once the aPTT is in the therapeutic range, a complete blood count and aPTT should be checked daily or as clinically indicated. Abbreviations: aPTT, activated partial thromboplastin time

Table 2. Recommended dosing of protamine for reversal of heparin therapy

Heparin: time since last dosing	Protamine dose
< 30 min	1 mg / 100 u heparin received
30-60 min	0.5 - 0.75 mg/ 100 u heparin received
60-120 min	0.375 - 0.5 mg/ 100 u heparin received
>120 min	0.25 - 0.375 mg/ 100 u heparin received
maximum dose	50 mg
infusion rate	10 mg/ml solution; rate < 5 mg/min

- low molecular weight heparin (LMWH)

- advantages: Subcutaneous administration. Heparin induced thrombocytopenia is rarely associated with LMWH.
- antidote: Omit two doses if an invasive procedure is required. Protamine is partially effective, dosage 1mg/100U heparin given within the last 3-4 hours.

Table 3. Low molecular weight heparin dosing

age	initial treatment dose	prophylactic dose
< 2 months	1.5 mg/kg bd	0.75 mg/kg bd
> 2 months	1 mg/kg bd	0.5 mg/kg bd

Therapeutic dose range may vary from 0.95-3.5mg/kg/bd

Note : LMWH have specific anti-factor Xa activity. Therapy is monitored using anti-FXa and not APTT (aim for anti FXa level 0.5-1U/mL), monitoring 4 h after dosage adjustment; weekly once therapeutic level attained. However, monitoring of anti-FXa levels may not presently be available in most laboratories.

• thrombolytic agents

- consider thrombolytic agents (recombinant tissue plasminogen activator, streptokinase) if there is major vessel occlusion causing critical compromise of organs or limbs
- supplementation with plasminogen (from FFP) enhances the thrombolytic effect
- thrombi already present for several days may be resistant to thrombolysis (failure rates ≈ 50%)
- monitoring
  - monitor fibrinogen levels, thrombin time, plasminogen levels before starting, 3-4 hours after starting and 3-4 times daily thereafter. Stop if fibrinogen < 100 mg/dL
  - imaging studies q4-12 hr to allow discontinuing treatment as soon as clot lysis achieved
  - complications: bleeding, embolisation

Table 4 - Thrombolytic regime in neonate

Drug	IV bolus dose	IV maintenance dose
Streptokinase	1000 units / kg	1000 units / kg / hour
Urokinase	4,400 U/kg over 20 mins	4,400 units / kg / hour for 6-12 hrs
Tissue plasminogen activator	0.5 mg / kg over 10 mins	0.015-0.2 mg / kg / hour
(dose for direct infusion into thrombus)		

Table 5. Recommendations for management of thrombolytic therapy

*Before initiating therapy:*

- exclude contraindications
- monitor full blood count, including platelets, fibrinogen
- obtain blood type, cross match
- ensure adequate supply of blood products, cryoprecipitate, aminocaproic acid
- obtain cranial ultrasound
- ensure adequate venous access for infusion and monitoring
- have compresses and topical thrombin ready for localised bleeding

*During therapy:*

- post sign on bed that patient is receiving thrombolytic therapy
- monitor PT, PTT, fibrinogen level every 4 h during infusion and 4h and 12h after infusion
- daily cranial ultrasound
- maintain fibrinogen > 150 mg/dL with cryoprecipitate (1unit/5kg); expect 20-50% decrease
- maintain platelet count > 100,000 / ml
- no IM injections
- no urinary catheterisation, rectal temperatures or arterial puncture
- minimal manipulation of patient
- avoid warfarin, antiplatelet agents

## GUIDELINES FOR THE USE OF SURFACTANT

### Introduction

- surfactant is expensive, however evidence for its effectiveness is very strong

*A systematic review of 35 RCTs on surfactant use: in 6000 infants there was a reduction in mortality of 30-40%, a reduction in pulmonary air leak, and decreased long term oxygen dependence.*

### Indication

Ideally for all infants who require mechanical ventilation for respiratory distress syndrome (RDS), which is due to surfactant deficiency. Due to costs, this is limited to:

- preterm infants  $\leq 32$  weeks or birth weight  $\leq 1.5$  kg
- more mature or larger infants if RDS is severe  
i.e. arterial alveolar (a/A)  $PO_2$  ratio of  $<0.22$  or Fraction of inspired oxygen ( $FiO_2$ )  $>0.5$

Calculation for a/A $PO_2$ ratio : $\frac{PaO_2 \text{ (mmHg)}}{(760-47)FiO_2 - PaCO_2 \text{ (mmHg)}}$
---

### Timing of therapy

- give first dose as early as possible to preterm infants on mechanical ventilation
- no benefit in administering surfactant  $> 24$  hours age or using more than 2 doses

### Types of surfactant and dosage

- *Survanta*, a natural surfactant, is the only preparation currently available in Malaysia.
  - dose : 4 ml/kg per dose. Give 1st dose as soon as possible preferably in first 2 hours.
  - repeat at 6 hours later if needed. Onset of action within minutes.

### Method of administration

- surfactant is delivered as a bolus directly through an endotracheal tube (ETT), over 15 minutes, either via
  - a catheter inserted into the ETT via a side port in the ventilator circuit , in 2 aliquots
  - on the ETT adaptor without the need of removing the infant from ventilator
  - into the side port on the ETT adaptor
- rapid installation over 5 minutes is not recommended as it results in an increase in CBFV (Cerebral Blood Flow Velocity) and  $PCO_2$  compared to slower 15-minute bolus
- infants who remained connected to the ventilator during surfactant installation have been shown to experience less oxygen desaturation compared to those who were disconnected. This also results in more homogenous distribution of surfactant within the lung
- infants must be monitored closely with a pulse oximeter and regular blood gas measurements. An indwelling intra-arterial line will be useful. Ventilator settings must be promptly wound down to reduce the risk of pneumothorax.
- a single dose may be sufficient if after dosing, the oxygen requirement falls  $< 30\%$ .

### Cost effectiveness

- studies on the cost-effectiveness of surfactant therapy show that in spite of the high cost of drug, its use reduces cost per survivor.

## NEWBORN AND ACID BASE BALANCE

The rate of metabolism in infants is twice as great in relation to body mass as in adults, which means twice as much acid is formed which leads to a tendency toward acidosis. Functional development of kidneys is not complete until the end of the first month and hence renal regulation of acid base may not be optimal.

**Table 1. Causes of acidosis and alkalosis**

### Causes of Acidosis

- Metabolic acidosis
  - renal failure
  - septicaemia
  - hypoxia
  - hypothermia
  - hypotension
  - cardiac failure
  - dehydration
  - hyperkalaemia
  - hyperglycaemia
  - anaemia
  - intraventricular haemorrhage
  - drugs (e.g. acetazolamide)
  - metabolic disorders (often associated with hypoglycaemia)
- Respiratory acidosis
  - asphyxia : damage to respiratory centre
  - obstruction to respiratory tract  
e.g. secretions, blocked endotracheal tube
  - respiratory conditions :
    - respiratory distress syndrome (RDS)
    - pneumonia
    - pulmonary oedema
    - apnoea

### Causes of Alkalosis

- Metabolic alkalosis
  - administration of sodium bicarbonate
  - pyloric stenosis
  - hypokalaemia
  - use of diuretics like thiazides and frusemide
- Respiratory alkalosis
  - asphyxia – overstimulation of respiratory centre
  - over ventilation while on mechanical ventilation

### Effects of acidosis and alkalosis in the body

- acidosis
  - depression of central nervous system (CNS)
  - disorientation and coma
  - increased depth and rate of respiration in metabolic acidosis and depressed respiration in respiratory acidosis
  - high  $\text{PaCO}_2$  in respiratory acidosis increases cerebral blood flow and risk of intraventricular haemorrhage
- alkalosis
  - over excitability of the CNS
  - decreased cerebral blood flow - causing cerebral ischaemia , convulsions

### Measurement of Acid Base Status

- done by analyzing following parameters in an arterial blood gas sample:

*Table 2. Normal values for arterial blood gas parameters*

pH	7.34-7.45
$\text{PaCO}_2$	5.3-6.0 kPa (40-45 mmHg)
$\text{PaO}_2$	8-10 kPa (60-75 mmHg)
$\text{HCO}_3$	20-25 mmol/L
Base Excess (BE)	$\pm 5$ mmol/L

## Interpretation of Blood Gases

- pH < 7.34 : *acidosis*
  - if PaCO<sub>2</sub> and HCO<sub>3</sub> are low and base deficit is high: *metabolic acidosis*
  - if PaCO<sub>2</sub> and HCO<sub>3</sub> are high and base excess is high: *respiratory acidosis*
  - if both PaCO<sub>2</sub> and base deficit are high: *mixed metabolic and respiratory acidosis*
- pH > 7.45 : *alkalosis*
  - if PaCO<sub>2</sub> is low : *respiratory alkalosis*
  - if HCO<sub>3</sub> and base excess are high : *metabolic alkalosis*

Acidosis and alkalosis may be partially or fully compensated by the opposite mechanism,

- low PaCO<sub>2</sub>: *hypocarbica*; high PaCO<sub>2</sub>: *hypercarbica*  
*Note: Permissive hypercapnia (PCO<sub>2</sub> 45-55mmHg) is one of ventilator techniques to reduce the risk of chronic lung disease of prematurity.*
- low PaO<sub>2</sub> : *hypoxaemia*; high PaO<sub>2</sub> : *hyperoxaemia*

## Management of Metabolic Acidosis and Alkalosis

- treat underlying cause when possible
- do not treat metabolic acidosis by hyperventilation (other than briefly while preparing to give NaHCO<sub>3</sub>). This may correct pH but has deleterious effects on cardiac output and pulmonary blood flow.
- volume expansion (i.e., bolus 10 mL/kg of 0.9% NaCl) should not be used to treat acidosis unless there are signs indicative of hypovolemia. A volume load is poorly tolerated in severe acidosis because of the decrease in myocardial contractility.
- NaHCO<sub>3</sub> treatment should be used only if significant metabolic acidosis is present (e.g., pH < 7.3 with base deficit > 7)
- dose of NaHCO<sub>3</sub> for treatment of metabolic acidosis can be calculated by:

*Dose in mmol of NaHCO<sub>3</sub> = Base deficit (mmol/L) x Body weight (kg) x 0.3*

- administer NaHCO<sub>3</sub> IV at a rate not exceeding 1 mEq/kg/min.
- the usual NaHCO<sub>3</sub> used in newborns is NaHCO<sub>3</sub> and the concentration is 0.5 mEq/mL, so it is hyperosmolar (900 mOsm/L)
- do not give NaHCO<sub>3</sub> unless infant is receiving assisted ventilation that is adequate. With inadequate ventilation, NaHCO<sub>3</sub> will worsen acidosis from liberation of CO<sub>2</sub>.

For chronic mild metabolic acidosis in small premature infants on hyperalimentation, maximize acetate and minimize chloride in the solution.

- metabolic alkalosis: usually iatrogenic in premature infants - diuretic use, gastrointestinal losses, and occurs in combination with contracted intravascular and ECF volumes

## Treatment of respiratory acidosis and alkalosis

- a steadily rising PaCO<sub>2</sub> at any stage in the disease is an indication that ventilatory assistance is likely to be needed
- a sudden rise may be an indication of acute changes in the infant's condition e.g. pneumothorax, collapsed lobes, misplaced endotracheal tube
- a swift rise in PaCO<sub>2</sub> often accompanied by hypoxia following weaning is often an indication that the infant is not ready for weaning
- a gradual rise in PaCO<sub>2</sub> at the end of the first week in a LBW infant on ventilator may be an indicator of the presence of a patent ductus arteriosus
- low PaCO<sub>2</sub> in a infant on a ventilator means overventilation, hence treatment is to wean down the ventilation. However in conditions like pulmonary hypertension or cerebral oedema a slightly low PaCO<sub>2</sub> may be necessary in the treatment.

## Interpretation of Blood Gases

- examples of Arterial Blood Gas (ABG) Interpretation

1. A 20 weeks' gestation and 1.1 kg BW infant has RDS. He is 20 hours old and is being nursed on nasal CPAP. His ABG shows:

pH	7.21
PaCO <sub>2</sub>	6.6 kPa
PaO <sub>2</sub>	7.5 kPa
HCO <sub>3</sub>	20 mmol/L
BE	-4 mmol/L

**Question (Q):** What does the ABG show?

**Answer (A):** Mild respiratory acidosis due to worsening Respiratory Distress Syndrome

**Q:** What is the next appropriate mode of therapy?

**A:** Mechanical ventilation

2. Below is the ABG of a 10 hour old 28 weeks' gestation infant :

pH	7.22
PaCO <sub>2</sub>	7.0 Pa
PaO <sub>2</sub>	10.0 kPa
HCO <sub>3</sub>	17 mmol/L
BE	-8 mmol/L

**Q:** What does the ABG show?

**A:** Mixed respiratory and metabolic acidosis

**Q:** Name a likely diagnosis

**A:** Respiratory distress syndrome

3. The following is the ABG of a 40 day old 26 weeks' gestation baby:

pH	7.38
PaCO <sub>2</sub>	8.0 Pa
PaO <sub>2</sub>	8.0 kPa
HCO <sub>3</sub>	35 mmol/L
BE	+10 mmol/L

**Q:** What does the ABG show?

**A:** Fully compensated respiratory acidosis by metabolic alkalosis

**Q:** What is a likely diagnosis?

**A:** Chronic lung disease

4. An infant of 30 weeks' gestation and BW 1.3 kg is being ventilated . ABG shows:

pH	7.35
PaCO <sub>2</sub>	3.0 Pa
PaO <sub>2</sub>	15.0 kPa
HCO <sub>3</sub>	12 mmol/L
BE	-12 mmol/L

**Q:** Interpret the ABG

**A:** Fully compensated metabolic acidosis by respiratory alkalosis and hyperoxaemia

**Q:** What is your next course of action?

**A:** Reduce FiO<sub>2</sub>, give a small dose of NaHCO<sub>3</sub>, treat any contributory cause of acidosis and wean down ventilation setting

5. A term infant is being ventilated for meconium aspiration. His ABG is as follows :

pH	7.16
PaCO <sub>2</sub>	10.0 Pa
PaO <sub>2</sub>	6.0 kPa
HCO <sub>3</sub>	16 mmol/L
BE	-10 mmol/L

**Q:** What is likely to have happened?

**A:** Pneumothorax

**Q:** What is your interpretation of the ABG

**A:** Mixed respiratory and metabolic acidosis with hypoxaemia

6. A 6 day old infant is being ventilated for a cyanotic heart disease. ABG shows :

pH	6.8
PaCO <sub>2</sub>	4.5 Pa
PaO <sub>2</sub>	3.0 kPa
HCO <sub>3</sub>	8 mmol/L
BE	-24 mmol/L

**Q:** What does the ABG show?

**A:** Severe metabolic acidosis with severe hypoxaemia

**Q:** What is your next course of action ?

**A:** Administer sodium bicarbonate, consider prostaglandin infusion, confirm heart defect and consider surgery

### Pearls

Conversion of kPa to mmHg is a factor of 7.5 kPa

## NEONATAL ENCEPHALOPATHY

### Definition

- Neonatal Encephalopathy (NE) is a clinical syndrome of disturbed neurological function, caused by failure to make a successful transition to extrauterine gas exchange
- manifests by a difficulty in initiating and maintaining spontaneous respiration, depression of muscle tone and reflexes, depressed consciousness and often seizures
- occurs in approximately 3.5 - 6/1000 live births; usually affects full term infants

*Note: The terminology NE is preferred to Hypoxic Ischemic Encephalopathy (HIE) as it is not always possible to document a significant hypoxic-ischemic insult and there are other possible aetiologies such as CNS malformation, infection, metabolic diseases, drug exposure, and neonatal stroke as possible causes of the encephalopathy.*

**Table 1. Diagnostic criteria for perinatal asphyxia as a cause of Neonatal Encephalopathy**

- profound metabolic or mixed acidemia (pH <7.00) in an umbilical cord arterial blood sample, if obtained
- persistence of an Apgar score of 0-3 for longer than 5 minutes
- neonatal neurologic sequelae (e.g. seizures, coma, hypotonia)
- multiple organ involvement (e.g. of the kidney, lungs, liver, heart, intestines)

*From the American Academy of Pediatrics (AAP) and  
The American College of Obstetrics and Gynecology (ACOG)*

### Hypoxic Ischaemic Encephalopathy (HIE)

- in HIE, the brain injury is caused by a deficit in oxygen supply.
- this can occur by
  - hypoxaemia - a decrease in oxygen saturation in the blood supply, or
  - ischaemia - a decrease in the amount of blood perfusing the brain
  - or both

**Table 2. Staging of neonatal hypoxic ischaemic encephalopathy (HIE)**

Variable	Stage I	Stage II	Stage III
Level of consciousness	alert	lethargy	coma
Muscle tone	normal or hypertonia	hypotonia	flaccidity
Tendon reflexes	increased	increased	depressed or absent
Myoclonus	present	present	absent
Seizures	absent	frequent	frequent
<b>Complex reflexes</b>			
Suck	active	weak	absent
Moro	exaggerated	incomplete	absent
Grasp	normal or exaggerated	exaggerated	absent
Doll's eyes	normal	overactive	reduced or absent
<b>Autonomic function</b>			
Pupils	dilated, reactive	constrictive, reactive	variable or fixed
Respirations	regular	variation in rate and depth, periodic	ataxic, apneic
Heart rate	normal or tachycardia	bradycardia	bradycardia
Electroencephalogram	normal	low voltage, paroxysmal	periodic
Outcome	no impairment	25% Impaired	92% Impaired

*Note: Only consistent in term infants or > 35 weeks gestation. Not consistent in premature infants  
adapted from Sarnat and Sarnat (1976)*



## Management

- adequate and effective resuscitation.
- monitor vital signs, as well as blood gases, urine output, blood sugar and electrolytes
- supportive measures:
  - nurse in thermoneutral environment. Avoid high environmental temperature as fever is associated with adverse outcome
  - maintain normoglycaemia, both hypo- and hyperglycemia can be harmful.
  - review infection risk and cover with antibiotics if necessary
  - maintain adequate hydration (do not dehydrate or over hydrate).
  - if metabolic acidosis is severe or persistent, slow infusion of sodium bicarbonate may be used with caution. (*see chapter on Acid Base Balance*)
- cerebral protection measures
  - maintain BP (Mean Arterial Pressure > 40 mmHg for term infants) with cautious use of inotrope infusion. Volume expansion can be used in case of hypovolaemia.
  - treat seizures promptly. (*see chapter on Neonatal Seizures*)
  - treat/prevent Intracranial Hypertension
    - ventilate to maintain PaCO<sub>2</sub> at 35-45 mmHg. Lowering PaCO<sub>2</sub> less than this may cause cerebral ischaemia. Maintain for 24 - 48 hours only.
    - IV mannitol (0.25g/kg over 20 minutes) may be used where there is raised intracranial pressure. It is contraindicated in oliguria. Maximum 2-3 doses q6 hourly
    - steroids are of no benefit
- treat complications that arise:

Table 3. Complications and management strategies

Organ system	Complication	Treatment
Central nervous system	cerebral oedema, periventricular, subdural / subarachnoid haemorrhage, periventricular leucomalacia, bleeding into choroid plexus, cerebellum, thalamus	treat for cerebral oedema, as described above
Renal	acute tubular necrosis, acute urinary retention	if oliguria (urine output < 1ml/kg/hr) - treat prerenal failure with adequate volume if in established renal failure - fluid restrict; maintain normal electrolyte levels - peritoneal dialysis may be needed
Cardiac	hypoxic damage to myocardium with cardiogenic shock and failure	use of inotropes and careful fluid balance
Lungs	meconium aspiration, Persistent Pulmonary Hypertension (PPHN)	See relevant chapter on PPHN
Gastrointestinal	stress ulcers, feed intolerance, necrotizing enterocolitis (NEC)	enteral feeding preferable to parenteral; avoid rapid increase in volume of feeds to decrease risk of NEC
Others	syndrome of inappropriate anti-diuretic hormone secretion (SIADH), hypomagnesaemia, hypocalcaemia, hypoglycaemia and bleeding disorder	- if SIADH occurs restrict fluids - if DIVC occurs correct haemostasis with FFP, cryoprecipitate, platelet or packed cell as indicated

## Investigations

- acute investigations have been described above.
- other investigations as in Table 4.
- a normal cranial imaging study *does not* rule out NE.

Table 4. Investigations

Investigation	Indication
<i>Cranial Ultrasound</i>	To exclude haemorrhage and other intracerebral abnormalities. Doppler studies (done after 24 hours of life) suggest that a resistive index of less than 0.5-0.6 is consistent with the diagnosis of HIE.
<i>Brain CT scan</i>	To exclude haemorrhage, cerebral oedema and other intracerebral abnormalities. May assist with prognosis. Extensive areas of low attenuation with apparent brightness of basal ganglia are associated with very poor prognosis (done after 1st week of life).
<i>Brain MRI</i>	MRI may provide prognostic information. Abnormalities of the thalami and basal ganglia are associated with an increased risk of subsequent abnormal developmental outcome. Superior to CT scans.
<i>Electroencephalogram (EEG)</i>	Severe abnormalities include burst suppression, low voltage or isoelectric EEG. Moderate abnormalities include slow activity The overall risks for death or disability were 95% for severely abnormal EEG, 64% for moderately abnormal EEG and 3 % for normal or mildly abnormal EEG.

## Follow up

- all infants with NE should be followed up for to look for development and neurological problems. Full term infants who suffer from Grade 2 or 3 encephalopathy are known to have a high incidence of neurologic damage
- manage epilepsy (see chapter on Epilepsy), developmental delay as appropriate
- remember to evaluate hearing and vision on follow-up and manage appropriately

## NEONATAL SEIZURES

Seizures are the most frequent manifestation of neonatal neurological diseases. It is important to recognize seizures, determine their aetiology and treat them because:

1. the seizures may be related to significant diseases that require specific treatment
2. the seizures may interfere with supportive measures e.g. feeding and assisted respiration for associated disorders
3. the seizures per se may lead to brain injury.

Table 1. Classification of neonatal seizures

Clinical seizure	EEG seizures	Manifestation
<b>Subtle</b>	common	<i>ocular phenomena</i> - tonic horizontal deviation of eyes common in term infants - sustained eye opening with fixation common in preterm infants - blinking  <i>oral-buccal-lingual movements</i> - chewing common in preterm infants - lip smacking, cry-grimace  <i>limb movements</i> - pedaling, stepping, rotary arm movements  <i>apnoeic spells</i> common in term infants
<b>Clonic</b>		
Focal	common	well localized clonic jerking; infant usually not unconscious
Multifocal	common	multifocal clonic movements; simultaneous or in sequence or non-ordered ( non-Jacksonian) migration
<b>Tonic</b>		
Focal	common	sustained posturing of a limb, asymmetrical posturing of trunk or neck
Generalized	uncommon	tonic extension of upper and lower limbs (mimic decerebrate posturing) tonic flexion of upper limbs and extension of lower limbs( mimic decorticate posturing) those with EEG correlates; autonomic phenomena e.g. increased blood pressure are prominent features.
<b>Myoclonic</b>	common	well localized, single or multiple, migrating jerks usually of limbs
Focal, Multifocal		
Generalized		single or several bilateral synchronous jerks or flexion movement occurring more in upper than lower limbs.

### Aetiology

- *Hypoxic ischaemic encephalopathy*
  - usually secondary to perinatal asphyxia.
  - most common cause of neonatal seizures (preterm and term)
  - seizures occur in the first day of life (DOL)
  - presents with subtle seizures; multifocal clonic or focal clonic seizures
  - if focal clonic seizures may indicate associated focal cerebral infarction

Table 2. Major aetiology in relation to time of seizure onset and relative frequency

Etiology	Time of onset <sup>1</sup>		Relative frequency <sup>2</sup>	
	0-3 days	> 3days	Premature	Full term
Hypoxic –ischemic encephalopathy	+		+++	+++
Intracranial hemorrhage	+	+	++	+
Intracranial infections	+	+	++	++
Developmental defects	+	+	++	++
Hypoglycaemia	+		+	+
Hypocalcaemia	+	+	+	+
Other metabolic disturbances & IEM	+			+
Epileptic Syndromes	+	+		+

footnote: 1. postnatal age

2. relative frequency of seizures among all etiologies:

+++ most common, ++ less common, +least common

Abbreviations. IEM, inborn errors of metabolism

- **Intracranial hemorrhage (ICH)**

- principally germinal matrix-intraventricular (GM-IVH), often with periventricular haemorrhagic (P VH) infarction in the premature infant
- in term infants ICH are principally (may occur with HIE) and subdural(associated with a trauma , presenting with focal seizures in the first 2 DOL)

- **Intracranial Infection**

- common organisms are group B streptococci, E. coli., toxoplasmosis, herpes simplex, coxsackie B, rubella and cytomegalovirus

- **Malformations of cortical development**

- neuronal migration disorder resulting in cerebral cortical dysgenesis e.g. lissencephaly, pachygyria and polymicrogyria

- **Metabolic disorder**

- hypoglycemia common in SGA infants and infants of diabetic mothers (IDM) (see protocol on Neonatal Hypoglycemia)
- hypocalcaemia has 2 major peaks of incidences:
  - first 2 to 3 DOL, in low birth weight infants, IDM and history of perinatal asphyxia.
  - later-onset of hypocalcaemia associated with endocrinopathy (maternal hypoparathyroidism, neonatal hypoparathyroidism) and heart disease (with or without Di George Syndrome), rarely with nutritional type (cow's milk, high phosphorus synthetic milk). Hypomagnesemia is a frequent accompaniment.
- inborn errors of metabolism: represent <1% of all neonates who have seizures but among neonates with intractable neonatal seizure, ~30% are due to IEM

Table 3. Inborn errors of metabolism presenting with neonatal seizures

Treatable	Non-treatable
Pyridoxine-dependent epilepsy	Nonketotic hyperglycinemia
Pyridoxal phosphate responsive epilepsy	(poor outcome though seizure may be better controlled with dextromethorphan)
Folinic acid-responsive seizures	Sulphite oxidase deficiency/
Biotinidase deficiency	Molybdenum cofactor deficiency
Glucose transporter 1 deficiency	Mitochondrial disorders
Serine deficiency syndromes	Peroxisomal disorder
Creatine deficiency syndromes	Neuronal ceroid lipofuscinoses
Phenylketonuria	Adenylosuccinate lyase deficiency
	(purine disorder)

## Seizures versus Jitteriness and Other Non-epileptic Movements

Some movements e.g. jitteriness and other normal movement during sleep (Myoclonic jerks or generalized myoclonic jerks as infant wakes from sleep) or when awake/ drowsy (roving sometimes dysconjugate eye movements, sucking not accompanied by ocular fixation or deviation) in newborn may be mistaken for seizures.

Table 3. Differentiating seizures form non-epileptic events, e.g. jitteriness

Clinical Features	Jitteriness	Seizure
Abnormality of gaze or eye movement	0	+
Movements exquisitely stimulus sensitive	+	0
Predominant movement	tremors <sup>1</sup>	clonic, jerking <sup>2</sup>
Movements cease with passive flexion of affected limb	+	0
Autonomic changes ( tachycardia, ↑ BP, apnoea, salivation, cutaneous vasomotor phenomena)	0	+

footnote: 1. alternating movements are rhythmical and of equal rate and amplitude

2. clonic, jerking – movements with a fast and slow component

## Management

- consensus is lacking on necessity for treatment of minimal or absent clinical manifestations.
- treatment with anticonvulsant is to prevent potential adverse effects on ventilatory function, circulation and cerebral metabolism ( threat of brain injury)
- controversy regarding identification of adequacy of treatment, elimination of clinical seizures or electrophysiology seizures. Generally majority attempt to eliminate all or nearly all clinical seizures.

## Duration of Anticonvulsant Therapy - Guidelines

Duration of therapy depends on the probability of recurrence of seizures if the drugs are discontinued and the risk of subsequent epilepsy. This can be determined by considering the neonatal neurological examination, cause of the seizure and the EEG.

### Neonatal Period

- if neonatal neurological examination becomes normal, discontinue therapy
- if neonatal neurological examination is persistently abnormal,
  - consider etiology and obtain electroencephalogram(EEG)
  - in most cases – continue phenobarbitone, discontinue phenytoin
  - and reevaluate in a month

### One Month after Discharge

- if neurological examination has become normal, discontinue phenobarbitone over 2 weeks
- if neurological examination is persistently abnormal, obtain EEG
- if no seizure activity or not overtly paroxysmal on EEG, discontinue phenobarbitone over 2 weeks
- if seizure activity is overtly paroxysmal continue phenobarbitone until 3 months of age and reassess in the same manner

Figure 1. Approach to neonatal seizures

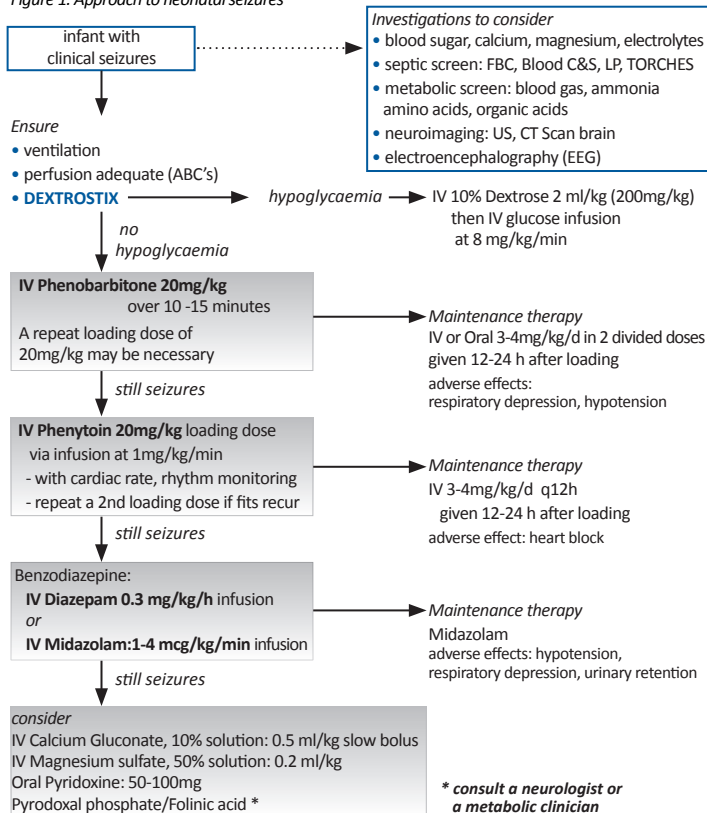


Table 4. Prognosis according to aetiology of neonatal seizures

Neurological Disorder	Normal Development (%) <sup>1</sup>
Hypoxic Ischemic Encephalopathy	50
Severe Intraventricular Haemorrhage with PVH infarction	10
Hypocalcaemia	
Early onset (depends on the prognosis of complicating illness, if no neurological illness present prognosis approaches later onset)	50
Later onset (nutritional type)	100
Hypoglycemia	50
Bacterial Meningitis	50
Developmental defect	0

footnote. 1. Prognosis is based on those cases with the stated neurological disease when seizures are a manifestation. This will differ from overall prognosis of the disease.

## NEONATAL HYPOGLYCAEMIA

### Definition

Blood glucose level < 2.6 mmol/l in a term or preterm infant

### Clinical Features

Symptoms of hypoglycaemia include:

- jitteriness and irritability
- apnoea and cyanosis
- hypotonia and poor feeding
- convulsions

Hypoglycaemia *may be asymptomatic* therefore monitoring is important for high risk infants (see Table 1).

### Management

#### Prevention and Early Detection

- identify babies at risk
- for *well* babies who are at risk:
  - immediate feeding: first feed can be given in Labour Room
  - supplement feeding until breastfeeding established
- for *unwell* babies
  - set up dextrose 10% drip
- regular glucometer monitoring
  - on admission and at 1, 2 and 4 hours later
  - 3 to 6 hourly pre-feeding samples once blood glucose stable for 24 - 48 hours

#### Hypoglycaemia

- repeat the glucometer test and send RBS stat.
- examine and document any symptoms
- note when the last feeding was given
- if on IV drip, check if the IV infusion of glucose is adequate and running well
- if blood sugar level (BSL) <1.5mmol/l or if the baby is symptomatic
  - intravenous bolus Dextrose 10% at 2-3 ml/kg
  - followed by dextrose 10% drip at 60-90ml/kg/day (for day 1 of life) to maintain normal blood glucose
  - if baby is already on dextrose 10% drip, consider increasing the rate or the glucose concentration (usually require 6-8 mg/kg/min of glucose delivery)
- if blood sugar level (BSL) 1.5 – 2.5 mmol/l
  - give supplementary feed (EBM or formula) as soon as possible.
  - if BSL remains < 2.6 mmol/l and baby refuses to feed, set up dextrose 10% drip.
  - if baby is on dextrose 10% drip, consider stepwise incrementing of the glucose infusion rate by 2 mg/kg/min until blood sugar is > 2.6 mmol/L
- glucose monitoring
  - if capillary blood sugar (dextrostix) is < 2.6 mmol/l, check glucometer half hourly
  - if capillary blood sugar > 2.6 mmol/l for 2 readings:
    - monitor hourly x 2, then 2 hourly X 2, then 4-6 hourly if blood sugar remains normal
- start feeding when capillary blood sugar remains stable and increase as tolerated. Reduce the IV infusion rate one hour after feeding increment.

**Table 1. High risk infants**

infants of diabetic mothers  
small for gestational age  
preterm infants  
macrosomic infants, weight > 4.0kg  
sick babies including those with:

- perinatal Asphyxia
- Rhesus disease
- polycythaemia
- sepsis
- hypothermia

### Persistent Hypoglycaemia

If hypoglycaemia persists despite intravenous dextrose, consult MO/ specialist and for district hospitals, consider early referral

- re-evaluate the infant
- confirm hypoglycaemia with RBS but treat as such while waiting for RBS result
- increase volume by 30ml/kg/day and/or increase the dextrose concentration to 12.5% or 15% . Concentrations of > 12.5% must be infused through a central line
- if hypoglycaemia still persists despite glucose delivery >10mg/kg/min, consider glucagon IV 30 – 100 mcg/kg over 20 mins. or IM 100 mcg/kg (maximum 3 doses ), infusion (1mg or 5-10 mcg/kg/hr) in particularly for infants of diabetic mothers. Glucagon should not exceed 0.5 mg/dose and not to be administered at concentrations >1 mg/mL . Glucagon is only useful where there is sufficient liver stores, thus should not be used for SGA babies or in adrenal insufficiency
- in others especially SGA, give intravenous hydrocortisone 2.5 -5 mg/kg /dose bd  
There may be hyperinsulinaemia in growth retarded babies as well.

### Recurrent or resistant hypoglycaemia

This condition should be considered when there is a failure to maintain normal blood sugar levels despite a glucose infusion of 12 mg/kg/min or when stabilization is not achieved by 7 days of life. High levels of glucose infusion may be needed in the infants to achieve euglycemia.

*Refer chapter on Recurrent Hypoglycaemia (Metabolic section)*

Table 2. Prescription to make up a 50mL solution of various dextrose infusions

Infusion concentration	Volume of 10% Dextrose	Volume of 50% Dextrose
12.5 %	46.5 ml	3.5 ml
15. %	44.0 ml	6.0 ml

### Pearls and pitfalls in management

- depending on the severity of hypoglycaemia, some oral feeds should be maintained as milk has more calories than 10% dextrose. Breastfeeding should be encouraged as it is more ketogenic.
- the recommended practice is to feed the baby with as much milk as is tolerated and to infuse glucose at a rate sufficient to prevent hypoglycaemia. The glucose infusion is then reduced slowly while milk feeds are maintained or increased.
- avoid giving multiple boluses as they can cause a rapid rise in blood glucose concentration which may be harmful to neurological function and may be followed by rebound hypoglycaemia
- any bolus given must be followed by a continuous infusion of glucose, initially providing 4-8 mg/kg/ min. There is no place for treatment with intermittent glucose boluses alone.
- ensure volume of intravenous fluid is appropriate for patient, taking into consideration concomitant problems like cardiac failure, cerebral oedema and renal failure. If unable to increase volume further, concentration of dextrose can be increased.

Glucose requirement = (mg/kg/min)	=	$\frac{\% \text{ of dextrose} \times \text{rate (ml/hr)}}{\text{weight (kg)} \times 6}$
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## NEONATAL JAUNDICE

### Introduction

Jaundice can be detected clinically when the level of bilirubin in the serum rises above 85  $\mu\text{mol/l}$  (5mg/dl)

### Causes of neonatal jaundice

- haemolysis due to ABO or Rh isoimmunisation, G6PD deficiency, microspheroctosis, drugs
- physiological jaundice
- cephalhaematoma, subaponeurotic haemorrhage
- polycythaemia
- sepsis e.g. septicaemia, meningitis, urinary tract infection and intra-uterine infection
- breastfeeding and breastmilk jaundice
- gastrointestinal tract obstruction: increase in enterohepatic circulation

**Table 1. Risk factors for bilirubin neurotoxicity**

preterm infants
small for gestational age
sepsis
acidosis
asphyxia
hypoalbuminaemia
jaundice < 24 hours of age

### Approach to an infant with jaundice

#### History

- age of onset
- previous infants with NNJ, kernicterus, neonatal death, G6PD deficiency
- mother's blood group (from antenatal history)
- gestation: the incidence of hyperbilirubinaemia increases with prematurity
- presence of abnormal symptoms such as apnoea, difficulty in feeding, feed intolerance and temperature instability

#### Physical examination

- general condition, gestation and weight, signs of sepsis, hydration status
- signs of kernicterus e.g. lethargy, hypotonia, seizure, opisthotonus, high pitch cry
- pallor, plethora, cephalhaematoma, subaponeurotic haemorrhage,
- signs of intrauterine infection e.g. petechiae, hepatosplenomegaly
- cephalo-caudal progression of severity of jaundice (see Table 2).

*Table 2. Clinical assessment of neonatal jaundice (Kramer's rule)*

Zone	Jaundice (detected by blanching the skin with finger pressure)	Estimated serum bilirubin ( $\mu\text{mol/L}$ )
1	head and neck	100
2	over upper trunk above umbilicus	150
3	lower trunk and thighs	200
4	over arms, legs and below knee	250
5	hands, feet	>250

*Note: This may be difficult in dark skinned infants*

### Management

Indications for referral to hospital:

- jaundice within 24 hours of life.
- jaundice below umbilicus (corresponds to serum bilirubin 200-250  $\mu\text{mol/L}$ )
- jaundice extending to sole of feet: **urgent referral, may need exchange transfusion**
- family history of significant haemolytic disease or kernicterus
- any unwell infant with jaundice
- prolonged jaundice more than 14 days (see chapter on Prolonged jaundice)

## Investigations

- total serum bilirubin
- G6PD status
- others as indicated:
  - infant's blood group, maternal blood group, direct Coomb's test (indicated in Day 1 jaundice and severe jaundice)
  - full blood count, reticulocyte count, peripheral blood film
  - blood culture, urine microscopy and culture (if infection is suspected)

## Treatment

### Phototherapy

- phototherapy lights should have a minimum irradiance of  $12 \mu\text{W}/\text{cm}^2/\text{nm}$ . Measure intensity of phototherapy light periodically using irradiance meters
- intensive phototherapy is above irradiance of  $30 \mu\text{W}/\text{cm}^2/\text{nm}$ .
- position light source 35-50 cm from top surface of the infant (when conventional fluorescent photolights are used.)
- expose infant appropriately
- cover infant's eyes
- turn infant every 2 hours
- monitor serum bilirubin levels as indicated
- monitor infant's temperature 4 hourly to avoid chilling or overheating
- ensure adequate hydration
- allow parental-infant interaction
- discontinue phototherapy when bilirubin is  $30 \mu\text{mol}/\text{L}$  below phototherapy level.
- in infants without haemolytic disease, the average bilirubin rebound after phototherapy is less than  $1 \text{ mg}/\text{dL}$  ( $17 \mu\text{mol}/\text{L}$ ). Discharge from hospital need not be delayed in order to observe the infant for rebound, and in most cases, no further measurement of bilirubin is necessary.
- turn off photolights during feeding and blood taking

Once the baby is on phototherapy, visual observation as a means of monitoring is unreliable. Serum bilirubin levels must guide the management.

Table 3. Guidelines for phototherapy and exchange transfusion (ET) in hospitalized infants of  $\geq 35$  weeks' gestation (derived from fig 1)

Hours of life	Total Serum Bilirubin levels mg/dL ( $\mu\text{mol}/\text{L}$ )					
	low risk ( $\geq 38$ wk and well)		medium risk $\geq 38$ wk + risk factors <b>or</b> 35-37 6/7 wk and well		high risk (35-37 6/7 wk + risk factors)	
	Intensive phototherapy	ET	Intensive phototherapy	ET	Intensive phototherapy	ET
< 24*						
24	12 (200)	19 (325)	10 (170)	17 (290)	8 (135)	15 (255)
48	15 (255)	22 (375)	13 (220)	19 (325)	11 (185)	17 (290)
72	18 (305)	24 (410)	15 (255)	21 (360)	13 (220)	18.5 (315)
96	20 (340)	25 (425)	17 (290)	22.5 (380)	14 (240)	19 (325)
> 96	21 (360)	25 (425)	18 (305)	22.5 (380)	15 (255)	19 (325)

1. start conventional phototherapy at TSB  $3 \text{ mg}/\text{dL}$  ( $50 \mu\text{mol}/\text{L}$ ) below the levels for intensive phototherapy.

2. Risk factors – isoimmune hemolytic disease; G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis or albumin  $< 3.0 \text{ g}/\text{dL}$

\*Infants jaundiced at < 24 hours of life are not considered healthy and require further evaluation

**Intensive phototherapy indications:**

- total bilirubin > 300  $\mu\text{mol/L}$
- early onset jaundice (first 48 hours)
- rapidly rising jaundice (more than 8.5  $\mu\text{mol/L/hr}$ )

**Additional notes:**

- immediate exchange transfusion is recommended if infants show signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonus, fever, high pitch cry) or if TSB is  $\geq 5 \text{ mg/dL}$  (85  $\mu\text{mol/L}$ ) above the exchange levels stated above.
- use total bilirubin level. Do not subtract direct reacting or conjugated bilirubin.
- during birth hospitalisation, ET is recommended if the TSB rises to these levels despite intensive phototherapy
- for readmitted infants, if the TSB level is above the ET level repeat the TSB measurement every 2 to 3 hours and consider ET if the TSB levels remain above the ET level for 6 hours under intensive phototherapy
- infants who are of lower gestation will require phototherapy and ET at lower levels, (please check with your specialist)

**Measures to prevent severe neonatal jaundice**

- inadequate breast milk flow in the first week may aggravate jaundice. Supportive measures should be there to promote successful breastfeeding. Supplements may be needed temporarily to ensure adequate hydration.
- interrupting breastfeeding in healthy term newborns is discouraged; frequent breastfeeding (8-10 times every 24 hours) should be continued. Supplementation with milk formula with or without phototherapy can be considered. Supplementing with water or dextrose water does not lower bilirubin level in healthy, breast-feeding infants.
- determine G6PD status before discharge. If deficient, baby should be observed for 5 days
- infants of mothers with blood group "O" and with a sibling who had severe neonatal jaundice should be observed for at least the first 24 hours of life.
- arrange follow-up for all neonates discharged < 48 hours after birth with a health care professional in an ambulatory setting, or at home within 2-3 days of discharge

**Table 4. Agents to be avoided in patients with G6PD Deficiency**

<b>Foods and Herbs to be avoided</b>	<b>Drugs that can be safely given in therapeutic doses</b>	
Fava Beans (Kacang Parang)	Paracetamol	Trimethoprim
Documented Chinese herbs/medicine	Ascorbic Acid	Tripeleennamine
<i>Chuen Lin</i>	Aspirin	Vitamin K
<i>San Chi</i>	Chloramphenicol	Mefloquine
<i>13 herbs</i>	Chloroquine	<b>Drugs to be avoided or contraindicated</b>
<i>12 herbs</i>	Colchicine	
Other traditional herbs/medications are also not to be taken unless with medical advice	Diphenhydramine	
	Isoniazid	
	Phenacetin	
	Phenylbutazone	
	Phenytoin	
	Probenecid	
	Procainamide	
	Pyrimethamine	
<b>Other chemicals to be avoided</b>	Quinidine	
Naphthalene (moth balls)	Streptomycin	
Mosquito coils and insect repellants which contains pyrethium	Sulfisoxazole	
		Bactrim

Fig 1: Guidelines for intensive phototherapy in infants  $\geq 35$  wks gestation

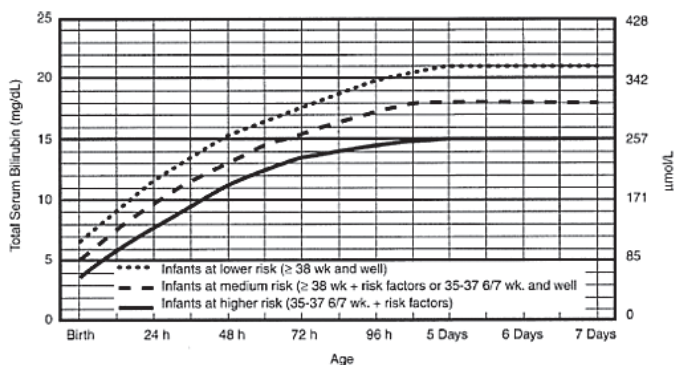
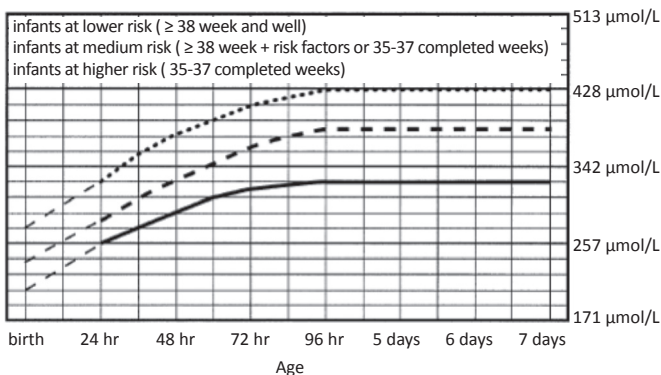


Fig 2: Guidelines for exchange transfusion in infants  $\geq 35$  wks gestation



1. The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy
2. Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, ophisthotonus, fever, high pitched cry) or if total serum bilirubin is  $\geq 5$  mg/dL (85  $\mu\text{mol/L}$ ) above these lines

## EXCHANGE TRANSFUSION

### Introduction

- Exchange transfusion (ET) is indicated for severe hyperbilirubinaemia.
- neonates with significant jaundice should be monitored closely and treated with intensive phototherapy

### Indications

- Blood exchange transfusion to lower the serum bilirubin level and reduce the risk of kernicterus
- Partial exchange transfusion
  - to correct polycythaemia with hyperviscosity
  - to correct severe anaemia without hypovolaemia.

### Preparation of infant

- informed consent from parents
- keep resuscitation equipment on standby
- maintain stable temperature, pulse and respiration.
- place a peripheral line for maintenance intravenous fluid.
- proper gentle restraint.
- continue feeding the child and *omit only the last feed* before the procedure. If < 4 hrs from last feed, empty gastric contents using a nasogastric tube aspiration prior to ET

### Grouping of Blood to be used

Rh isoimmunisation:	ABO compatible, Rh negative blood
Other conditions:	cross-match with baby and mother's blood
Emergency (rarely):	'O' Rh negative blood

### Procedure (Exchange Transfusion)

- volume to be exchanged is twice blood volume (2x80mls/kg)
- use fresh whole blood preferably less than 5 days old
- place a cardiac monitor and record baseline observations on the neonatal exchange blood transfusion sheet. The following observations are recorded every 15 minutes: heart rate, respiration, oxygen saturation.
- strict aseptic technique with gown and mask
- cannulate umbilical vein to depth *not* > 5-7cm (for push-pull technique through an umbilical venous catheter). (*see chapter on Procedures for umbilical vein cannulation*)
- use 5-8 mls/kg aliquots of blood for removal and replacement (< 10% of blood volume) Maximum volume per cycle - 20 mls for term infants
- the assisting nurse keeps a record of the amount of blood given or withdrawn, and medication given.

### Isovolumetric or continuous technique

- indication: when umbilical vein cannulation is not possible e.g. umbilical sepsis, failed cannulation
- blood is replaced as a continuous infusion into a large peripheral vein while removing small amount blood from an arterial catheter at regular intervals.
  - in smaller infants, e.g. 1.5 kg baby, total volume for exchange is 240 mls. Delivering 120mls / hour, allowing 10 ml of blood to be removed every 5 mins for 2 hours.

## Points to note

- blood volume to exchange = 160mls/kg body weight {2 x blood volume (80 mL/kg)}
- pre-warm blood. Do not overheat blood.
- rate of exchange is 4-5 minutes per cycle:  
*1 min 'out', 1 min 'in', 1-2 min 'pause'; excludes time to discard blood and draw from blood bag*
- total exchange time should be about 90 - 120 mins.
- start exchange with removal of blood, so that there is always a deficit to avoid cardiac overload
- dilute and give:
  - 1 ml of 4.2% sodium bicarbonate for every 100mls of blood exchanged
  - 1 ml of 10% calcium gluconate for every 160mls of blood exchanged
  - *never give the two (NaHCO<sub>3</sub> & Ca gluconate) solutions together. Use a peripheral vein and not the umbilical vein (UVC).*
- shake blood bag gently and frequently to prevent settling of red blood cells
- remove UVC after procedure unless a second ET is anticipated and the UVC insertion was difficult
- continue intensive phototherapy after the ET
- repeat ET may be required in 6 hours for infants with high rebound of serum bilirubin
- feed after 4-6 hours if patient is well and a repeat ET not required.
- if child is anaemic (pre-exchange Hb <12 g/dL) give an extra aliquot volume of blood (10 mls/kg) at the end of transfusion at a rate of 5 mls/kg/hr after the ET

**Table 1. Complications of ET**

### *Catheter related*

- infection
- haemorrhage
- necrotizing enterocolitis
- air embolism
- portal and splenic vein thrombosis (late sequelae)

### *Haemodynamic problems*

- overload cardiac failure
- hypovolaemic shock
- arrhythmia (catheter tip near sinus node in right atrium)
- bradycardia with calcium bolus

### *Electrolyte imbalance*

- hyperkalemia
- hypocalcemia
- hyper- and hypo-glycaemia
- metabolic acidosis, alkalosis (late breakdown of citrate)

## Investigations

### *Pre-exchange (1st volume of blood removed)*

- serum bilirubin
- full blood count
- blood cultures as indicated (through peripheral venous blood)
- others as indicated if patient is unwell

### *4 to 6 hour post-exchange*

- serum bilirubin

### *Post-exchange*

(always discard the blood remaining in the UVC first before sampling)

- serum bilirubin
- full blood count
- dextrostix
- serum electrolytes
- serum calcium
- others as indicated

### **Partial Exchange Transfusion**

- to correct *hyperviscosity due to polycythaemia*

(central haematocrit or packed cell volume, PCV of > 65%)

$$\text{Volume exchanged (in mL)} = \frac{\text{Blood volume} \times (\text{PCV initial} - \text{PCV desired})}{\text{PCV initial}}$$

- to correct *anaemia without hypovolaemia*

$$\text{Volume exchanged (in mL)} = \frac{\text{Blood volume (mL)} \times (\text{Hb desired} - \text{Hb initial})}{(\text{Hb donor} - \text{Hb initial})}$$

*Where blood volume for term infant is 80 ml/kg body weight*

## Follow-up

- long term follow-up to monitor hearing and neurodevelopmental assessment

## PROLONGED JAUNDICE IN THE NEWBORN

### Definition

Visible jaundice (or serum bilirubin, SB >85  $\mu\text{mol/L}$ ) that persists beyond 14 days of life in a term infant or 21 days in a preterm infant.

**Table 1. Causes of prolonged jaundice**

Unconjugated Hyperbilirubinaemia	Conjugated Hyperbilirubinaemia
septicaemia or urinary tract infection (UTI)	biliary tree abnormalities
breast milk Jaundice	biliary atresia - extra, intra-hepatic
hypothyroidism	choledochal cyst
haemolysis	paucity of bile ducts
G6PD deficiency	- Alagille syndrome, non-syndromic
congenital spherocytosis	idiopathic neonatal hepatitis syndrome
galactosaemia	septicaemia or UTI
Gilbert syndrome	congenital infection (TORCHES)
	metabolic disorders
	citrin deficiency
	galactosaemia
	progressive familial intrahepatic cholestasis (PFIC)
	alpha-1 antitrypsin deficiency
	Total Parenteral Nutrition

*If unconjugated hyperbilirubinaemia:*

- admit if infant is unwell. Otherwise follow-up until jaundice resolves.
- important investigations are; Thyroid Function Tests, Urine FEME, C&S and reducing sugar, and FBC, reticulocyte count & Peripheral Blood Film.
- exclude UTI and hypothyroidism.
- congenital hypothyroidism is a neonatal emergency. Check Screening TSH result if done at birth. (*see chapter on Congenital Hypothyroidism*)
- where indicated, investigate for galactosaemia
- breast milk Jaundice is a diagnosis of exclusion. Child must be well, have appropriate weight gain, feeds well with yellow stools. Management is to continue breastfeeding.

*If conjugated hyperbilirubinaemia:*

(conjugated bilirubin > 2mg/dL or > 15% of total bilirubin)

- investigate for **biliary atresia** and neonatal hepatitis syndrome.

- admit and observe colour of stool for 3 consecutive days.
- further investigations: LFT, Hep B and C status, TORCHES, VDRL tests, alpha-1 antitrypsin and a metabolic (IEM) screen.  
( $\gamma\text{GT}$ , GALT assay, Tandem Mass Spectrometry /IEM screen,  $\pm$  urine organic acids & plasma amino acid [refer chapter on IEM] )
- consider Alagille syndrome
- **suspect biliary atresia if the stool is pale over 3 consecutive days.**

Refer paediatric surgery and plan for:

- *Ultrasound of the hepatobiliary system*
  - preferably done after 4 hours of fasting
  - dilated intrahepatic bile ducts and an absent gall bladder
  - raises the suspicion of extra hepatic biliary atresia

- HIDA Scan
  - increased accuracy of scan if oral phenobarbitone 5mg/kg given for 5 days, prior to the scan.
  - low uptake with normal excretion: neonatal hepatitis syndrome.
  - normal uptake with absent excretion: extrahepatic biliary atresia
- liver biopsy as indicated
  - biliary atresia can be confirmed in 85% by biopsy
  - ensure PT and aPTT normal before biopsy. Give Vitamin K 1 mg IV, if needed
  - platelet count  $\geq 40,000 /\text{mm}^3$  before biopsy
- operative cholangiogram followed by definitive surgery if necessary.
  - this is now the investigation of choice in most centres.

### Biliary atresia

- biliary atresia can be treated successfully by the Kasai procedure.
- this procedure must be performed within the first 2 months of life.
- with early diagnosis and biliary drainage through a Kasai procedure before 60 days of age, successful long-term biliary drainage is achieved in >80% of children. In later surgery good bile flow is achieved only in 20-30%.
- liver transplantation is indicated later if there is failure to achieve or maintain bile drainage

### Neonatal Hepatitis Syndrome

- follow up with LFT fortnightly. Watch out for liver failure and bleeding tendency (vitamin K deficiency).
- repeat Hepatitis B & C screening at 6 weeks
- most infants with idiopathic neonatal hepatitis make a complete recovery



## APNOEA IN THE NEWBORN

### Definition

Pause in breathing lasting >15 sec (term) or >20sec (preterm) during which the infant may develop cyanosis ( $\text{SpO}_2 < 80\%$ ) and bradycardia (heart rate < 100 per min). In very immature infants, shorter duration of apnoea may produce bradycardia and cyanosis.

Types:

- **Central** : absence of respiratory effort with no gas flow
- **Obstructive**: continued ineffective respiratory effort with no gas flow
- **Mixed** central and obstructive

**Periodic breathing**: regular sequence of respiratory pauses of 10-20 sec interspersed with periods of hyperventilation (4-15 sec) and occurring at least 3x/ minute, not associated with cyanosis or bradycardia.

**Table 1. Aetiology**

Symptomatic of underlying problems, commoner ones of which are:

Respiratory conditions	Metabolic disorder
RDS, pulmonary haemorrhage, pneumothorax, upper airway obstruction, sedative drugs	hypoglycaemia, hyponatraemia, hypocalcaemia
Sepsis	Cardiac failure, congenital heart disease,
Hypoxaemia	Anaemia
Hypothermia	Aspiration, gastro-oesophageal reflux
Central nervous system abnormality	Necrotizing enterocolitis, abdomen distension
intraventricular haemorrhage, asphyxia,	Vagal reflex
increased intracranial pressure, seizures	nasogastric tube insertion, suctioning, feeding

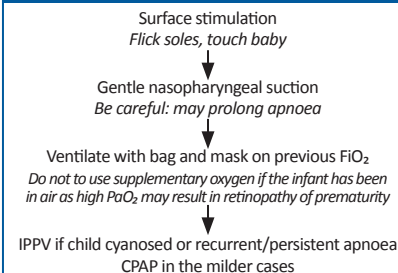
### Recurrent apnoea of prematurity

Occurs > 3 days of life with no underlying pathological condition. May occur earlier in ELBW infants. Most disappear by 34- 36 weeks, but may persist > 40 weeks 'corrected' age.

### Management

- immediate resuscitation (Table 2)
- review possible causes (Table 1) and institute specific therapy i.e. septic workup if suspected sepsis and commence antibiotics Remember to check blood glucose via glucometer.
- prevent recurrence:
  - maintain a thermoneutral environment
  - nursing prone may reduce episodes of apnoea.
  - titrate the  $\text{FiO}_2$  to keep the  $\text{PaO}_2$  between 50 - 80 mmHg
  - monitoring: pulse oximeter, cardio-respiratory monitor
  - drug therapy: IV Aminophylline, oral Theophylline
  - if repeated attacks:
    - regular prophylactic tactile/surface stimulation
    - nasal CPAP (3 - 4 cm of  $\text{H}_2\text{O}$ ) or IPPV (usually low settings)

**Table 2. Immediate resuscitation**



## NEONATAL SEPSIS

### Definition

Neonatal sepsis generally falls into two main categories:

- early onset (*generally acquired from the mother*)
- late onset: sepsis occurring > 72hrs after birth  
(*acquired from the nursery environment or from the community*)

### Clinical features

#### Signs and symptoms of Sepsis

- temperature instability:
  - hypo or hyperthermia
- change in behaviour:
  - lethargy, irritability
  - change in tone  
(‘baby just doesn’t seem right)
- skin:
  - poor perfusion, mottling
  - pallor, jaundice
  - scleraema
- feeding problems:
  - feeding intolerance, vomiting
  - diarrhea,
  - abdominal distension
- cardiopulmonary:
  - tachycardia, hypotension
  - tachypnoea, respiratory distress, apnoea
- metabolic:
  - hypo or hyperglycaemia, metabolic acidosis

**Table 1. Risk factors for sepsis**

#### Any stage

prematurity  
neutropenia due to other causes

#### Early onset sepsis

maternal GBS (group B streptococcus) carrier  
maternal HVS positive  
prolonged rupture of membranes (PROM) (>18 hours)  
preterm labour/PPROM  
maternal fever  
maternal urinary tract infection  
discoloured / foul-smelling liquor  
clinical chorioamnionitis

#### Late Onset Sepsis

overcrowded nursery  
inadequate hand washing  
central lines  
colonization of patients by certain organisms  
infection from family members or contacts

### Investigations

- full blood count : Hb, TWBC with differential count, platelet count
- blood cultures (at least 1ml of blood)
- where available :
  - serial CRP 24 hours apart
  - ratio of immature forms over total of neutrophils + immature forms - IT ratio > 0.2  
is an early predictor of infection during the first week or two of life
- where indicated :
  - lumbar puncture
  - chest, abdominal X-ray
  - culture of endotracheal tube aspirate
  - urine culture
  - maternal high vaginal swab culture

## Management

- antibiotics
  - start immediately when diagnosis is suspected and after all appropriate specimens taken. Do not wait for culture results.
  - trace culture results after 48 – 72 hours. Adjust antibiotics according to results. If cultures are negative and infection is clinically unlikely, stop antibiotics.
- antibiotic treatment
  - Early onset sepsis*
    - IV C. Penicillin/Ampicillin and Gentamicin
    - specific choice of antibiotics when specific organisms suspected/confirmed
    - change antibiotics according to sensitivity results
  - Late onset sepsis*
    - for community acquired infection, start on
      - Cloxacillin/Ampicillin and Gentamicin for non-CNS infection and
      - C. Penicillin and Cefotaxime for CNS infection
    - for nosocomial infections
      - choice of antibiotics depends on the prevalent organisms in the nursery and their sensitivities
      - for units where CONS / MRSE/ MRSA are common, consider Vancomycin
      - for non-ESBL gram negative rods, consider cephalosporin
      - for ESBLs consider carbapenams
      - for *Pseudomonas* consider Ceftazidime
      - if anaerobic infections (e.g. Intraabdominal sepsis), consider Metronidazole
      - consider fungal sepsis if patient is not responding to antibiotics especially if preterm or with indwelling long lines
  - duration of antibiotics
    - 7-10 days for pneumonia or proven neonatal sepsis
    - 14 – 21 days for GBS meningitis
    - at least 21 days for Gram-negative meningitis
  - IV Immunoglobulin may be considered in VLBW babies with sepsis
  - consider removing central lines
  - complications and supportive therapy
    - *respiratory*: ensure adequate oxygenation with blood gas monitoring and initiate oxygen therapy or ventilator support if needed
    - *cardiovascular*: support BP and perfusion to prevent shock.
    - *haematological*: monitor for DIVC
    - *CNS*: seizure control and monitor for SIADH
    - *metabolic*: monitor for hypo/hyperglycaemia, electrolyte and acid-base imbalance

## CONGENITAL SYPHILIS

Decision to treat an infant for congenital syphilis depends on

- identification of presence of maternal syphilis
- adequacy of maternal treatment
- evidence of clinical, laboratory or radiographic syphilis in the infant
- comparison of infant's/ cord VDRL with maternal's VDRL

**Table 1. Selecting infants who need treatment**

Which infants to treat ?
<p>The following infants require treatment</p> <ul style="list-style-type: none"> <li>• <i>Infants suggestive of congenital syphilis</i> <ul style="list-style-type: none"> <li>- clinical                             <ul style="list-style-type: none"> <li>non immune hydrops, IUGR, jaundice, hepatosplenomegaly, rhinitis, skin rash, pseudoparalysis of extremity</li> </ul> </li> <li>- laboratory                             <ul style="list-style-type: none"> <li>cord blood VDRL 4X maternal level</li> </ul> </li> </ul> </li> <li>• <i>Infants with presumed congenital syphilis</i> <ul style="list-style-type: none"> <li>- infant with positive cord blood VDRL</li> </ul> </li> <li>• <i>mothers - untreated/unknown/inadequate treatment</i> <ul style="list-style-type: none"> <li>- treatment &gt; 38 weeks gestation</li> <li>- or treatment ≤ 4 weeks before delivery</li> <li>- treatment with erythromycin</li> <li>- treated but VDRL did not decrease at least 4 fold</li> </ul> </li> </ul>

**Table 2. Investigations**

<p><i>infants with signs of congenital syphilis.</i></p> <ul style="list-style-type: none"> <li>lumbar puncture: CSF for counts, proteins and VDRL status</li> <li>X-ray of long bones, CXR</li> </ul> <p><i>check VDRL/TPHA status of mother</i> /father/partner</p> <p>If father's VDRL negative, check TPHA</p> <p><i>TPHA titres (not necessary)</i></p>
--

### Treatment

- *infants with congenital syphilis and presumed congenital syphilis*
  - IM Procaine Penicillin 50,000 units/kg IM daily x 10 - 14 days
  - IV C. Penicillin 50,000 units/kg/dose 12hrly X 1st 7 days then 8hrly for 10 - 14 days
  - IV/IM Ceftriaxone 75mg/kg (< 30 days old) or 100mg/kg daily(> 30 days old)

*Note: If >1 day of treatment is missed, the entire course should be restarted*
- *mother with positive VDRL but infant's cord blood VDRL negative:*
  - IM Benzathine Penicillin 50,000 units/kg single dose
- refer the parents to the STD clinic for management.

*Note:*

1. Tetracycline, doxycycline or erythromycin does not have an established and well-evaluated high rate of success as injection penicillin in the treatment of syphilis.
2. Penetration of tetracycline, doxycycline and erythromycin into the CSF is poor.

**Notification** for infants with: - clinical features of syphilis  
- VDRL titres > 4 fold that of the mother's.

### Follow-up

- clinical examination and serological tests at intervals for a total period of 2 years;
- every 3 months until VDRL non reactive or decrease by 4 fold (should decline by 3 months and non reactive by 6 months)
- retreatment if:
  - clinical signs and symptoms persist or recur.
  - 4-fold rise of titre in VDRL
  - failure of VDRL titre to decrease 4 fold in 1 year for early syphilis

## OPHTHALMIA NEONATORUM

### Definition

Conjunctivitis occurring within the 1st 4 weeks of life

### Gonococcal

Bilateral purulent conjunctival discharge within first few days of life.

#### Treatment:

- systemic:
  - Ceftriaxone 50mg/kg (max. 125mg) IV or IM once daily for 2-3 days *or*
  - Cefotaxime 50mg/kg/day IV in two divided doses 12 hourly for 2-3 days
- disseminated infection : duration 7 days; If meningitis : 10-14 days*
- local:
  - irrigate eyes with sterile normal saline and at least hourly as long as necessary to eliminate discharge. Topical antibiotics are optional.
- refer to ophthalmologist for assessment
- check VDRL of the infant to exclude congenital syphilis, screen for C. trachomatis and HIV. Screen both parents for Gonococcal infections, syphilis and HIV.
- parents should be referred to STD clinic for further management.
- on discharge, infants should be seen at 2 weeks with repeat eye swab gram stain and C&S

### Non- Gonococcal

Include *Staph aureus*, *Strep viridans*, *Haemophilus*, *E.coli*, *Pseudomonas* infections

#### Treatment:

- local – Neomycin eye ointment 0.5% after feed, both eyes *or*  
Ceftazidime 5% bd to qid for a week  
*(change according to sensitivity ,duration according to response)*

### Chlamydial

Unilateral or bilateral conjunctivitis with peak incidence at 2 weeks of life

#### Treatment:

- during 1st week of life :
  - oral Erythromycin 20mg/kg/d (< 2kg), or 30 mg/kg/d (>2 kg) in divided doses
- >1 week age:
  - oral Erythromycin 40mg/kg/d PO in divided doses
  - duration of treatment = 14 days*
- local Rx: tetracycline ointment 1% q6H for 7-14 days
- *systemic treatment is essential. Local treatment is unnecessary if systemic treatment given.*
- refer both parent to STD clinic for further management
- refer to ophthalmologist for assessment of ocular complications

### Gonococcal Infections in Older Children

- suspect child abuse.
- children over 45 kg or 12 years old should receive adult regimens.
- for children < 45 kg or < 12 years old with uncomplicated vulvovaginitis and urethritis
  - Ceftriaxone 125mg IM single injection *or*
  - Spectinomycin 40mg/kg IM single injection

*Input from Dr Joseph Alagaratnam , Consultant Paediatric Ophthalmologist HKL , is acknowledged.*

## PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS

### Introduction

Gestational age is the most important determinant of the incidence of patent ductus arteriosus (PDA). The other risk factors for PDA are lack of antenatal steroids, respiratory distress syndrome (RDS) and need for ventilation.

### Clinical Features

- wide pulse pressure/ bounding pulses
- systolic or continuous murmur
- tachycardia
- lifting of xiphisternum with heart beat
- hyperactive precordium
- apnoea
- increase in ventilatory requirements

### Complications

- congestive cardiac failure
- renal impairment
- intraventricular haemorrhage (IVH)
  - risk of subsequent neurological impairment, disability
- pulmonary haemorrhage
- necrotizing enterocolitis
- chronic lung disease

### Management

- confirm PDA with cardiac ECHO if available
- medical therapy
  - fluid restriction. Care with fluid balance to avoid dehydration
  - no role for diuretics
  - IV or oral Indomethacin 0.1 mg/kg/day daily dose for 6 days -contraindicated if
    - infants with proven or suspected infection that is untreated.
    - bleeding, especially active gastrointestinal or intracranial.
    - platelet count  $< 60 \times 10^9/L$
    - NEC or suspected NEC
    - duct dependant congenital heart disease
    - impaired renal function creatinine  $> 140$  micromol/L or blood urea  $> 14$  mmol/L
    - monitor urine output and renal function. If urine output  $< 0.6$  ml/kg/hr after a dose given, withhold next dose until output back to normal.
    - monitor for GIT complications e.g. gastric bleeding, perforation
- surgical ligation
  - persistence of a symptomatic PDA and failed 2 courses of Indomethacin
  - if medical treatment fails or contraindicated
- in older preterm infant who is asymptomatic,
  - i.e. only cardiac murmur present in an otherwise well baby – no treatment required.
  - follow-up as necessary. Most PDAs in this group will close spontaneously

### Pearls and pitfalls in management

- higher success rate in PDA closure if indomethacin is given in the first 2 weeks of life
- oral indomethacin: ensure suspension is freshly prepared, well mixed before serving
- IV indomethacin is unstable once the vial is opened

## PERSISTENT PULMONARY HYPERTENSION

### Definition

Persistent pulmonary hypertension (PPHN) of the newborn is defined as a failure of normal pulmonary vasculature relaxation at or shortly after birth, resulting in impedance to pulmonary blood flow which exceeds systemic vascular resistance, such that unoxygenated blood is shunted to the systemic circulation.

Some known precipitating factors contributing to failure of pulmonary vasculature relaxation are:

- hypoxia
- meconium
- cold stress
- lung disease
- hypoglycaemia
- sepsis

### Diagnosis

- *history*
  - presence of precipitating factors during antenatal, intrapartum, postnatal periods
- *respiratory signs*
  - signs of respiratory distress (tachypnoea, grunting, nasal flaring, chest retractions)
  - onset at birth or within the first 4 to 8 hours of life
  - marked lability in pulse oximetry
- *cardiac signs*
  - central cyanosis (differential cyanosis between the upper and lower body may be noted clinically, by pulse oximetry and blood gasses)
  - prominent precordial impulse
  - low parasternal murmur of tricuspid incompetence
- *radiography*
  - lung fields
    - normal, parenchymal lesions if lung disease is present, or oligoemia
  - cardiac shadow
    - normal sized-heart, or cardiomegaly (usually right atrial or ventricular enlargement)
- *echocardiography- important to:*
  - exclude congenital heart disease.
  - define pulmonary artery pressure using tricuspid incompetence, ductal shunt velocities.
  - define the presence, degree, direction of shunt through the duct / foramen ovale.
  - define the ventricular outputs.

### Differential Diagnosis

In centres where there is a lack of readily available echocardiography and/or Paediatric Cardiology services, the challenge is to differentiate PPHN from Congenital Cyanotic Cardiac diseases. Differentiating points between the two are:

- babies with congenital cyanotic heart diseases are seldom critically ill at delivery
- bradycardia is almost always due to hypoxia, not a primary cardiac problem
- infants with cyanotic lesions usually do not have respiratory distress
- the infant with PPHN usually had some perinatal hypoxia and handles poorly
- the cyanosed cardiac baby is usually pretty happy, but blue

## Management

### General measures

- preventing and treating
  - hypothermia, hypoglycaemia, hypocalcaemia, hypovolaemia, anaemia
- avoid excessive noise, discomfort and agitation.
- minimal handling

### Sedation

- morphine – given as an infusion at 20 mcg/kg/hr. Morphine is said to be a safe sedative and analgesic even in the preterm infants.
- midazolam – its use cannot be recommended among the preterm population especially those with a gestational age less than 34 weeks, in view of deleterious effects on the cerebral circulation leading to an increase in adverse long term neurodevelopmental outcomes.

### Ventilation

- conventional ventilation – adopt ‘gentle ventilatory’ approach by
  - avoidance of hyperventilation (i.e. hypocarbia and hyperoxia).
  - hypocarbia causes neuronal cell death leading to white matter necrosis and periventricular leukomalacia. Aim for a  $p\text{CO}_2$  of 35-55mmHg.
  - hyperoxia leads to chronic oxygen dependency and bronchopulmonary dysplasia. Aim for a  $p\text{O}_2$  of at least 50 mm Hg.
  - ventilating to achieve a tidal volume of 5mls/kg<sup>3</sup>
  - short inspiratory time (0.2-0.3 sec) to prevent alveolar overdistension
  - inadvertently increasing ventilatory settings may lead to overdistention of the lungs and high mean airway pressures compromising venous return to the heart which further aggravates systemic hypotension as cardiac output is compromised
- High Frequency Oscillatory ventilation (HFOV)
  - may be effective in PPHN secondary to a pulmonary pathology (role is controversial)

### Circulatory support

- Inotropes improve cardiac output and enhances systemic oxygenation. Poorly substantiated in PPHN, especially with the use of iNO, though the pulmonary vasodilating effect help improve cardiac output and systemic blood pressure.
- However, inotropes are still recommended in institutions without facilities for iNO
 

Dopamine	5 – 15 mcg/kg/min
Dobutamine	5 – 15 mcg/kg/min
Adrenaline	0.1 – 1.0 mcg/kg/min

### Vasodilators

- inhaled nitric oxide (iNO)- selective pulmonary vasodilator (dose 5 - 20 ppm)
  - in term and near term infants (> 34 weeks gestational age)
  - it reduces the need for Extracorporeal membrane oxygenation (ECMO)

*There is insufficient evidence to support iNO use for preterm infants < 34 weeks age.*

- Tolazoline, Prostacycline and Sildenafil

### Extracorporeal membrane oxygenation (ECMO)

ECMO is effective in PPHN, though usage has declined since the use of iNO and HFOV.

*Practices not recommended for routine use*

- sodium bicarbonate
- magnesium sulphate
- paralysing agents



## PERINATALLY ACQUIRED VARICELLA

### Introduction

- in maternal infection (onset of rash) **within 5 days before and 2 days after delivery** 17-30% infants develop neonatal varicella with lesions appearing at 5-10 days of life.
- **mortality is high (20%-50%)**. Cause of death is due to severe pulmonary disease or widespread necrotic lesions of viscera.
- when maternal varicella occurs 5-21 days before delivery, lesions typically appear in the first 4 days of life and prognosis is good with no associated mortality. The mild course is probably due to the production and transplacental passage of maternal antibodies that modify the course of illness in new-borns.
- infants born to mothers who develop varicella between 7 days antenatally and 14 days postnatally should receive
  - 125µ Zoster immunoglobulin (ZIG) as soon as possible. If vesicles develop to give
  - acyclovir 20 mg/kg over 1 hour every 8hrly (total 60mg /kg/day) for 7 days.
  - if Zoster immunoglobulin *is not available*
    - give IV Immunoglobulin 400 mg/kg ( this is less effective) *and* acyclovir 20 mg/kg over 1 hour every 8hrly (total 60mg /kg/day) for 7 days.
- women with varicella at time of delivery should be isolated from their newborns, breast-feeding is contraindicated. Mother should express breast milk in the mean time and commence breast-feeding when all the lesions have crusted.
- neonates with varicella lesions should be isolated from other infants but not from their mothers.
- infants whose mothers develop Zoster before or after delivery have maternal antibodies and they will not need ZIG.

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## RESPIRATORY MEDICINE

- 28** Viral Bronchiolitis
- 29** Croup
- 30** Pneumonia
- 31** Asthma



## VIRAL BRONCHIOLITIS

### Aetiology and Epidemiology

- a common respiratory illness especially in infants aged 1 to 6 months old
- Respiratory Syncytial Virus (RSV) remains the commonest cause of acute bronchiolitis in Malaysia
- although it is endemic throughout the year, cyclical periodicity with annual peaks occur, in the months of November, December and January.

### Clinical Features

- typically presents with a mild coryza, low grade fever and cough
- tachypnoea, chest wall recession, wheeze and respiratory distress subsequently develop. The chest may be hyperinflated and auscultation usually reveals fine crepitations and sometimes rhonchi.
- a majority of children with viral bronchiolitis has mild illness and about 1% of these children require hospital admission

Table 1. Guideline for hospital admission in viral bronchiolitis

	Home Management	Hospital management
Age < than 3 months	No	Yes
Toxic – looking	No	Yes
Chest recession	Mild	Moderate/Severe
Central cyanosis	No	Yes
Wheeze	Yes	Yes
Creptitations on auscultation	Yes	Yes
Feeding	Well	Difficult
Apnoea	No	Yes
Oxygen saturation	>95%	<93%
High risk group	No	Yes

### Chest X-ray

- a wide range of radiological changes are seen in viral bronchiolitis;
  - hyperinflation (most common)
  - segmental
  - lobar collapse/consolidation
- a chest X-ray is *not routinely required*, but recommended for children with:
  - severe respiratory distress
  - unusual clinical features
  - an underlying cardiac or chronic respiratory disorder
  - admission to intensive care

### Management

#### General measures

- careful assessment of the respiratory status and oxygenation is critical
- arterial oxygenation by pulse oximetry (SpO<sub>2</sub>) should be performed at presentation and maintained above 93%
  - administer supplemental humidified oxygen if necessary
- monitor for signs of impending respiratory failure:
  - inability to maintain satisfactory SpO<sub>2</sub> on inspired oxygen > 40%, or a rising pCO<sub>2</sub>
- very young infants are at risk of apnoea require greater vigilance



### Nutrition and Fluid therapy

- **Feeding.** Infants admitted with viral bronchiolitis frequently have poor feeding, are at risk of aspiration and may be dehydrated. Small frequent feeds as tolerated can be allowed in children with moderate respiratory distress. Naso-gastric feeding, although not universally practiced, may be useful in these children who refuse to feed and also to empty the dilated stomach.
- **Intravenous fluids** for children with severe respiratory distress, cyanosis, apnoea. Fluid therapy should be restricted to maintenance requirement of 100 ml/kg/day for infants, in the absence of dehydration.

### Pharmacotherapy

- **Inhaled  $\beta_2$ -agonists.** Pooled data have indicated a modest clinical improvement with the use of  $\beta_2$ -agonist. A trial of nebulised  $\beta_2$ -agonist, given in oxygen, may be considered in infants with viral bronchiolitis. Vigilant and regular assessment of the child should be carried out if such a treatment is provided.
- **Inhaled steroids.** Randomised controlled trials of the use of inhaled steroids for treatment of viral bronchiolitis demonstrated no meaningful benefit.
- **Antibiotics** are recommended for all infants with
  - recurrent apnoea and circulatory impairment,
  - possibility of septicaemia
  - acute clinical deterioration
  - high white cell count
  - progressive infiltrative changes on chest radiograph.

## CROUP

### Aetiology and epidemiology

It is a clinical syndrome characterised by barking cough, inspiratory stridor, hoarse voice and respiratory distress of varying severity. It is the result of viral inflammation of the larynx, trachea and bronchi, hence the term laryngotracheobronchitis.

The most common pathogen is parainfluenza virus (74%), (types 1, 2 and 3).

The others are Respiratory Syncytial Virus, Influenza virus type A and B, Adenovirus, Enterovirus, Measles, Mumps and Rhinoviruses and rarely *Mycoplasma pneumoniae* and *Corynebacterium Diphtheriae*

### Clinical Features

- low grade fever, cough and coryza for 12-72 hours, followed by
- increasingly bark-like cough and hoarseness
- stridor that may occur when excited, at rest or both
- respiratory distress of varying degree

### Diagnosis

- croup is a *clinical diagnosis*. Studies show that it is safe to visualise the pharynx to exclude acute epiglottitis, retropharyngeal abscess etc. However, in severe croup, it is advisable to examine the pharynx under controlled conditions (ICU/OT)
- neck Radiograph is not necessary, unless the diagnosis is in doubt, such as in the exclusion of a foreign body.

## Assessment of severity

### Clinical Assessment of Croup (Wagener)

#### • Severity

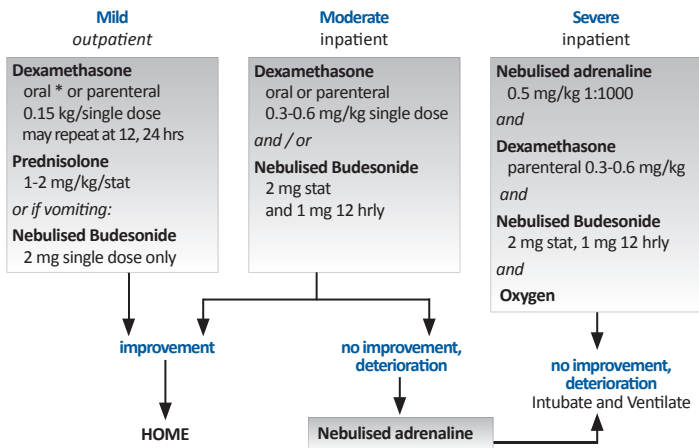
- mild: stridor with excitement or at rest, with no respiratory distress.
- moderate: stridor at rest with intercostal, subcostal or sternal recession.
- severe: stridor at rest with marked recession, decreased air entry and altered level of consciousness.
- pulse oximetry is helpful but not essential
- arterial blood gas is not helpful because the blood parameters may remain normal to the late stage. The process of blood taking may distress the child.

## Management

### Indications for hospital admission

- moderate and severe viral croup
- poor oral intake
- family lives a long distance from hospital; lacks reliable transport
- toxic looking
- age less than 6 months
- unreliable caregivers at home

Figure 1. Algorithm for the management of viral croup



Note: With the use of steroids + adrenaline in severe croup (the sustained action of steroids combined with quick action of adrenaline), the rate of intubation has been reduced from 3% to nil in many centres. The decision to intubate under controlled conditions (in Operation Theatre or Intensive Care Unit, with standby for tracheostomy) is made on clinical criteria, which suggests increasing respiratory distress.

The indications for oxygen therapy include:

- severe viral croup
- percutaneous  $\text{SaO}_2 < 93\%$

Caution: With oxygen therapy, the  $\text{SaO}_2$  may be normal despite progressive respiratory failure and a high  $\text{PaCO}_2$ . Hence clinical assessment is most important.

Antibiotics are not recommended unless bacterial super-infection is strongly suspected or the patient is very ill. IV fluids are not necessary except for those unable to drink.

# PNEUMONIA

## Definition

There are two clinical definitions of pneumonia:

- *bronchopneumonia*: a febrile illness with cough, respiratory distress with evidence of localised or generalised patch infiltrates
- *lobar pneumonia*: similar to bronchopneumonia except that the physical findings and radiographs indicate lobar consolidation.

## Aetiology

The specific aetiological agents is not identified in 40% to 60% of cases. It is difficult to distinguish viral from bacterial disease based on a combination of findings. A helpful indicator in predicting aetiological agents is the age group. The majority of lower respiratory tract infections are viral in origin, e.g. respiratory syncytial virus, influenza A and B, adenovirus and parainfluenza virus. The predominant bacterial pathogens are shown in Table 1.

Table 1. Pathogens for pneumonia

Age	Bacterial Pathogens
newborns	<i>Group B streptococcus, Escherichia coli, Klebsiella species, Enterobacteriaceae</i>
1- 3 months	<i>Chlamydia trachomatis</i>
preschool	<i>Streptococcus pneumoniae, Haemophilus influenzae type b, Staphylococcus aureus</i> Less common: group A <i>Streptococcus, Moraxella catarrhalis, Pseudomonas aeruginosa</i>
school	<i>Mycoplasma pneumoniae, Chlamydia pneumoniae</i>

## Assessment of severity of pneumonia

The predictive value of respiratory rate for the diagnosis of pneumonia may be improved by making it age specific. Tachypnoea is defined as follows :

< 2 months age: > 60 /min

2- 12 months age: > 50 /min

12 months – 5 years age: > 40 /min

Assessment of severity is essential for optimal management of pneumonia, and can be categorised based on the respiratory signs and symptoms as shown in Table 2:

Table 2. Assessment of severity of pneumonia

age < 2 months	age 2 months - 5 years
<i>Severe pneumonia</i>	<i>Mild pneumonia</i>
severe chest indrawing	fast breathing
or fast breathing	<i>Severe pneumonia</i>
<i>Very severe pneumonia</i>	chest indrawing
not feeding	<i>Very severe pneumonia</i>
convulsions	not able to drink
abnormally sleepy or difficult to wake	convulsions
fever/ low body temperature	drowsiness
hypopnoea with slow irregular breathing	malnutrition

## Investigations and assessment

Children with bacterial pneumonia cannot be reliably distinguished from those with viral disease on the basis of any single parameter: clinical, laboratory or chest X-ray findings.

- *chest radiograph*
  - indicated when clinical criteria suggests pneumonia
  - does not diagnose aetiological agent
  - not always necessary if facilities are not available or the pneumonia is mild

- **white blood cell count**
  - increased counts with predominance of polymorphonuclear cells suggests bacterial cause
  - leucopenia can either suggest a viral cause or severe overwhelming infection
- **blood culture**
  - non-invasive gold standard for determining the precise aetiology of pneumonia
  - sensitivity is low: positive blood cultures in 10%-30% of patients with pneumonia
  - should be performed in severe pneumonia or if poor response to first line antibiotics
- **pleural fluid analysis**
  - if there is significant pleural effusion diagnostic pleural tap will be helpful
- **serology**
  - serology is performed in patients with suspected atypical pneumonia, i.e. from *Mycoplasma pneumoniae*, *Chlamydia*, *Legionella* and *Moraxella catarrhalis* are
  - acute phase serum titre > 1:160 or paired samples taken 2-4 weeks apart showing a 4 fold rise is a good indicator of *Mycoplasma pneumoniae* infection.
  - This test should be considered for children aged five years or older.

### Assessment of oxygenation

The best objective measurement of hypoxia is by pulse oximetry which avoids the need for arterial blood gases. It is a good indicator of the severity of pneumonia

### Criteria for hospitalization

- community acquired pneumonia can be treated at home
- it is crucial to identify indicators of severity in children who may need admission. Failure to recognise the severity of pneumonia may lead to death. The following indicators can be used as a guide for admission:
  - children aged 3 months and below, whatever the severity of pneumonia.
  - fever ( more than 38.5 °C ), refusal to feed and vomiting
  - fast breathing with or without cyanosis
  - associated systemic manifestation
  - failure of previous antibiotic therapy
  - recurrent pneumonia
  - severe underlying disorder ( i.e. immunodeficiency )

### Antibiotics

When treating pneumonia, the clinical, laboratory and radiographic findings should be considered. Other factors are age of the child, local epidemiology of respiratory pathogens and sensitivity to microbial agents and the emergence of antimicrobial resistance. The severity of the pneumonia and drug costs also impact on selection of therapy.

The majority infections are caused by viruses and do not require any antibiotic. However, it is also very important to be vigilant to choose appropriate antibiotics especially in the initial treatment to reduce further mortality and morbidity.

Table 3. Bacterial pathogens of children and the recommended antimicrobial agents to be used

Pathogen	Antimicrobial agent
Beta-lactam susceptible	
<i>Streptococcus pneumoniae</i>	penicillin, cephalosporins
<i>Haemophilus influenzae</i> type b	ampicillin, chloramphenicol, cephalosporins
<i>Staphylococcus aureus</i>	cloxacillin
Group A <i>Streptococcus</i>	penicillin, cephalosporin
<i>Mycoplasma pneumoniae</i>	macrolides , e.g. erythromycin, azithromycin
<i>Chlamydia pneumoniae</i>	macrolides , e.g. erythromycin, azithromycin
<i>Bordetella pertussis</i>	macrolides , e.g. erythromycin, azithromycin

## INPATIENT MANAGEMENT

### Antibiotics

For children with severe pneumonia, the following antibiotics are recommended:

Table 4. Suggested antimicrobial agents for inpatient treatment of pneumonia

1st line	<i>beta-lactam drugs</i> : benzylpenicillin, amoxycillin, ampicillin, amoxycillin-clavulanate
2nd line	<i>cephalosporins</i> : cefotaxime, cefuroxime, ceftazidime
3rd line	<i>carbapenem</i> : imipenam
others	<i>aminoglycosides</i> : gentamicin, amikacin

- *second line antibiotics* need to be considered when :
  - there are no signs of recovery
  - patients remain toxic and ill with spiking temperature for 48 - 72 hours
- a macrolide antibiotic is used if *Mycoplasma* or *Chlamydia* are the causative agents
- a child admitted to hospital with severe community acquired pneumonia must receive parenteral antibiotics. As a rule, in severe cases of pneumonia, combination therapy using a second or third generation cephalosporins and macrolide should be given. Staphylococcal infections and infections caused by Gram negative organisms such as *Klebsiella* have been frequently reported in malnourished children.

### Staphylococcal infection

*Staphylococcus aureus* is responsible for a small proportion of cases. A high index of suspicion is required because of the potential for rapid deterioration. It is chiefly a disease of infants and has a significant mortality rate. Radiological features include the presence of multilobar consolidation, cavitation, pneumatoceles, spontaneous pneumothorax, empyema and pleural effusion. Treatment with high dose cloxacillin (200 mg/kg/day) for a longer duration and drainage of empyema will result in good outcome in the majority of cases.

### Supportive treatment

#### • Fluids

Oral intake should ceased when a child is in severe respiratory distress. In severe pneumonia, secretion of anti-diuretic hormone is increased which means that dehydration is uncommon. It is important that the child should not be overhydrated.

#### • Oxygen

Oxygen reduces mortality associated with severe pneumonia. It should be given especially to children who are restless, tachypnoeic with severe chest indrawing, cyanosed or not tolerating feeds. It is important to maintain the  $\text{SaO}_2 > 95\%$ .

#### • Cough syrup

Not recommended as it causes suppression of cough and may interfere with airway clearance. Adverse effects and overdosage have been reported.

#### • Temperature control

To reduce discomfort from symptoms, as paracetamol will not abolish the fever

#### • Chest physiotherapy

This assists in the removal of tracheobronchial secretions: removes airway obstruction, increase gas exchange and reduce the work of breathing.

There is no evidence that chest physiotherapy should be routinely done in pneumonia.

## OUTPATIENT MANAGEMENT

In children with mild pneumonia, their breathing is fast but there is no chest indrawing. Antibiotics can be prescribed orally. The mother is advised to return in two days for reassessment, or earlier if the child is getting worse.

## ASTHMA

The International Studies on Asthma And Allergy (ISAAC) has shown that the prevalence of asthma among school age children is 10%.

### Definition

Chronic airway inflammation leading to increase airway responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or early morning. It is often associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment.

Reversible and variable airflow limitation as evidenced by > 15% improvement in PEFR (Peak Expiratory Flow Rate), in response to administration of bronchodilator.

**Table 1. Important points in history**

current symptoms  
pattern of symptoms  
precipitating factors  
present treatment  
previous hospital admission  
typical exacerbations  
home/ school environment  
impact on life style  
history of atopy  
response to prior treatment  
prolonged URTI symptoms  
family history

**Table 2. Physical examination**

#### *Signs of chronic illness*

Harrison sulci  
hyperinflated chest  
eczema / dry skin  
hypertrophied turbinates

#### *Signs in acute exacerbation*

tachypnoea  
wheeze, rhonchi  
hyperinflated chest  
accessory muscles  
cyanosis  
drowsiness  
tachycardia

**NOTE: ABSENCE OF PHYSICAL FINDINGS  
DOES NOT EXCLUDE ASTHMA!**

### Management of Chronic Asthma

#### *Assessment of Severity*

- classification based on frequency, chronicity and severity of symptoms (Table 3)

#### *Management according to severity (GINA guidelines)*

In 2006, the Global Initiatives on Asthma (GINA) has proposed the management of asthma from severity based to control based. The change is due to the fact that asthma management based on severity is on expert opinion rather than evidence based, with limitation in deciding treatment and it does not predict treatment response. Asthma assessment based on levels of control is based on symptoms and the three levels of control are well controlled, partly control and uncontrolled.

**Table 4. Levels of Asthma Control (GINA 2006)**

	Characteristics					
	daytime symptoms	limitation of activities	nocturnal symptoms or awakenings	need for reliever	lung function test	exacerbations
<b>Controlled</b>						
<i>All of the following:</i>	none	none	none	none	normal	none
<b>Partly Controlled</b>						
<i>Any measure present in any week:</i>	> 2 / week	any	any	2 / week	< 80% predicted or personal best	≥ 1 a year
<b>Uncontrolled</b>	≥ 3 features of partly controlled asthma present in any week					1 / week

Table 3. Classification of severity of childhood asthma

category	clinical parameter
<b>Intermittent</b>	daytime symptoms < once a week nocturnal symptoms < once a month no exercise induced symptoms brief exacerbations not affecting sleep and activity normal lung function
<b>Persistent</b> (Threshold for preventive treatment)	
<i>Mild persistent</i>	daytime symptoms > once a week nocturnal symptoms > twice a month exercise induced symptoms exacerbations once a month affecting sleep and activity PEFR / FEV <sub>1</sub> > 80%
<i>Moderate Persistent</i>	daytime symptoms daily nocturnal symptoms > once a week exercise induced symptoms exacerbations > twice a month affecting sleep and activity PEFR / FEV <sub>1</sub> 60 – 80%
<i>Severe Persistent</i>	daytime symptoms daily daily nocturnal symptoms daily exercise induced symptoms frequent exacerbations > twice a month affecting sleep and activity PEFR / FEV <sub>1</sub> < 60%

**Note**

- This division is arbitrary, groupings may merge. An individual's classification may change from time to time.
- There are a few patients who have very infrequent but severe or life threatening attacks with completely normal lung function and no symptoms between episodes. This type of patient remains very difficult to manage.

Abbreviations. PEFR = Peak Expiratory Flow Rate; FEV<sub>1</sub> = Forced Expiratory Volume in One Second

**Prevention**

Identifying and avoiding the following common triggers may be useful

- environmental allergens

These include house dust mites, animal dander, insects like cockroach, mould and pollen.

Useful measures include damp dusting, frequent laundering of bedding with hot water, encasing pillow and mattresses with plastic/vinyl covers, removal of carpets from bed rooms, frequent vacuuming and removal of pets from the household.

- cigarette smoke
- respiratory tract infections - commonest trigger in children.
- food allergy - uncommon trigger, occurring in 1-2% of children
- exercise

Although it is a recognised trigger, activity should not be limited. Taking a  $\beta_2$ -agonist prior to strenuous exercise, as well as optimizing treatment, are usually helpful.

**Drug Therapy**

- see Tables 5, and 6 (on next page) for drug delivery methods and dosages.

Table 5. Delivery systems available &amp; recommendation for the different ages

Age (years)	Oral	MDI + Space + Mask	MDI + Spacer	Dry Powder Inhaler
< 5	+	+	-	-
5 - 8	-	+	-	-
> 8	-	+	+	+

Table 6. Drug dosages for asthma

Drug	Formulation	Dosage
<i>Relieving Drugs</i>		
<b>Rapid acting <math>\beta_2</math>-agonists</b>		
salbutamol	oral metered dose inhaler dry powder inhaler	0.15 mg/kg/dose TDS-QID/PRN 100-200 mcg/dose QID/PRN 100-200 mcg/dose QID/PRN
terbutaline	oral metered dose inhaler dry powder inhaler	0.075 mg/kg/dose TDS-QID/PRN 250-500 mcg/dose QID/PRN 500-1000 mcg/dose QID/PRN (maximum 4000 mcg/daily)
fenoterol	metered dose inhaler	200 mcg/dose QID/PRN
Ipratropium bromide	metered dose inhaler	40-60mcg /dose TDS/QID/PRN
<i>Preventive Drugs</i>		
<b>Corticosteroids</b>		
prednisolone	oral	1-2 mg/kg/day in divided doses
beclomethasone dipropionate	metered dose inhaler dry powder inhaler	low dose: <400 mcg/day moderate dose: 400-800 mcg/day high dose: 800-1200 mcg/day
budesonide	metered dose inhaler dry powder inhaler	low dose: <400 mcg/day moderate dose: 400-800 mcg/day high dose: 800-1200 mcg/day
fluticasone propionate	metered dose inhaler dry powder inhaler	low dose: <200 mcg/day moderate dose: 200-400 mcg/day high dose: 400-600 mcg/day
ciclesonide	metered dose inhaler	low dose: 160 mcg/day high dose: 320 mcg day
Sodium cromoglycate	dry powder inhaler metered dose inhaler	20mg QID 1-2mg QID or 5-10mg BID-QID
Theophylline	oral syrup slow release	5 mg/kg/dose TDS/QID 10 mg/kg/dose BD
<b>Long acting <math>\beta_2</math>-agonist</b>		
salmeterol	metered dose inhaler dry powder inhaler	50-100 mcg/dose BD 50-100 mcg/dose BD
<b>Combination</b>		
salmeterol /fluticasone	metered dose inhaler dry powder inhaler	25/50mcg, 25/125mcg, 25/250mcg 50/100mcg, 50/250mcg, 50/500mcg
budesonide/Formoterol	dry powder	160/4.5mcg, 80/4.5mcg
<b>Antileukotrienes (Leukotriene modifier)</b>		
montelukast	oral	4 mg granules 5mg/tablet nocte <i>chewable</i> 10mg/tablet nocte

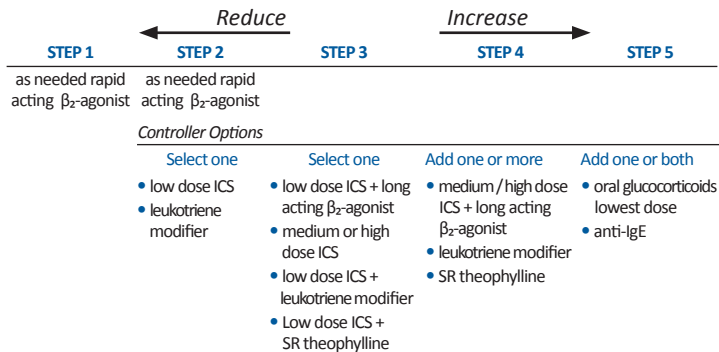
Note: Dry powder inhaler devices available include rothaler, diskhaler, turbohaler, accuhaler and easyhaler.



## Treatment of Chronic Asthma

- asthma management based on levels of control is a step up and step down approach as shown in Figure 1.

Figure 1. Chronic asthma: management based on control



### NOTE:

- Patients should commence treatment at the step most appropriate to the initial severity. A short rescue course of prednisolone may help establish control promptly.
- Explain to parents and patient about asthma and all therapy
- Ensure both compliance and inhaler technique optimal before progression to next step.
- Step-up; assess patient after 1 month of initiation of treatment and if control is not adequate, consider step-up after looking into factors as in 3.
- Step-down; review treatment every 3 months and if control sustained for at least 4-6 months, consider gradual treatment reduction.

Abbreviations. ICS, inhaled corticosteroids; SR, sustained release

## Monitoring

### Assessment during follow-up

- assess severity
- response to therapy
  - interval symptoms
  - frequency and severity of acute exacerbation
  - morbidity secondary to asthma
  - quality of life
  - PEF monitoring on each visit
- compliance
  - frequency and technique, reason and excuses
- education
  - technique, factual information, written action plan, PEF monitoring may not be practical for all asthmatics but is essential especially for those have poor perception of symptoms and those with life threatening attacks

## MANAGEMENT OF ACUTE ASTHMA

### Assessment of Severity

#### Initial (Acute assessment)

- Diagnosis
  - symptoms e.g. cough, wheezing, breathlessness, pneumonia
- Triggering factors
  - food, weather, exercise, infection, emotion, drugs, aeroallergens
- Severity
  - respiratory rate, colour, respiratory effort, conscious level

Table 7. The initial assessment - the first step in the management of acute asthma

	Mild <i>admission unlikely</i>	Moderate (may need admission)	Severe (admission needed)
altered consciousness	no	no	yes
physical exhaustion	no	no	yes
talks in:	sentences	phrases	words
pulsus paradoxus	not palpable	may be palpable	palpable
central cyanosis	absent	absent	present
rhonchi	present	present	silent chest
use of accessory muscle	absent	moderate	marked
sternal retraction	absent	moderate	marked
initial PEF	> 60 %	40 - 60 %	< 40 %
oxygen saturation	> 93 %	91 - 93 %	< 90 %

#### Note:

1. Chest X Ray is rarely helpful in the initial assessment unless complications like pneumothorax, pneumonia or lung collapse are suspected

2. Initial ABG is indicated only in acute severe asthma

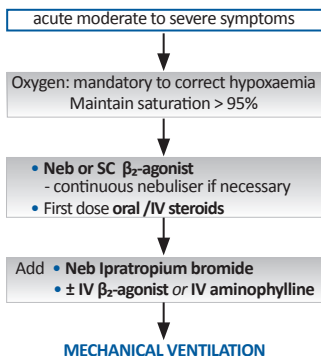
#### Criteria for admission

- failure to respond to standard home treatment
- failure of those with mild or moderate acute asthma to respond to nebulised  $\beta_2$ -agonists
- relapse within 4 hours of nebulised  $\beta_2$ -agonists
- severe acute asthma

#### Management considerations

- monitor pulse, colour, PEFR, ABG and SpO<sub>2</sub>. Close monitoring for at least 4 hours.
- hydration - give maintenance fluids.
- role of aminophylline debated due to its potential toxicity. To be used with caution.
- antibiotics indicated only if bacterial infection suspected.
- avoid sedatives and mucolytics.
- efficacy of prednisolone in the first year of life is poor.
- on discharge, patients must be provided with an Asthma Action Plan to assist parents or patients to prevent/terminate asthma attacks. The plan must include:
  - how to recognize worsening asthma
  - how to treat worsening asthma
  - how & when to seek medical attention

Figure 1. Algorithm for management of acute asthma



Abbreviations.  
Neb, nebuliser;  
SC, subcutaneous

Table 8. Drug dosages for acute asthma

Drug	Formulation	Dosage
<b>β<sub>2</sub>-agonists</b>		
salbutamol	nebuliser solution 5 mg/ml or 2.5 mg/nebule	0.15 mg/kg/dose (max 5 mg) or < 2 years old : 2.5 mg/dose > 2 years old : 5.0 mg/dose continuous : 500 mcg/kg/hr
	intravenous	bolus: 5-10 mcg/kg over 10 min Infusion: start 0.5-1.0 mcg/kg/min increased 1.0 mcg/kg/min every 15 min to a maximum of 20 mcg/kg/min
terbutaline	nebuliser solution 10 mg/ml, 2.5 mg/ml or 5 mg/ml respule	0.2-0.3 mg/kg/dose, or < 20 kg: 2.5 mg/dose > 20 kg: 5.0 mg/dose
	parenteral	5-10 mcg/kg/dose
fenoterol	nebuliser solution	0.25-1.5 mg/dose
<b>Steroids</b>		
prednisolone	oral	1-2 mg/kg/day in divided doses (for 3-7 days)
hydrocortisone	intravenous	4-5 mg/kg/dose 6 hourly
methylprednisolone	intravenous	1-2 mg/kg/dose 6-12 hourly
Ipratropium bromide	nebuliser solution 250 mcg/ml	< 5 years old : 250 mcg 4-6 hourly > 5 years old : 500 mcg 4-6 hourly
	intravenous	6 mg/kg slow bolus (if not previously on theophylline) followed by infusion 0.5-1.0 mg/kg/hr

Note:

- salbutamol MDI vs nebulizer  
 < 6 year old: 6 x 100 mcg puff = 2.5 mg Salbutamol nebules  
 > 6 year old: 12 x 100 mcg puff = 5.0 mg Salbutamol nebules
- aminophylline : No significant role but can be used in a control environment like ICU

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# CARDIOLOGY

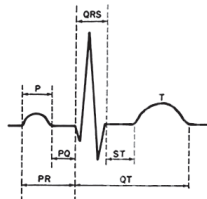
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## PAEDIATRIC ELECTROCARDIOGRAPHY

Age related changes in the anatomy and physiology of infants and children produce normal ranges for electrocardiographic features that differ from adults and vary with age. Awareness of these differences is the key to correct interpretation of paediatric ECG.

Figure 1. The ECG cycle



ECG should be interpreted systematically

- Heart rate
- Rhythm
- P wave axis, amplitude, duration
- PR interval
- QRS axis, amplitude, duration
- ST segment and T waves
- QT interval and QTc

(QTc = measured QT interval / square root of R-R interval)

Table 1. normal values for ECG in children

Age	Heart Rate (bpm)	
	Mean	Range
< 1 day	119	94 – 145
1 – 7 days	133	100 – 175
3 – 30 days	163	115 – 190
1 – 3 months	154	124 – 190
3 – 6 months	140	111 – 179
6 – 12 months	140	112 – 177
1 – 3 years	126	98 – 163
3 – 5 years	98	65 – 132
5 – 8 years	96	70 – 115
8 – 12 years	79	55 – 107
12 – 16 years	75	55 – 102

Table 2. Normal values in the paediatric ECG

Age	PR interval (ms)	QRS duration (ms)	R wave (S wave) amplitude (mm)	
			Lead V1	Lead V6
Birth	80 – 160	< 75	5 – 26 (1 – 23)	0 – 12 (0 – 10)
6 months	70 – 150	< 75	3 – 20 (1 – 17)	6 – 22 (0 – 10)
1 year	70 – 150	< 75	2 – 20 (1 – 20)	6 – 23 (0 – 7)
5 years	80 – 160	< 80	1 – 16 (2 – 22)	8 – 25 (0 – 5)
10 years	90 – 170	< 85	1 – 12 (3 – 25)	9 – 26 (0 – 4)



Table 3. QRS axis and QRS progression

Age group	ECG Characteristics
Premature infants ( $< 35$ weeks gestation)	Left & posterior QRS axis Relative LV dominant; smaller R in V1, taller R in V6
Full term infant	Right axis deviation ( $30^\circ$ to $180^\circ$ ) RV dominant Tall R in V1, Deep S in V6, R/S ratio $> 1$ in V1 T wave in V1 may be upright for 48 hours
1 to 6 months	Less right axis deviation ( $10^\circ$ to $120^\circ$ ) RV remains dominant Negative T waves across right praecordial leads
6 months to 3 years	QRS axis $< 90^\circ$ R wave dominant in V6 R/S ratio $\leq 1$ in V1
3 to 8 years	Adult QRS progression in praecordial leads LV dominant, Dominant S in V1, R in V6 Q wave in V5-6 (amplitude $< 5$ mm)

### Important normal variants

- T wave inversion of right praecordial leads (V1 – V3): normal findings from day 2 of life until late teens. An upright T wave in V1 before 8 years old is indicative of RVH
- Q wave may be present in leads I, aVL, V5 and V6 provided amplitude  $< 5$  mm
- RSR' pattern of right praecordial leads: normal in some children provided QRS duration  $< 10$  msec and R' amplitude  $< 15$  mm (infants) or 10 mm (children)
- elevated J point: normal in some adolescents

### Criteria for Right Ventricular Hypertrophy

- R  $> 20$  mm in V1 at all ages
- S  $> 14$  mm (0 to 7 days);  $> 10$  mm (1 week - 6 mths);  $> 7$  mm (6 mths - 1 year);  $> 5$  mm ( $> 1$  year) in V6
- R/S ratio  $> 6.5$  (0 - 3 mths); 4.0 (3 - 6 mths); 2.4 (6 mths - 3 years); 1.6 (3 to 5 years); 0.8 (6 to 15 years) in V1
- T wave upright in V4R or V1 after 72 hrs of life
- presence of Q wave in V1

### Criteria for Left Ventricular Hypertrophy

- S  $> 20$  mm in V1
- R  $> 20$  mm in V6
- S (V1) + R (V6)  $> 40$  mm over 1 year of age;  $> 30$  mm if  $< 1$  year
- Q wave  $> 4$  mm in V5-6
- T wave inversion in V5-6

# CONGENITAL HEART DISEASE IN THE NEWBORN

## Introduction

Congenital heart diseases (CHD) encompass a spectrum of structural abnormalities of the heart or intrathoracic vessels.

Commonly presents in the newborn with central cyanosis, heart failure, sudden collapse or heart murmur.

## Central Cyanosis

- bluish discoloration of lips and mucous membranes
- caused by excess deoxygenated haemoglobin ( $> 5 \text{ Gm/dL}$ )
- confirmed by pulse oxymetry ( $\text{SpO}_2 < 85\%$ ) or ABG

## Heart Failure

clinical presentation may mimic pulmonary diseases or sepsis:

- tachypnoea
- hepatomegaly
- tachycardia
- weak pulses

## Sudden Collapse

can be difficult to be distinguished from sepsis or metabolic disorders:

- hypotension
- metabolic acidosis
- extreme cyanosis
- oliguria

Table 2. Causes of heart failure in the newborn

<b>structural heart lesions</b>
<i>obstructive left heart lesions</i>
hypoplastic left heart syndrome, critical aortic stenosis, severe coarctation of aorta
<i>severe valvular regurgitation</i>
truncal arteriosus with truncal valve regurgitation
<i>large left to right shunts</i>
patent ductus arteriosus, ventricular septal defects, truncus arteriosus, aortopulmonary collaterals
<i>obstructed pulmonary venous drainage</i>
total anomalous pulmonary venous drainage
<b>myocardial diseases</b>
<i>cardiomyopathy</i>
infant of diabetic mother, familial, idiopathic
<i>ischaemic</i>
anomalous origin of left coronary artery from pulmonary artery, perinatal asphyxia
<i>myocarditis</i>
<i>arrhythmias</i>
atrial flutter, SVT, congenital heart block
<b>extracardiac</b>
<i>severe anaemia</i>
<i>neonatal thyrotoxicosis</i>
<i>fulminant sepsis</i>

Table 1. Causes of cyanosis in the newborn

<b>cyanotic heart diseases</b>
<i>obstructed pulmonary flow</i>
pulmonary atresia, critical pulmonary stenosis, tetralogy of Fallot
<i>discordant ventriculo-arterial connection</i>
transposition of great arteries
<i>common mixing</i>
single ventricle, truncus arteriosus, tricuspid atresia, total anomalous pulmonary venous drainage
<b>primary pulmonary disorders</b>
<i>parenchymal disease</i>
meconium aspiration syndrome, respiratory distress syndrome, congenital pneumonia
<i>extraparenchymal disease</i>
pneumothorax, congenital diaphragmatic hernia
<b>persistent pulmonary hypertension of newborn</b>
<i>primary</i>
<i>secondary</i>
meconium aspiration, perinatal asphyxia, congenital diaphragmatic hernia
<b>severe polycythaemia</b>
<b>methaemoglobinaemia</b>

Table 3. Congenital heart lesions that may present with sudden collapse

<i>duct-dependent systemic circulation</i>
coarctation of aorta, critical aortic stenosis, hypoplastic left heart syndrome, interrupted aortic arch
<i>duct-dependent pulmonary circulation</i>
pulmonary atresia with intact ventricular septum, tricuspid atresia with pulmonary atresia, single ventricle with pulmonary atresia, critical pulmonary stenosis
<i>transposition of great arteries without septal defect</i>
<i>obstructed total anomalous pulmonary drainage</i>

## Challenges and Pitfalls

- cyanosis is easily missed in the presence of anaemia.
- difficulty to differentiate cyanotic heart disease from non-cardiac causes
- indistinguishable clinical presentations between left heart obstructive lesions and severe sepsis or metabolic disorders
- possibility of congenital heart disease not considered in management of sick infant

### Clinical Approach to infants with Congenital Heart Disease

#### History

- antenatal scans (cardiac malformation, fetal arrhythmias, hydrops)
- family history of congenital heart disease
- maternal illness: diabetes, rubella, teratogenic medications
- perinatal problems: prematurity, meconium aspiration, perinatal asphyxia

#### Physical Examination

- dysmorphism: Trisomy 21, 18 and 13, Turner syndrome, DiGeorge syndrome
- central cyanosis
- differential cyanosis (SpO<sub>2</sub> lower limbs < upper limbs)
- tachypnoea
- weak or unequal pulses
- heart murmur
- hepatomegaly

#### Investigations

- chest X-ray
- hyperoxia test: administer 100% oxygen via headbox at 15 L/min for 15 mins.  
ABG taken from right radial artery  
cyanotic heart diseases: pO<sub>2</sub> < 100 mmHg; rise in pO<sub>2</sub> is < 20 mmHg  
(note: in severe lung diseases & PPHN, pO<sub>2</sub> can be < 100 mmHg)
- echocardiography

Table 4. Summary of clinical approach to cyanotic newborns

cause	history, signs	chest X-ray	ABG	hyperoxia test	Echo
<b>cyanotic heart disease</b>	no / mild respiratory distress; heart murmur	abnormal heart size, pulmonary vasculature	low pO <sub>2</sub> normal pCO <sub>2</sub>	no rise in pO <sub>2</sub>	usually diagnostic
<b>primary lung disease</b>	respiratory distress	abnormal lungs	low pO <sub>2</sub> high pCO <sub>2</sub>	pO <sub>2</sub> > 100 mmHg	normal
<b>persistent pulmonary hypertension</b>	suggestive history (MAS, asphyxia, sepsis)	may be abnormal (lungs)	differential cyanosis	inconclusive	right to left shunt across PFO or PDA
<b>methemoglobinemia</b>	normal	normal	normal	pO <sub>2</sub> > 100 mmHg	normal

MAS, meconium aspiration syndrome; PFO, patent foramen ovale; PDA, patent ductus arteriosus

#### General principles of management

- initial stabilization – secure airway, adequate ventilation, circulatory support
- correct metabolic acidosis, electrolyte, hypoglycaemia; prevent hypothermia
- empirical treatment with IV antibiotics
- early cardiology consultation
- IV Prostaglandin E infusion if duct-dependent lesions suspected  
starting dose: 10 – 40 ng/kg/min; maintenance: 2 – 10 ng/kg/min  
adverse effects: apnoea, fever, hypotension
- unresponsive to IV prostaglandin E, consider:
  - transposition of great arteries, obstructed total anomalous pulmonary venous drainage
  - blocked IV line
  - non-cardiac diagnosis
- arrangement to transfer to regional cardiac center once stabilized

# CONGENITAL HEART DISEASE

## SPECIFIC MANAGEMENT STRATEGIES FOR COMMON LESIONS

### LEFT TO RIGHT SHUNTS

#### Atrial septal defects (ASD)

- *small defects*: - no treatment
- *large defects*: - elective closure at 4-5 years age

#### Ventricular septal defects (VSD)

- *small defects*:
  - no treatment; high rate of spontaneous closure
  - SBE prophylaxis
  - yearly follow up for aortic valve prolapse, regurgitation
  - surgical closure indicated if prolapsed aortic valve
- *moderate defects*:
  - anti-failure therapy if heart failure
  - surgical closure if:
    - heart failure not controlled by medical therapy
    - persistent cardiomegaly on chest X-ray
    - elevated pulmonary arterial pressure
    - aortic valve prolapse or regurgitation
    - one episode of infective endocarditis
- *large defects*:
  - early primary surgical closure
  - pulmonary artery banding followed by VSD closure in multiple VSDs

#### Persistent ductus arteriosus (PDA)

- *small PDA*:
  - no treatment if there is no murmur
  - if murmur present: elective closure as risk of endarteritis.
- *moderate to large PDA*:
  - anti-failure therapy if heart failure
  - timing, method of closure (surgical vs transcatheter) depends on symptom severity, size of PDA and body weight

#### Atrioventricular septal defects (AVSD)

- *partial AVSD*:
  - elective surgical repair at 4 to 5 years old;
  - earlier if symptomatic or severe AV valve regurgitation
- *complete AVSD*:
  - primary surgical repair < 6 months age to prevent pulmonary vascular disease
  - In selected patients - e.g. with severe AV valve regurgitation and older patients, conservative treatment is an option as surgical outcomes are poor

### OBSTRUCTIVE LESIONS

#### Pulmonary stenosis (PS)

- *mild*:
  - no treatment
  - (*peak systolic gradient* < 50 mmHg)
- *moderate-severe*:
  - transcatheter balloon valvuloplasty is treatment of choice
  - (*gradient* > 50 mmHg)
- *neonatal critical PS*: characterized with cyanosis and RV dysfunction
  - temporary stabilization with IV Prostaglandin E infusion
  - early transcatheter balloon valvuloplasty

*SBE prophylaxis is indicated in all cases*

## Coarctation of the aorta (CoA)

- *neonatal severe CoA*: frequently associated with large malaligned VSD and intractable heart failure
  - sick infants require temporary stabilization
    - mechanical ventilation
    - correction of metabolic acidosis, hypoglycaemia, electrolyte imbalances
    - IV Prostaglandin E infusion
  - early surgical repair (single-stage CoA repair + VSD closure or 2 stage CoA repair followed by VSD closure at later date)
- *asymptomatic / older children*
  - with discrete CoA*:
    - presents with incidental hypertension or heart murmur
    - choice of treatment (primary transcatheter balloon angioplasty, stent implantation or surgical repair)
    - depends on morphology of CoA and age of presentation

## CYANOTIC HEART LESIONS

### Tetralogy of Fallot (TOF)

- most TOFs suitable for single stage surgical repair at 1 to 2 years age
- indications for modified Blalock Taussig shunt:
  - hypercyanotic spells or severe cyanosis < 6 months age when child is too young for total repair
  - small pulmonary arteries; to promote growth before definitive repair
  - anomalous coronary artery crossing in front of right ventricular outflow tract - precludes transannular incision; repair with conduit required at later age
- following surgical repair, patients need life-long follow up for late right ventricular dysfunction; some may require pulmonary valve replacement

### Transposition of the great arteries (TGA)

- *simple TGA*:
  - IV Prostaglandin E infusion promotes intercirculatory mixing at PDA
  - early balloon atrial septostomy (BAS) if restrictive interatrial communication
  - surgical repair of choice: arterial switch operation at 2 to 4 weeks age
  - left ventricular regression may occur if repair not performed within 4 weeks of life
- *TGA with VSD*:
  - do not usually require intervention during early neonatal period; may develop heart failure at 1 to 2 months age
  - elective one-stage arterial switch operation + VSD closure before 3 months age
- *TGA with VSD and PS*:
  - Blalock Taussig shunt during infancy followed by Rastelli repair at 4 to 6 years age

### Pulmonary atresia with intact ventricular septum

- IV prostaglandin E infusion to maintain ductal patency in early neonatal period
- further management strategy depends on the degree of right ventricular hypoplasia

### Truncus arteriosus

- surgical repair (VSD closure and RV-to-PA conduit) before 3 months of age

### Tetralogy of Fallot with pulmonary atresia

- IV prostaglandin E infusion is often required during early neonatal period
- further management strategy depends on the anatomy of the pulmonary arteries and presence of aortopulmonary collaterals

### Single ventricle

includes 3 main categories of lesions:

- *double inlet ventricles*:  
double inlet left ventricle, double inlet right ventricle
- *atretic or stenosed atrioventricular connections*:  
tricuspid atresia, mitral atresia, hypoplastic left heart syndrome
- *miscellaneous lesions which preclude biventricular circulation*:  
unbalanced AV septal defect, double outlet right ventricle with remote VSD, congenital corrected transposition of great arteries, heterotaxy syndromes

Requires staged management approach for eventual Fontan procedure

### Total anomalous pulmonary venous drainage

- 4 major anatomic types: supracardiac, cardiac, infracardiac and mixed
- management strategy depends on presence of pulmonary venous obstruction
  - *obstructed pulmonary venous drainage (frequent in infracardiac type)*
    - presents with respiratory distress and heart failure
    - initial stabilization: oxygen, diuretics, positive pressure ventilation
    - surgical repair immediately after initial stabilization
  - *unobstructed pulmonary venous drainage*
    - early surgical repair is required

## HYPERCYANOTIC SPELL

### Introduction

Sudden severe episodes of intense cyanosis caused by reduction of pulmonary flow in patients with underlying Tetralogy of Fallot or other cyanotic heart lesions. This is due to spasm of the right ventricular outflow tract or reduction in systemic vascular resistance (e.g. hypovolaemia) with resulting increased in right to left shunt across the VSD.

### Clinical Presentation

- peak incidence age: 3 to 6 months
- often in the morning, can be precipitated by crying, feeding or defaecation
- severe cyanosis, hyperpnoea, metabolic acidosis
- in severe cases, may lead to syncope, seizure, stroke or death
- there is a reduced intensity of systolic murmur during spell

### Management

- treat this as a *medical emergency*
- knee-chest/squatting position:
  - place the baby on the mother's shoulder with the knees tucked up underneath.
  - this provides a calming effect, reduces systemic venous return and increases systemic vascular resistance
- administer 100% oxygen
- give IV/IM/SC morphine 0.1 – 0.2 mg/kg to reduce distress and hyperpnoea

If above measures fail:

- give IV Propranolol 0.05 – 0.1 mg/kg slow bolus over 10 mins
- alternatively, IV Esmolol 0.5 mg/kg slow bolus over 1 min, followed by 0.05 mg/kg/min for 4 mins.
  - can be given as continuous IV infusion at 0.01 – 0.02 mg/kg/min.
  - Esmolol is an ultra short acting beta blocker
- volume expander (crystalloid or colloid) 20 ml/kg rapid IV push to increase preload
- give IV sodium bicarbonate 1 mEq/kg to correct metabolic acidosis
- heavy sedation, intubation and mechanical ventilation

In resistant cases, consider

- IV Phenylephrine / Noradrenaline infusion to increase systemic vascular resistance and reduce right to left shunt
- emergency Blalock Taussig shunt

*Other notes:*

- a single episode of hypercyanotic spell is an indication for early surgical referral (either total repair or Blalock Taussig shunt).
- oral propranolol 0.2 – 1 mg/kg/dose 8 to 12 hourly should be started soon after stabilization while waiting for surgical intervention.

## HEART FAILURE

### Definition

Defined as the inability to provide adequate cardiac output to meet the metabolic demand of the body.

### Causes of heart failure (see Table 1)

- congenital structural heart lesions, more commoner during infancy
- primary myocardial and acquired valvular diseases, more common in older children

### Clinical presentation

- varies with age of presentation
- symptoms of heart failure in infancy
  - feeding difficulty: poor suck, prolonged time to feed, sweating during feed
  - recurrent chest infections
  - failure to thrive
- signs of heart failure in infancy
  - resting tachypnoea, subcostal recession
  - tachycardia
  - hyperactive praecordium, praecordial bulge
  - hepatomegaly
  - poor peripheral pulses, poor peripheral perfusion
  - wheezing
- common signs of heart failure in adults, i.e. increased jugular venous pressure, leg oedema and basal lung crackles are *not usually* found in children

Table 1. Causes of heart failure

<b>congenital heart disease</b> left to right shunt lesions VSD, PDA, AVSD, ASD <i>obstructive left heart lesions</i> hypoplastic left heart syndrome, coarctation of aorta, aortic stenosis <i>common mixing with unrestricted pulmonary flow</i> truncus arteriosus, TAPVD, tricuspid atresia with TGA, single ventricle, pulmonary atresia with VSD, large aortopulmonary collateral <i>valvular regurgitation</i> AV valve regurgitation, Ebstein anomaly, semilunar valve regurgitation <i>myocardial ischaemia</i> anomalous origin of left coronary artery from pulmonary artery	<b>myocardial disease</b> <i>primary cardiomyopathy</i> idiopathic, familial <i>secondary cardiomyopathy</i> - drug-induced: anthracycline - infection: post viral myocarditis, Chagas disease - ischaemic: Kawasaki disease - myopathic: muscular dystrophy, Pompe disease, mitochondrial disorders - metabolic: hypothyroidism - arrhythmia-induced – congenital heart block, atrial ectopic tachycardia - others – iron overload (thalassaemia) acute myocarditis viral, rheumatic, Kawasaki disease
<b>acquired valvular disease</b> <i>chronic rheumatic valvular diseases</i> <i>post infective endocarditis</i>	<b>miscellaneous</b>



## Treatment

### General measures

- oxygen supplementation, propped up position
- keep warm & gentle handling
- fluid restriction to  $\frac{3}{4}$  normal maintenance if not dehydrated or in shock
- optimize caloric intake; low threshold for nasogastric feeding;  
    consider overnight continuous infusion feeds
- correct anaemia, electrolyte imbalance, treat concomitant chest infections

### Antifailure medications

- frusemide (loop diuretic)
  - dose: 1 mg/kg/dose OD to QID, oral or IV
  - continuous IV infusion at 0.1 – 0.5 mg/kg/hour if severe fluid overload
  - use with potassium supplements (1 - 2 mmol/kg/day) or add potassium sparing diuretics
- spironolactone (potassium sparing diuretic, modest diuretic effect)
  - dose: 1 mg/kg/dose BD
- captopril
  - angiotensin converting enzyme inhibitor, afterload reduction agent
  - dose: 0.1 mg/kg/dose TDS, gradual increase up to 1 mg/kg/dose TDS
  - monitor potassium level (risk of hyperkalaemia)
- digoxin
  - role controversial
  - useful in heart failure with excessive tachycardia, supraventricular tachyarrhythmias
- IV inotropic agents - i.e. Dopamine, Dobutamine, Adrenaline, Milrinone
  - used in acute heart failure, cardiogenic shock, post-op low output syndrome

### Specific management

- establishment of definitive aetiology is of crucial importance
- specific treatment targeted to underlying aetiology. Examples:
  - surgical/transcatheter treatment of congenital heart lesion
  - pacemaker implantation for heart block
  - control of blood pressure in post-infectious glomerulonephritis
  - high dose aspirin  $\pm$  steroid in acute rheumatic carditis

# ACUTE RHEUMATIC FEVER

## Introduction

An inflammatory disease of childhood resulting from untreated *Streptococcus pyogenes* (group A streptococcus) pharyngeal infections.  
Peak incidence 5 to 15 years; more common in females.

Table 1. Diagnostic criteria for Acute Rheumatic Fever

Major Criteria	Minor Criteria	Investigations
carditis <sup>1</sup> polyarthritis, polyarthralgia or aseptic monoarthritis chorea erythema marginatum subcutaneous nodules	fever (temperature > 38 °C) ESR > 30 mm/h or CRP > 30 mg/L prolonged PR interval	FBC - anaemia, leucocytosis ESR and CRP elevated. Throat swab, ASOT Blood culture CXR, ECG. Echocardiogram
<b>Making the Diagnosis</b>		
initial episode of ARF	Recurrent attack of ARF (known past ARF or RHD)	1. Evidence of carditis : - cardiomegaly - cardiac failure - pericarditis - tachycardia out of proportion to fever, sleep - pathological or changing murmurs
2 major criteria or 1 major + 2 minor criteria	2 major criteria or 1 major + 2 minor criteria or 3 minor criteria	
<b>PLUS</b> evidence of a preceding group A streptococcal infection		

ARF, Acute Rheumatic Fever; RHD, Rheumatic Heart Disease

Source: Australian 2005 Guidelines

## Treatment

Aim to suppress inflammatory response so as to minimize cardiac damage, provide symptomatic relief and eradicate pharyngeal streptococcal infection

- bed rest. Restrict activity until acute phase reactants return to normal
- anti-streptococcal therapy
  - IV C. Penicillin 50 000U/kg/dose 6H
  - or oral Penicillin V 250 mg 6H (<30kg), 500 mg 6H (>30kg) for 10 days
  - oral Erythromycin for 10 days if allergic to penicillin.
- anti-inflammatory therapy
  - *mild / no carditis*:  
oral Aspirin 80-100 mg/kg/day in 4 doses for 2-4 weeks, taper over 4 weeks
  - *pericarditis, or moderate to severe carditis*:  
oral Prednisolone 2 mg/kg/day in 2 divided doses for 2 - 4 weeks, taper with addition of aspirin as above.
- anti-failure medications
  - diuretics, ACE inhibitors, digoxin (to be used with caution).

Consider early referral to paediatric cardiologist if heart failure persists or worsens during the acute phase despite aggressive medical therapy. Surgery may be indicated.

## Secondary Prophylaxis of Rheumatic Fever

- IM Benzathine Penicillin 0.6 mega units (<30 kg)  
or 1.2 mega units (>30 kg) every 3 to 4 weeks
- oral Penicillin V 250 mg twice daily
- oral Erythromycin 250 mg twice daily if allergic to Penicillin

## Duration of prophylaxis

- until age 21 years or 5 years after last attack of ARF whichever was longer
- lifelong for patients with carditis and valvular involvement.

## INFECTIVE ENDOCARDITIS

### Introduction

An uncommon condition in children but has a high morbidity and mortality if untreated.

Underlying risk factors include:

- congenital heart disease
- repaired congenital heart defects
- congenital or acquired valvular heart diseases
- immunocompromised patients with indwelling central catheters

Common symptoms are unexplained remitting fever > 1 week, loss of weight, loss of appetite and myalgia.

Table 1. Modified Duke Criteria for the Diagnosis of Infective Endocarditis

Major Criteria	Minor Criteria
<ul style="list-style-type: none"> <li>• blood culture positive: typical microorganisms from two separate blood cultures: <i>Viridans streptococci</i>, <i>Streptococcus bovis</i>, HACEK group,<sup>1</sup> <i>Staphylococcus aureus</i> community-acquired enterococci</li> <li>• evidence of endocardial involvement on echocardiogram</li> </ul> <p><i>1. fastidious gram negative bacteria from Haemophilus spp, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens and Kingella kingae</i></p>	<ul style="list-style-type: none"> <li>• predisposing heart condition, prior heart surgery, indwelling catheter</li> <li>• fever, temperature &gt; 38°C</li> <li>• vascular phenomena: <ul style="list-style-type: none"> <li>- major arterial emboli</li> <li>- septic pulmonary infarcts</li> <li>- mycotic aneurysm</li> <li>- intracranial hemorrhage,</li> <li>- conjunctival hemorrhages</li> <li>- Janeway's lesions</li> </ul> </li> <li>• immunologic phenomena: <ul style="list-style-type: none"> <li>- glomerulonephritis</li> <li>- Osler's nodes</li> <li>- Roth's spots</li> <li>- rheumatoid factor</li> </ul> </li> <li>• microbiological evidence: positive blood culture not meeting major criterion</li> </ul>

Table 2. Definition of Infective Endocarditis According to the Modified Duke Criteria

definite IE	possible IE	rejected IE
<ul style="list-style-type: none"> <li>• pathological criteria <ol style="list-style-type: none"> <li>1. microorganisms by <ul style="list-style-type: none"> <li>- culture</li> <li>- histological examination of vegetation or intracardiac abscess specimen</li> </ul> </li> <li>2. pathological lesions with active endocarditis</li> </ol> </li> <li>• clinical criteria: <ol style="list-style-type: none"> <li>2 major or</li> <li>1 major + 3 minor or</li> <li>5 minor</li> </ol> </li> </ul>	<ul style="list-style-type: none"> <li>- 1 major + 1 minor criteria</li> <li>- 3 minor</li> </ul>	<ul style="list-style-type: none"> <li>• firm alternative diagnosis</li> <li>• resolution of symptoms with antibiotic therapy &lt; 4 days</li> <li>• no pathological evidence of IE at surgery or autopsy</li> <li>• not meet criteria for possible IE</li> </ul>

IE, Infective Endocarditis

### Investigations

- blood culture
- C- Reactive protein/ESR
- full blood count
- urine FEME
- Chest X-ray
- echocardiography

## Management

- ensure 3 blood cultures taken before antibiotic therapy.  
Do not wait for echocardiography.
- use empirical antibiotics, until culture results available (refer Table 3) .

*Table 3: Antibiotic choices for Infective endocarditis in Children  
(Adapted from Malaysian CPG on antibiotic usage)*

Indication	preferred regime	alternative regime
Empirical Therapy For Infective Endocarditis	IV Penicillin G 200 000 U/kg per day in 4–6 divided doses x 4 weeks AND IV/IM Gentamicin 3 mg/kg per day in 3 divided doses x 2 weeks	IV Vancomycin 30 mg/kg per day in 2 divided doses x 4–6 weeks AND IV/IM Gentamicin 3 mg/kg per day in 3 divided doses x 2 weeks
<i>Streptococcus viridans</i> endocarditis	IV Vancomycin 30 mg/kg per day in 2 divided doses x 4–6 weeks AND IV/IM Gentamicin 3 mg/kg per day in 3 divided doses x 2 weeks	IV Vancomycin 30 mg/kg per day in 2 divided doses x 4–6 weeks AND IV/IM Gentamicin 3 mg/kg per day in 3 divided doses x 2 weeks
<i>Enterococcus</i> endocarditis	IV Penicillin G 300 000 U/kg/day in 4–6 divided doses x 4 - 6 weeks AND IV Gentamicin 3 mg/kg/day in 3 divided doses x 4 - 6 weeks	
Methicillin sensitive <i>Staphylococcus</i> endocarditis	IV Cloxacillin 200mg/kg/day in 4-6 divided doses x 6 weeks +/- IV/IM Gentamicin 3mg/kg/day in 3 divided doses x 3 - 5 days	
Penicillin allergy	IV Cefazolin 100mg/kg/day in 3 divided doses x 6 weeks	IV Vancomycin 40 mg/kg /day in 2 - 3 divided doses x 4-6 weeks
Methicillin Resistance	IV Vancomycin 40 mg/kg/day in 2 - 4 divided doses x 6 weeks	
Culture- Negative Endocarditis	IV Ampicillin-sulbactam 300mg/kg/day in 4-6 divided doses x 4-6 weeks AND IV Gentamicin 3mg/kg/day in 3 divided doses x 4-6 weeks	IV Vancomycin 40 mg/kg /day in 2 - 3 divided doses x 4-6 weeks AND IV/IM Gentamicin 3mg/kg/day in 3 divided doses x 4-6 weeks AND IV Ciprofloxacin 20-30 mg/kg/day in 2 divided doses x 4-6 weeks
Fungal Endocarditis <i>Candida spp</i> or <i>Aspergillosis</i>	IV Amphotericin B > 6 weeks AND Valve replacement surgery AND Long-term (lifelong) therapy with oral azole	

Table 4. Guidelines on IE prophylaxis

Endocarditis prophylaxis recommended	Endocarditis prophylaxis not recommended
<i>High-risk category</i>	<i>Negligible-risk category</i>
prosthetic cardiac valves	isolated secundum atrial septal defect
previous bacterial endocarditis	repaired atrial and ventricular septal defects,
complex cyanotic congenital heart disease	patent ductus arteriosus (after 6 mths)
surgical systemic pulmonary shunts or conduits	mitral valve prolapse without regurgitation
<i>Moderate-risk category</i>	functional, or innocent heart murmurs
other congenital cardiac malformations	previous Kawasaki disease
(other than above and below)	without valvar dysfunction
acquired valvar dysfunction	previous rheumatic fever
(e.g. rheumatic heart disease)	without valvar dysfunction
hypertrophic cardiomyopathy	cardiac pacemakers and implanted defibrillators
mitral valve prolapse with regurgitation	

Table 5. Common procedures that require IE prophylaxis

<i>Oral, dental procedures</i>	<i>Gastrointestinal procedures</i>
extractions, periodontal procedures	sclerotherapy for esophageal varices
placement of orthodontic bands (but not brackets)	oesophageal stricture dilatation
intraligamentary local anaesthetic injections	endoscopic retrograde cholangiography
prophylactic cleaning of teeth	biliary tract surgery
<i>Respiratory procedures</i>	surgical operations involving intestinal mucosa
tonsillectomy or adenoidectomy	<i>Genitourinary procedures</i>
surgical operations involving respiratory mucosa	cystoscopy
rigid bronchoscopy	urethral dilation
flexible bronchoscopy with biopsy	

Table 6. Antibiotic guidelines for IE prophylaxis

*Endocarditis Prophylactic Regimens for Dental, Oral, Respiratory Tract and Esophageal Procedures*

#### Standard general prophylaxis

Oral Amoxicillin 50 mg/kg (max 2 Gm)

one hour before procedure

or

IV/IM Ampicillin 50 mg/kg (max 2 Gm)

#### Penicillin allergy

Oral Clindamycin 20 mg/kg (max 600 mg)

or

Oral Cephalexin 50 mg/kg (max 2 Gm)

or

Oral Azithromycin/clarithromycin 50 mg/kg (max 500 mg)

or

Oral Erythromycin 20 mg/kg (max 3 Gm)

or

IV Clindamycin 20 mg/kg (max 600 mg)

*Note: give oral therapy 1 hour before procedure ;*

*IV therapy 30 mins before procedure*

# KAWASAKI DISEASE

## Introduction

A systemic febrile condition affecting children usually < 5 years old.

Aetiology remains unknown, possible bacterial toxins or viral agents with genetic predisposition. Also known as mucocutaneous lymph node syndrome.

Table 1. Diagnostic criteria for Kawasaki Disease

Diagnostic Criteria
<ul style="list-style-type: none"><li>• fever lasting at least 5 days.</li><li>• at least 4 out of 5 of the following:<ul style="list-style-type: none"><li>- bilateral non-purulent conjunctivitis</li><li>- mucosal changes of the oropharynx (injected pharynx, red lips, dry fissured lips, strawberry tongue).</li><li>- changes in extremities (oedema and/or erythema of the hands or feet, desquamation, beginning periungually).</li><li>- rash (usually truncal), polymorphous but non vesicular.</li><li>- cervical lymphadenopathy</li></ul></li><li>• illness not explained by other disease process.</li></ul>

## Clinical Pearls

Diagnosis is via criteria listed in Table 1.

Other helpful signs:

- indurated BCG scar
- perianal excoriation, irritability
- altered mental state
- aseptic meningitis
- transient arthritis
- diarrhoea, vomiting, abdominal pain
- hepatosplenomegaly
- hydrops of gallbladder
- sterile pyuria

## Investigations

- full blood count
  - anaemia, leucocytosis, thrombocytosis.
- ESR and CRP elevated
- serum albumin < 3g / dl; Raised alanine aminotransaminase
- urine >10 wbc / hpf
- chest X-ray, ECG.
- echocardiogram in the acute phase and repeat at 6-8 weeks or earlier if indicated.

Most important complication is coronary vasculitis, usually within 2 weeks of illness, affecting up to 25% of untreated children. Usually asymptomatic, it may manifest as myocardial ischaemia, infarction, pericarditis, myocarditis, endocarditis, heart failure and arrhythmias.

## Incomplete Kawasaki Disease

Patients who do not fulfill the classic diagnostic criteria outlined above. Tends to occur in infants and the youngest patients. High index of suspicion should be maintained for the diagnosis of incomplete KD. Higher risk of coronary artery dilatation or aneurysm occurring.

Echocardiography is indicated in patients who have prolonged fever with:

- two other criteria,
- subsequent unexplained periungual desquamation,
- two criteria + thrombocytosis
- rash without any other explanation.

## Atypical Kawasaki Disease

For patients who have atypical presentation, such as renal impairment, that generally is not seen in Kawasaki Disease.

### Treatment

#### Primary treatment

- IV Immunoglobulins 2 Gm/kg infusion over 10 - 12 hours.  
Therapy < 10 days of onset effective in preventing coronary vascular damage.
- Oral Aspirin 30 mg/kg/day for 2 weeks or until patient is afebrile for 2-3 days.

**Maintenance:** Oral Aspirin 3-5 mg/kg daily (anti-platelet dose) for 6 - 8 weeks or until ESR and platelet count normalise.  
If coronary aneurysm present, then continue aspirin until resolves.  
Alternative: Oral Dipyridamole 3 - 5 mg/kg daily

#### Kawasaki Disease not responding to Primary Treatment

Defined as persistent or recrudescent fever ≥ 36hours after initial IVIG infusion.

**Treatment:** Repeat IV Immunoglobulins 2 Gm/kg infusion over 10 - 12 hours

Table 2. Risk stratification and long term follow up

risk level	treatment	physical activity	follow up	invasive testing
<b>Level I</b> no coronary artery changes	none beyond 6-8 weeks	no restrictions beyond 6-8 weeks	cardiovascular risk assessment, counselling at 5yr intervals	none
<b>Level II</b> transient coronary artery ectasia; none after 6-8 weeks	none beyond 6-8 weeks	no restrictions beyond 6-8 weeks	cardiovascular risk assessment, counselling at 3 to 5yr intervals	none
<b>Level III</b> one small-medium coronary artery aneurysm, major coronary artery	low dose aspirin until aneurysm regression documented	age <11 yr old: no restriction beyond 6-8 weeks . avoid contact sports if on aspirin	annual echocardiogram and ECG, and cardiovascular risk assessment counselling	angiography if non-invasive test suggests ischemia
<b>Level IV</b> > 1 large or giant coronary artery aneurysm, or multiple or complex aneurysms in same coronary artery, without destruction	long term aspirin & warfarin (target INR 2.0-2.5) or LMWH in giant aneurysms	avoid contact sports	biannual echocardiogram and ECG; annual stress test	angiography at 6-12 mo or sooner if indicated; repeated study if non-invasive test, clinical or laboratory findings suggest ischemia
<b>Level V</b> coronary artery obstruction	long term aspirin; warfarin or LMWH if giant aneurysm persists. also consider β-blockers	avoid contact sports	biannual echocardiogram and ECG; annual stress test	angiography to address therapeutic options

LMWH, low molecular weight heparin

### Vaccinations

The use of Immunoglobulins may impair efficacy of live-attenuated virus vaccines. Delay these vaccinations for at least 3-6 months.

### Prognosis

Complete recovery in children without coronary artery involvement.  
Most (80%) 3 - 5 mm aneurysms resolve; 30% of 5 - 8 mm aneurysms resolve.  
Prognosis worst for aneurysms > 8 mm in diameter. Mortality in 1 - 2 %, usually from cardiac complications within 1 - 2 months of onset.

## VIRAL MYOCARDITIS

### Introduction

Defined as inflammation of the myocardium with myocellular necrosis. Viruses are found to be most important cause of acute myocarditis. Other causes include Mycoplasma, typhoid fever, diphtheria toxins etc.

### Clinical presentation

Vary from asymptomatic ECG abnormalities to acute cardiovascular collapse, even sudden death. There may be prodromal symptoms of viremia, including fever, myalgia, coryzal symptoms or gastroenteritis.

The diagnosis is made clinically, with a high index of suspicion, with the following presentation that cannot be explained in a healthy child:

- tachycardia
- respiratory distress
- other signs of heart failure
- arrhythmia

### Management

Depends on the severity of the illness. patients with heart failure require intensive monitoring and haemodynamic support. treatment of heart failure (refer Heart Failure chapter) consider early respiratory support with mechanical ventilation in severe cases

### Specific treatment

Treatment with IV immunoglobulins and immunosuppressive drugs have been studied but the effectiveness remains controversial and routine treatment with these agents cannot be recommended at this moment

### Prognosis

One third of patients recover. One third improve clinically with residual myocardial dysfunction. The other third does poorly and develops chronic heart failure, which may cause mortality or require heart transplantation

Table 1. Useful investigations for myocarditis

#### electrocardiogram (ECG)

- sinus tachycardia
- non-specific ST segment, T wave abnormalities
- pathological Q wave
- T wave inversion
- low QRS voltages (<5mm in any precordial lead)
- arrhythmia - heart block, ventricular ectopics

#### chest x-ray

- cardiomegaly  
(normal heart size doesn't exclude myocarditis)
- pleural effusion

#### echocardiography

- findings often varied and non-specific, although rarely entirely normal*
- global left ventricular dilatation and hypocontractility
  - pericardial effusion
  - functional mitral regurgitation
  - other structural abnormalities especially coronary artery anomalies need to be excluded

#### cardiac biomarkers

- Troponin T, Troponin I
- creatinine kinase (CK) and CK-MB

#### microbiological studies, including polymerase chain reaction (PCR)

- enterovirus 71, coxsackie B virus, adenovirus
- parvovirus B19, cytomegalovirus, echovirus
- Mycoplasma, Salmonella typhi*

#### contrast enhanced MRI

- myocardial oedema, focal myocardial enhancement, regional wall motion abnormalities.



## PAEDIATRIC ARRHYTHMIAS

### BRADYARRHYTHMIA

#### Sinus node dysfunction

- criteria for sinus bradycardia

Table 1. ECG criteria

Age Group	Heart Rate
infants to < 3 years	<100 bpm
children 3 – 9 years	< 60 bpm
children 9 – 16 years	< 50 bpm
adolescents > 16 years	< 40 bpm

Table 2. 24 hours Ambulatory ECG criteria

Age Group	Heart Rate
infants to 1 year of age	< 60 bpm sleeping, < 80 bpm awake
children 1 – 6 years	< 60 bpm
children 7 – 11 years	< 45 bpm
adolescents, young adults	< 40 bpm
highly trained athletes	< 30 bpm

#### Systemic causes of sinus bradycardia:

- hypoxia
- intracranial lesions
- hypothyroidism
- electrolytes abnormalities i.e. hypokalaemia, hypocalcaemia
- sepsis
- acidosis
- anorexia nervosa

#### Causes of sinus node dysfunction

- right atrial dilatation due to volume loading
- cardiomyopathies
- inflammatory conditions: myocarditis, pericarditis, rheumatic fever
- post atrial surgery: Mustard, Senning, Fontan, ASD closure, cannulation for cardiopulmonary bypass

#### Atrioventricular block

##### Classification

- 1st degree - prolonged PR interval
- 2nd degree
  - Mobitz type 1 (Wenckebach): progressive PR prolongation before dropped AV conduction
  - Mobitz type 2: abrupt failure of AV conduction without prior PR prolongation
  - high grade – 3:1 or more AV conduction
- 3rd degree (complete heart block): AV dissociation with no atrial impulses conducted to ventricles

Note: 2nd degree (Type 2 and above) and 3rd degree heart block are *always* pathological

## Aetiology

- congenital – in association with positive maternal antibody (anti-Ro and anti-La); mother frequently asymptomatic
- congenital heart diseases: atrioventricular septal defect (AVSD), congenital corrected transposition of great arteries (L-TGA), left atrial isomerism
- congenital long QT syndrome
- surgical trauma: especially in VSD closure, TOF repair, AVSD repair, Konno procedure, LV myomectomy, radiofrequency catheter ablation
- myopathy: muscular dystrophies, myotonic dystrophy, Kearns-Sayre syndrome
- infection: diphtheria, rheumatic fever, endocarditis, viral myocarditis

## Acute Management of symptomatic bradycardia with haemodynamic instability

- treat the underlying systemic causes of bradycardia
- drugs:
  - IV atropine
  - IV isoprenaline infusion
  - IV adrenaline infusion
- transcutaneous pacing if available

Patients who are not responding to initial acute management should be referred to cardiologist for further management. Emergency transvenous pacing or permanent pacing may be required.

## TACHYARRHYTHMIA

### Classification

- atrial tachycardia – AF, EAT, MAT
- conduction system tachycardia or supraventricular tachycardia – AVRT, AVNRT, PJRT
- ventricular tachycardia – VT, VF

### Description

- Atrial flutter (AF)
  - saw tooth flutter waves
  - variable AV conduction
- Ectopic atrial tachycardia (EAT)
  - abnormal P wave axis
  - P wave precedes QRS
  - variable rate
  - “warm up” and “cool down” phenomenon
- Multifocal atrial tachycardia (MAT)
  - irregularly irregular
  - multiple different P wave morphologies, bizarre and chaotic
  - no two RR intervals the same
- Atrioventricular re-entry tachycardia (AVRT)
  - P wave follows QRS

Figure 2. Atrial flutter



Figure 3. Ectopic atrial tachycardia



Figure 4. Multifocal atrial tachycardia



Figure 5. Atrioventricular re-entry tachycardia



Figure 6. Atrioventricular nodal re-entry tachycardia



- Atrioventricular nodal re-entry tachycardia (AVNRT)
  - P wave not visible, superimposed on QRS
- Permanent junctional reciprocating tachycardia (PJRT)
  - inverted P waves in II, III, aVF appear to precede QRS complex
  - long RP interval
- Ventricular tachycardia (VT)
  - wide QRS complex
  - P wave may be dissociated from the QRS complex
- Ventricular fibrillation (VF)
  - chaotic, irregular rhythm

Figure 7. Permanent junctional reciprocating tachycardia



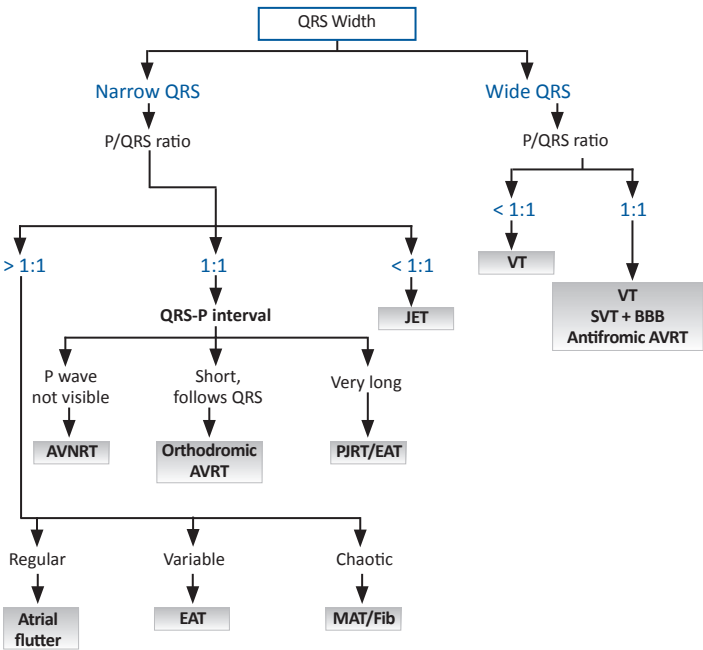
Figure 8. Ventricular tachycardia



Figure 8. Ventricular fibrillation

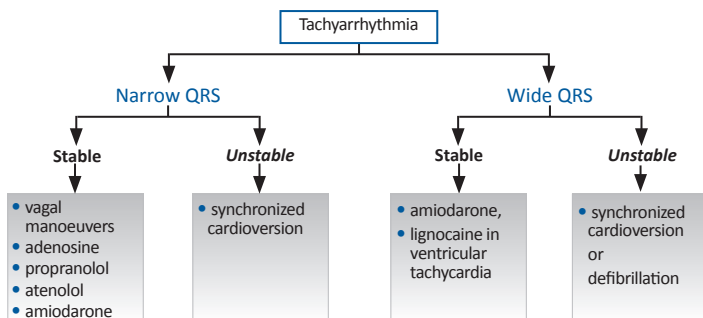


Figure 2. Algorithm for identifying tachycardia



Abbreviations. VT, ventricular tachycardia; JET< junctional ectopic tachycardia; SVT, supraventricular tachycardia; BBB, bundle branch block; AVRT, atrioventricular re-entry tachycardia; AVNRT, atrioventricular nodal re-entry tachycardia; PJRT, permanent junctional reciprocating tachycardia; EAT, ectopic atrial tachycardia; MAT, multifocal atrial tachycardia; Fib, fibrillation.

Figure 3. Algorithm for management of acute tachyarrhythmia



### Narrow QRS complex tachycardia

#### Haemodynamically stable

- vagal manoeuvres:
  - icepack/iced water for infants – apply to face for a maximum of 30 seconds
  - Valsalva manoeuvres if child is old enough (blow into a pinched straw)
- IV Adenosine: 0.1mg/kg (max 6mg) rapid push. Increase by 0.1mg/kg every 2 mins until tachycardia terminated or up to a maximum of 0.5mg/kg (maximum: 18 mg).
- IV propranolol 0.02mg/kg test dose, then 0.1mg/kg over 10 minutes
- IV amiodarone: 25mcg/kg/min for 4 hours then 5 -15mcg/kg/min until conversion

#### Haemodynamically unstable

- synchronized DC conversion at 0.5 to 1 joule/kg

### Wide QRS complex tachycardia

#### Haemodynamically stable

- IV amiodarone (same as above)
- IV procainamide
- IV lignocaine

#### Haemodynamically unstable

- synchronized cardioversion at 0.5 to 1.0 joule/kg
- in pulseless patients, defibrillate at 2 to 4 joules/kg

### Pitfalls in management

- to consult a cardiologist if these acute measures fail to revert the tachycardia.
- in Wolff-Parkinson-White syndrome, digoxin is contraindicated because paroxysm of atrial flutter or fibrillation can be conducted directly into the ventricle.
- adenosine unmasks the atrial flutter by causing AV block and revealing more atrial beats per QRS complex
- in wide QRS complex tachycardia with 1:1 ventriculoatrial conduction, it is reasonable to see if adenosine will cause cardioversion, thereby making a diagnosis of a conduction system dependent SVT
- a follow up plan should be made in consultation with cardiologist

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## NEUROLOGY

- 42 Status Epilepticus
- 43 Child with a first unprovoked seizure
- 44 Febrile Convulsions
- 45 Epilepsy
- 46 Meningitis
- 47 Acute Demyelination
- 48 Acute Flaccid Paralysis
- 49 Guillain Barré syndrome
- 50 Coma
- 51 Brain Death



# STATUS EPILEPTICUS

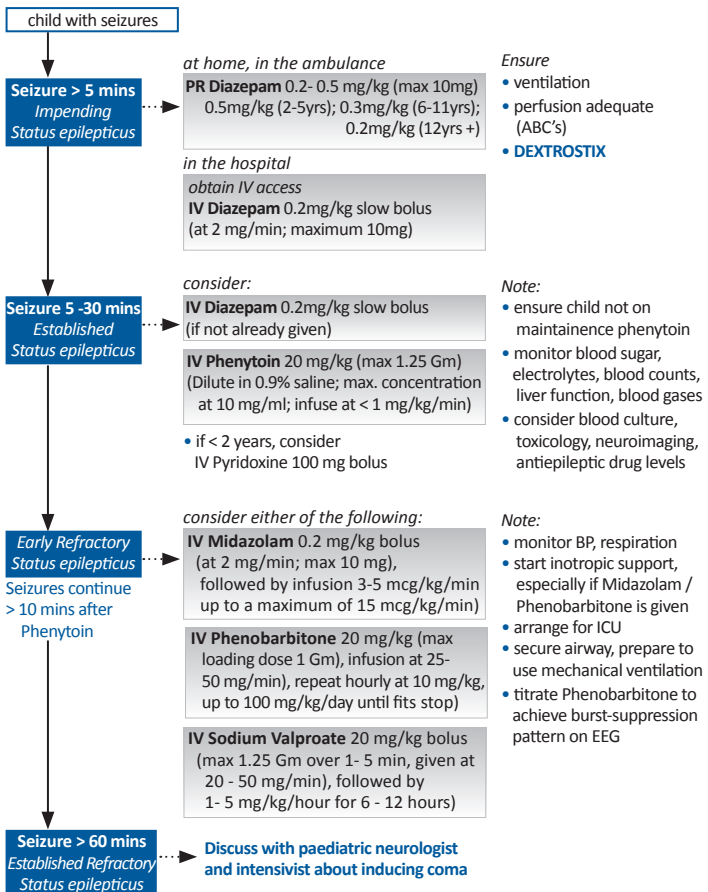
## Definition

- any seizure lasting > 30 minutes *or*
- intermittent seizures, without regaining full consciousness in between, for > 30 minutes

However, any seizure > 5 minutes is unlikely to abort spontaneously, and should be treated aggressively. Furthermore, there is evidence of progressive, time-dependent development of pharmaco-resistance if seizures continue to perpetuate.

*Refractory status epilepticus:* seizures lasting for >60 minutes or not responding to adequate doses of benzodiazepine and second line medications.

Figure 1. Algorithm for Status Epilepticus





## Salient Points

- apart from terminating seizures, management of SE should include, identifying and treating underlying cause
- presence of SE may mask usual signs and symptoms of meningitis or encephalitis, resulting in a danger of overlooking life-threatening infections.
- common mistakes in failing to treat status epilepticus (SE) are *under-dosing* of anticonvulsant and *excessive time lag* between doses/steps of treatment

## APPROACH TO A CHILD WITH A FIRST UNPROVOKED SEIZURE

### Definition

One or multiple *unprovoked afebrile* seizures within 24 hours with recovery of consciousness between seizures

### Notes:

- 30-50% of first unprovoked seizures in children will recur
- 70-80% of second seizure will recur
- detailed history to determine if event is a seizure or a paroxysmal non-epileptic event - e.g. syncope, breath holding spell, gastro-esophageal reflex.
- thorough clinical examination to look for any possible underlying aetiology
- need to exclude acute provoking factors

### What Investigations Need To Be Done?

- routine investigations such as FBC, BUSE, Ca, Mg, RBS if
  - child unwell (vomiting, diarrhoea etc)
  - child not 'alert', lethargic or failure to return to baseline alertness
- lumbar puncture indicated if there is suspicion of brain infection
- toxicology screening considered if there is suspicion of drug exposure
- EEG is recommended after all first *afebrile unprovoked* seizure
  - EEG helps classify seizure type, epilepsy syndrome and predict recurrence
- neuroimaging (MRI preferred) indicated for:
  - persisting postictal focal deficit (Todd's paresis)
  - condition of child not returned to baseline within several hours after seizure

### Is Treatment Required?

- treatment with anticonvulsant NOT indicated in all first afebrile seizure as it does not prevent development of epilepsy or influence long term remission
- treatment after first unprovoked seizure can be considered if:
  - neurological deficit in child
  - unequivocal epileptic activity on EEG
  - risks of having further seizures unacceptable
  - brain imaging shows structural abnormality

## FEBRILE CONVULSIONS

### Definition

Convulsions occurring in association with fever in children between 3 months and 6 years of age, in whom there is no evidence of intracranial pathology or metabolic derangement.

There is no comprehensive local epidemiological data. Studies in Western Europe quote a figure of 3-4% of children < 5 years experiencing febrile convulsions.

**Table 1. Classification of febrile convulsions**

Simple Febrile Convulsions	Complex Febrile Convulsions
<ul style="list-style-type: none"> <li>• duration &lt; 15 minutes</li> <li>• generalised seizure.</li> <li>• does not recur during the febrile episode</li> </ul>	<ul style="list-style-type: none"> <li>• duration &gt; 15 minutes</li> <li>• focal features</li> <li>• &gt; 1 seizure during the febrile episode</li> <li>• residual neurological deficit post-ictally, such as Todd's paralysis</li> </ul>

### Management

- not all children need to be admitted. The main reasons for admission are: -
  - to exclude intracranial pathology especially infection
  - fear of recurrent fits
  - to investigate and treat the cause of fever besides meningitis or encephalitis
  - to allay parental anxiety, especially if they are staying far from the hospital
- investigations
  - the need for blood counts, blood sugar, lumbar puncture, urinalysis, chest X-ray, blood culture etc, will depend on clinical assessment of the individual case.
  - lumbar puncture
    - *must be done if* (unless contraindicated – see chapter on “Meningitis”)
      - any signs of intracranial infection
      - prior antibiotic therapy
      - persistent lethargy and not fully interactive 6 hours after the seizure
    - *strongly recommended if*
      - age < 12 months old
      - first complex febrile convulsion
      - in district hospital without paediatrician
      - parents have a problem bringing the child in again if deterioration at home
  - serum calcium and electrolytes are rarely necessary
  - EEG is not indicated even if multiple recurrences or complex febrile convulsions
- parents should be counselled on the benign nature of the condition (Table 2).

**Table 2. Prognosis in febrile seizures**

*Febrile convulsions are benign events with excellent prognosis*

- 3 – 4 % of population have febrile convulsions
- 30 % recurrence after 1st attack
- 48 % recurrence after 2nd attack
- 2 – 7 % develop subsequent afebrile seizure or epilepsy
- no evidence of permanent neurological deficits following febrile convulsions or even febrile status epilepticus
- no deaths were reported from simple febrile convulsions

- control fever
  - take off clothing and tepid sponging.
  - antipyretic e.g. syrup or rectal Paracetamol 15 mg/kg 6 hourly.
  - antipyretic is indicated for patient's comfort, but has not been shown to reduce the recurrence rate of febrile convulsion.
- parents should also be advised on first aid measures during a convulsion:
  - do not panic, remain calm. Note time of onset of the fit
  - loosen the child's clothing especially around the neck
  - place the child in the left lateral position with the head lower than the body.
  - wipe any vomitus or secretion from the mouth
  - do not insert any object into the mouth even if the teeth are clenched.
  - do not give any fluids or drugs orally
  - stay near the child until the convulsion is over and comfort the child as he/she is recovering
- rectal Diazepam
  - parents of children with high risk of recurrent febrile convulsion should be supplied with rectal diazepam (dose : 0.5 mg / kg)
  - they should be advised on how to administer it in case the convulsion lasts more than 5 minutes
- prevention of *recurrent* febrile convulsions
  - anticonvulsants are no longer recommended for prevention of recurrent febrile convulsions because:
    - the risks and potential side effects of medications outweigh the benefits
    - no medication has been shown to prevent the future onset of epilepsy.
    - febrile convulsions have an excellent outcome with no neurological deficit nor any effect on intelligence.

**Table 3. Risk factors for *recurrent* febrile convulsions**

- family history of febrile convulsion
- age < 18 months
- low degree of fever (< 40 °C) during first febrile convulsion
- brief duration (< 1 hr) between onset of fever and convulsion

\* No risk factor < 15 % recurrence  
 ≥ 2 risk factors > 30 % recurrence  
 ≥ 3 risk factors > 60 % recurrence

**Table 4. Risk factors for subsequent *epilepsy***

- neurodevelopmental abnormality
- complex febrile convulsion
- family history of epilepsy

# EPILEPSY

## Definition

a neurological condition characterised by recurrent unprovoked epileptic seizures

An *epileptic seizure* is the clinical manifestation of an abnormal and excessive discharge of a set of neurons in the brain.

An *epileptic syndrome* is a complex of signs and symptoms that define a unique epilepsy condition. Syndromes are classified on the basis of seizure type(s), clinical context, EEG features and neuroimaging

Epilepsy should be viewed as a symptom of an underlying neurological disorder and not as a single disease entity.

**Table 1. Differential diagnosis of seizures**

Neonates and infants	Young children	Childhood and Adolescents
jitteriness	breath holding spells	vasovagal syncope
benign myoclonus	reflex anoxic seizures	migraine
apnoea	parasomnia	narcolepsy
gastro-oesophageal reflux	benign paroxysmal vertigo	panic attacks
shuddering attacks	paroxysmal choreoathetosis	pseudoseizures
benign paroxysmal torticollis	tics and ritualistic movements	<b>Any Age</b>
hyperekplexia	rage attacks	drug-induced dystonia
		cardiac dysrhythmias

## Management and Investigations

- detailed history of the seizures. Also note birth history, developmental milestones, family history.
- look for dysmorphism, neurocutaneous signs; do thorough CNS, developmental examination.
- investigations are recommended when a *second* afebrile seizure occurs:
  - routine biochemical tests only if clinical features suggest a biochemical disorder, e.g. hypoglycaemia or hypocalcaemia
  - ECG may be performed if suspicion of a cardiac dysrhythmia.
  - EEG is important to support the clinical diagnosis of epileptic seizures, classify the epileptic syndrome, selection of anti-epileptic drug and prognosis. It also helps in localization of seizure foci in intractable epilepsy
- neuroimaging (preferably MRI) is indicated for any child with
  - epilepsy occurring in the first year of life, except febrile seizures
  - partial epilepsy except benign rolandic epilepsy
  - developmental delay or regression

**Table 2. ILAE Classification of seizure types**

<b>Partial</b>
simple
complex
partial seizure with secondary generalisation
<b>Generalised</b>
absence
atypical absences
myoclonic
tonic-clonic
tonic
clonic
atonic
<b>Unclassified</b>
infantile spasms

ILAE = International League Against Epilepsy

**Table 3. Classification of epilepsies and epileptic syndromes (ILAE 1989)**

<b>Focal or Partial epilepsies &amp; syndromes</b>	<b>Generalized epilepsies and syndromes</b>
<i>Idiopathic</i> benign childhood epilepsy with centrotemporal (Rolandic) spikes childhood epilepsy with occipital paroxysms primary reading epilepsy	<i>Idiopathic</i> benign neonatal familial convulsions benign neonatal convulsions benign myoclonic epilepsy in infancy childhood absence epilepsy juvenile absence epilepsy juvenile myoclonic epilepsy epilepsy with grand mal seizures on awakening
<i>Symptomatic</i> epileptia partialis continua syndrome characterised by specific modes of precipitation temporal lobe epilepsy frontal lobe epilepsy	<i>Cryptogenic or symptomatic</i> West syndrome Lennox-Gastaut syndrome epilepsy with myoclonic atstatic seizures epilepsy with myoclonic absences
<b>Epilepsies and syndromes undetermined, whether focal or generalised</b> neonatal seizures severe myoclonic epilepsy in infancy epilepsy with CSWS (Continuous spike waves of slow sleep) acquired epileptic aphasia (Landau-Kleffner syndrome)	<i>Symptomatic</i> early myoclonic encephalopathy early infantile epileptic encephalopathy other symptomatic generalised epilepsies not defined above specific syndromes
<b>Special syndromes; situation-related seizures</b> febrile convulsions isolated seizures or isolated status epilepticus seizures occurring only with an acute metabolic or toxic event	

### Principles of anticonvulsant therapy for Epilepsy

- treatment recommended  $\geq 2$  episodes (recurrence risk up to 80%)
- attempt to classify the seizure type(s) and epileptic syndrome. Monotherapy as far as possible. Choose most appropriate drug, increase dose gradually until epilepsy controlled or maximum dose reached or side effects occur.
- add on the second drug if first drug failed. Optimise second drug, then try to withdraw first drug. (alternative monotherapy)
- rational combination therapy (usually 2 or maximum 3 drugs) i.e. combines drugs with different mechanism of action and consider their spectrum of efficacy, drug interactions and adverse effects.
- monitor drug levels (usually with carbamazepine, phenytoin, phenobarbitone) to check compliance, if seizures not well controlled despite adequate doses or in situations of polypharmacy where drug interaction is suspected.
- when withdrawal of medication is planned (generally being seizure free for 2 years), consideration should be given to epilepsy syndrome, likely prognosis and individual circumstances before attempting slow withdrawal of medication over 3-6 months (maybe longer if clonazepam or phenobarbitone). If seizures recur, the last dose reduction is reversed and medical advice sought.

Table 4. Selecting anticonvulsants according to seizure type

seizure type	first line	second line
<b>Partial seizures</b>		
simple partial	carbamazepine	lamotrigine
complex partial	valproate	topiramate
secondarily generalised		levetiracetam, phenytoin phenobarbitone, clonazepam
<b>Generalised seizures</b>		
tonic-clonic	valproate	lamotrigine
clonic		topiramate, clonazepam carbamazepine <sup>1</sup> , phenytoin <sup>1</sup> phenobarbitone
absence	valproate	lamotrigine, clonazepam
atypical absence	valproate	lamotrigine
atonic, clonic		topiramate, clonazepam
myoclonic	valproate, clonazepam	topiramate, phenobarbitone piracetam, levetiracetam lamotrigine <sup>2</sup>
infantile spasms	adrenocorticotrophin (ACTH), prednisolone, vigabatrin <sup>3</sup>	nitrazepam, clonazepam valproate

footnote: 1. may aggravate myoclonus/absence seizure in Idiopathic Generalised Epilepsy

2. may cause seizure aggravation in SMEI and JME

3. especially for patients with Tuberose sclerosis

Table 5. Side effects and serious toxicities of anticonvulsants.

seizure type	common side effects	serious toxicity
carbamazepine	drowsiness, dizziness, ataxia, diplopia, rash	agranulocytosis Steven-Johnson syndrome <sup>1</sup>
clonazepam	drowsiness, hypotonia, salivary and bronchial hypersecretion, paradoxical hyperactivity and aggressiveness	
lamotrigine	dizziness, somnolence, insomnia, rash	Steven-Johnson syndrome
levetiracetam	somnolence, asthenia, dizziness, irritability, behavioural change	
phenobarbitone	behavioural disturbance, cognitive dysfunction, drowsiness, ataxia, rash	
phenytoin	ataxia, diplopia, dizziness, rash, sedation hirsutism, gum hypertrophy	megaloblastic anemia
topiramate	weight loss, somnolence, mental slowing, word-finding difficulty, hypohidrosis	renal calculi
valproate	nausea, epigastric pain, tremor, alopecia, weight gain, hair loss, thrombocytopaenia	hepatic toxicity (< 2 years age) hepatitis, pancreatitis, encephalopathy
vigabatrin	drowsiness, dizziness, mood changes, weight gain	peripheral visual field constriction (tunnel vision)

footnote: 1. Steven-Johnson syndrome occur more frequently in children of Chinese and Malay ethnicity

The patients with “Intractable Epilepsy”

Please re-evaluate for the following possibilities:-

- as it a seizure or non-epileptic event?
- anticonvulsant dose not optimised
- poor compliance to anticonvulsant
- wrong classification of epilepsy syndrome, thus wrong choice of anticonvulsant
- anticonvulsant aggravating seizures
- lesional epilepsy, hence a potential epilepsy surgery candidate
- progressive epilepsy or neurodegenerative disorder

When to refer to a Paediatric Neurologist?

- poor seizure control despite monotherapy with 2 two different anticonvulsants
- difficult to control seizures beginning in the first year of life
- seizures and developmental regression
- structural lesion on neuroimaging

Advice for Parents

- educate and counsel on epilepsy
- emphasize compliance if on anticonvulsant.
- don’t stop the medication by themselves. This may precipitate breakthrough seizures.
- in photosensitive seizures - watch TV in brightly lit room. Avoid sleep deprivation.
- use a shower with bathroom door unlocked.
- no cycling in traffic, climbing sports or swimming alone.
- know emergency treatment for seizure.
- inform teachers and school about the condition

Table 6. Anticonvulsants that **aggravate** seizure types

phenobarbitone
absence seizures
clonazepam
tonic status in LGS
carbamazepine
absence, myoclonic, GTC seizures
lamotrigine
SMEI
myoclonic seizures in JME
phenytoin
absence, myoclonic seizures
vigabatrin
myoclonic, absence seizures

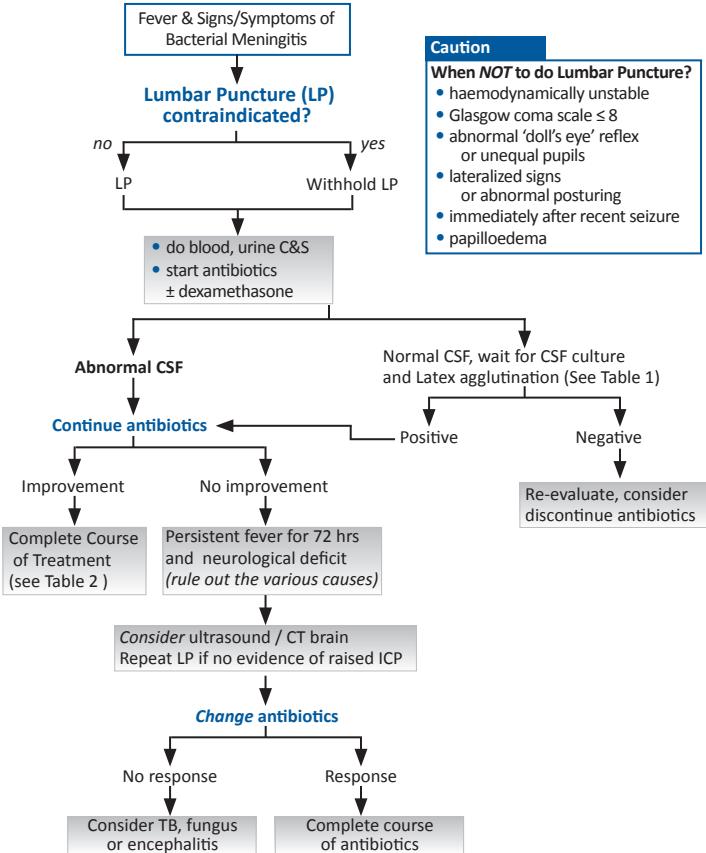
GTC, generalised tonic-clonic;  
LGS, Lennox-Gastaut syndrome;  
SMEI, severe myoclonic epilepsy of infancy;  
JME, juvenile myoclonic epilepsy

# MENINGITIS

## Introduction

Meningitis is still a major and sometimes fatal problem in Paediatrics. Morbidity is also high. About 30% of survivors have some sequelae of their disease. However, these complications can be reduced if meningitis is treated early.

Figure 1. Approach to children with fever and signs / symptoms of bacterial meningitis



Note: In cases of aseptic meningitis or encephalitis please send CSF and serum for viral serology e.g. for JE IgM and HSV CSF PCR.



Table 1. Cerebrospinal fluid values in neurological disorders with fever

Condition	Leukocytes (mm <sup>3</sup> )	Protein (g/l)	Glucose (mmol/l)	Comments
Acute bacterial meningitis	100 - >50,000	Usually 1- 5	<0.5 - 1.5	Gram stain may be positive
Partially treated bacterial meningitis	1 - 10,000 usually ↑ PMN, but may have lymphocytes	> 1	low	CSF may be sterile in pneumococcal, meningococcal meningitis
Tuberculous meningitis	10 - 500 early PMN, later ↑ lymphocytes	1 - 5	0 - 2.0	Smear for AFB, TB PCR positive in CSF. ESR ↑
Fungal meningitis	50 - 500 lymphocytes	0.5 - 2	normal or low	CSF for Indian ink / cryptococcal antigen
Encephalitis	10 - 1,000	normal / 0.5-1	normal	Send for CSF virology
Encephalopathy	<10 lymphocytes	normal	normal	May not be febrile

Table 2. Recommended antibiotic therapy according to likely pathogen

Age Group	Initial Antibiotic	Likely Organism	Duration (if uncomplicated)
< 1 month	C Penicillin + Cefotaxime	Group B <i>Streptococcus</i> <i>E. coli</i>	21 days
1 - 3 months	C Penicillin + Cefotaxime	Group B <i>Streptococcus</i> <i>E. coli</i> <i>H. influenzae</i> <i>Strep. pneumoniae</i>	10 - 21 days
> 3 months	C Penicillin + Cefotaxime or Ceftriaxone	<i>H. influenzae</i>	7 - 10 days
		<i>Strep. pneumoniae</i>	10 - 14 days
		<i>N. meningitidis</i>	7 days

Note:

1. Terminate inappropriate antibiotics when infective organism has been identified.
2. Ceftriaxone gives more rapid sterilisation of CSF than either Cefotaxime or Cefuroxime.
3. Ideally, MIC of the antibiotics for susceptible organisms (especially *S. pneumoniae*) is required to decide on the antibiotic of choice. For example:-  

MIC level	Drug of choice:
• MIC < 0.1 mg/L (sensitive strain)	C Penicillin
• MIC 0.1- < 2 mg/L (relatively resistant)	Ceftriaxone or Cefotaxime
• MIC > 2 mg/L (resistant strain)	Vancomycin + Ceftriaxone or Cefotaxime
4. Penicillin resistance in community acquired *S. pneumoniae* in Hospital Kuala Lumpur is 16.9 %
5. Extend duration of treatment if complications e.g. subdural empyema, brain abscess.

Table 3. Normal cerebrospinal (CSF) values

	Neonates	Infants	Older children
Cells/mm <sup>3</sup>	< 30	< 10	< 5
Glucose mmol/l*	1.1 - 3.3	3.9 - 5.0	2.8 - 4.4
Protein g/l	0.2 - 1.5**	0.15 - 0.45	0.2 - 0.4

\* RBS must be taken before LP. Normal CSF glucose ≥ 60% RBS

\*\* CSF protein: values up to 3g/l may be found in preterm infants

Table 4. Gram stain characteristics

<i>Streptococcus pneumoniae</i>	gram positive extracellular diplococci.
<i>Neisseria meningitidis</i>	gram negative intracellular diplococci
<i>Haemophilus influenzae</i>	gram negative coccobacilli

### Use of Steroids to decrease the sequelae of bacterial meningitis

- best effect achieved if the steroid is given before or with the first antibiotic dose
- dose: Dexamethasone 0.15 mg/kg 6 hly for 4 days or 0.4 mg/kg 12 hly for 2 days
- give steroids if CSF at LP is turbid and the patient has not received prior antibiotics

### Supportive measures

- monitor temperature, pulse, B/P and respiration 4 hourly and input/output
- nil by mouth if unconscious
- careful fluid balance required. Often, maintenance IV fluids is sufficient. However, if SIADH occurs, reduce to 2/3 maintenance for the initial 24 hours. Patient may need more fluid if dehydrated.
- if fontanel is still open, note the head circumference daily. Consider cranial ultrasound or CT scan if effusion or hydrocephalus is suspected
- fit chart
- daily CNS assessment is essential
- observe for 24 hours after stopping therapy and if there is no complication, patient can be discharged

*If persistent fever in a patient on treatment for meningitis, consider:*

- thrombophlebitis and injection sites e.g. intramuscular abscess
- intercurrent infection e.g. pneumonia, UTI or nosocomial infection
- resistant organisms. Inappropriate antibiotics or inadequate dosage
- subdural effusion, empyema or brain abscess
- antibiotic fever

**Follow up** (Long term follow up is important)

- note development of child at home and in school.
- note head circumference.
- ask for any occurrence of fits or any behavioural abnormalities.
- assess vision, hearing and speech
- request for a formal hearing assessment in cases of proven meningitis
- until child speaks normally or speaks intelligibly to others (usually until 4 years old)

### Prognosis depends on

- age: worse in younger patients
- duration of illness prior to effective antibiotics treatment
- causative organism: more complications with *H. influenzae* and *S. pneumoniae*
- presence of focal signs

**Table 5. Indication for cranial CT scan**

*Useful to detect complications*

- prolonged depression of consciousness
- prolonged focal or late seizures
- focal neurological abnormalities
- enlarging head circumference
- suspected subdural effusion or empyema

**Table 6. Indications for subdural drainage**

- rapid increase in head circumference with no hydrocephalus
  - focal neurological signs
  - increased intracranial pressure
  - suspected subdural empyema
- Most do not need treatment*

# ACUTE DEMYELINATION

## Introduction

These disorders consist of monophasic and polyphasic (recurrent) diseases with acquired immune injury to the white matter in the central nervous system.

## Optic neuritis

- acute loss of vision (decreased visual acuity) of one or both eyes
- often associated with pain on eye movements and colour desaturation
- A relative afferent pupillary defect is present
- CT/MRI may show swelling and abnormal signal of optic nerves.

## Acute transverse myelitis

- spinal cord dysfunction, with motor weakness, numbness of both legs and/or arms, often associated with urinary retention
- maximal deficits occurring between 4 hours to 21 days after symptom onset
- MRI may demonstrate swelling +/- abnormal signal in the spinal cord

## Acute Disseminated Encephalomyelitis (ADEM)

- acute neurological deficits, often multifocal (weakness, numbness, ataxia) with at least 2 of the following:
  - (1) prodromal illness in the last 28 days
  - (2) fever
  - (3) neck stiffness
  - (4) headache
  - (5) seizures
  - (6) altered level of consciousness or behaviour
- MRI shows multiple areas of abnormal signal in the white matter

**Table 1. ADEM: Common differential diagnoses**

<i>CNS infection</i>
bacterial, tuberculous meningitis
Herpes simplex encephalitis
<i>Demyelination of the peripheral nervous system</i>
Guillain Barré syndrome
Chronic inflammatory demyelinating polyneuropathy (CIDP)
<i>Acute stroke</i>
<i>Mitochondrial disorders</i>

## Other Investigations (as needed)

- cerebrospinal fluid - FEME, cultures, oligoclonal banding, Herpes virus PCR (optional: lactate, viral studies)
- infection screen - virology, mycoplasma, etc.
- vasculitis screen (ESR, C3, C4, antinuclear factor)
- evoked potentials - visual, auditory and somatosensory

## Treatment

### Supportive measures

- vital sign monitoring, maintain blood pressure
- assisted ventilation for "cerebral / airway protection"
- anticonvulsants for seizures
- antibiotics, Acyclovir for CNS infections if febrile, awaiting cultures, PCR result

### Definitive immunotherapy

- IV Methylprednisolone 20 - 30 mg/kg/day (max 1 gm) daily for 3 to 5 days then oral Prednisolone 1 mg/kg/day (max 60 mg) daily to complete 2 weeks.
- Severe episodes of demyelination that respond to initial therapy may benefit from a longer course, tapering over 4 to 6 weeks
- If no response, consider: IV Immunoglobulins 2 gm/kg over 2 - 5 days (or referral to a paediatric neurologist)

**If recurring demyelinating episodes, consider referral to a paediatric neurologist**

## ACUTE FLACCID PARALYSIS

### Introduction

Acute Flaccid Paralysis (AFP) occurs when there is rapid evolution of motor weakness (< than 4 days), with a loss of tone in the paralysed limb. This excludes weakness due to trauma and spastic paralysis.

AFP is a **medical emergency** as unnecessary delays can result in death and disability.

Children with AFP need to be assessed and managed carefully. Figure 1 describes a simple algorithm to follow.

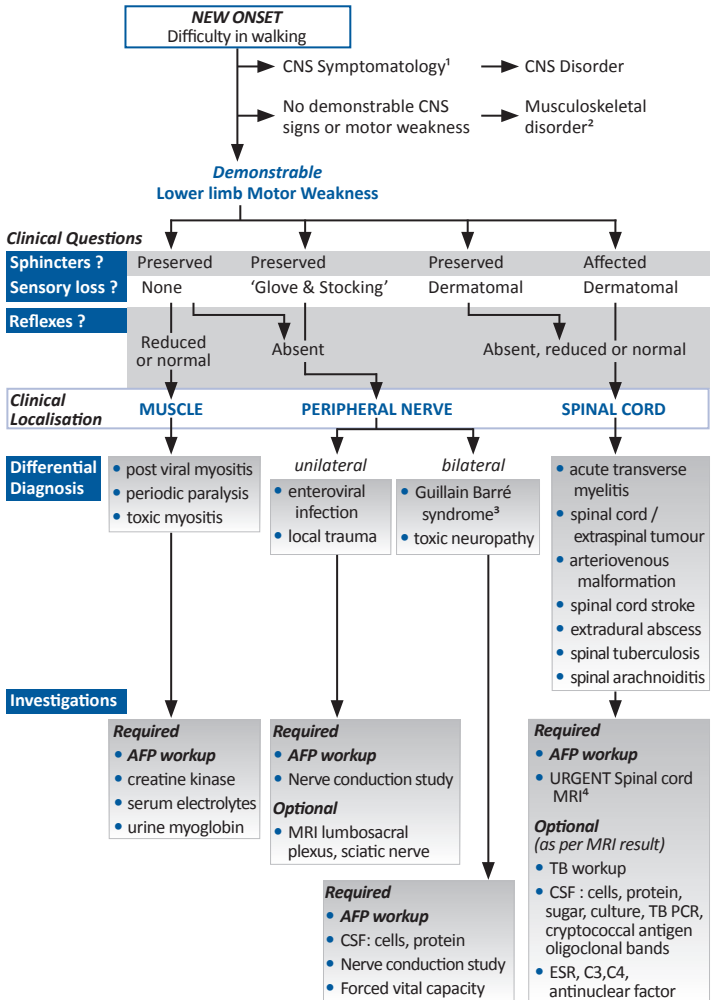
### AFP surveillance in children

- collecting stools for enterovirus in children with AFP is an important part of the Global Polio Eradication Initiative (GPEI)
- for Malaysia to remain a polio-free country we need to prove that none of our cases of AFP are caused by poliovirus infection. To do this we have to report enough cases, send stools for enterovirus isolation using a standardised protocol, and follow up children with AFP to determine the outcome.
- the new target “background rate” for AFP in the GPEI is 2 per 100,000 children below age 15 per year

Table 1. Protocol for AFP surveillance in Malaysia

Step	Timing	Description
Case Detection	at diagnosis	Follow case definition for AFP
Case Reporting	within 24 hours	Fax forms to 03-2693 8094 (Virology Unit, IMR; Tel no: 03-2616 2677)
Timing of stool specimens	within 2 weeks of onset of paralysis	2 stool specimens collected no less than 24 hours apart
Collection of specimens		Fresh stool, or rectal swabs containing fecal material (at least 8g – size of an adult thumb). Place in a sterile glass bottle
Transport of stools	as soon as able	Maintain a cold chain of 2 - 8 °C. Transport in dry ice if transportation will take > 24 hours Caution: avoid desiccation, leakage; ensure adequate documentation
Follow up of patients	60 days from paralysis	To determine whether there is residual paralysis on follow up

Figure 1. Clinical approach to children with AFP



Notes: 1. headache, vomiting, seizures, encephalopathy, cranial nerve deficits, ataxia, brisk tendon reflexes, upgoing plantar response  
 2. soft tissue, joint or bony causes of walking difficulty  
 3. GBS in children may present in a variety of ways. Refer next page.  
 4. Standard spinal MRI must begin with a screening sagittal T2-weighted image of the whole spine, then adequate study of the affected area(s) in both sagittal and axial planes. Contrast with gadolinium is often needed.

# GUILLAIN BARRÉ SYNDROME

## Introduction

Guillain Barré syndrome (GBS) is a post-infectious inflammatory disorder affecting the peripheral nerves.

**Table 1. Clinical pearls on GBS in children**

- weakness may begin in the face or upper limbs, or may be asymmetrical at onset. However, at full evolution is almost always bilateral, symmetrical, proximal predominant limb weakness.
- sensory symptoms, e.g. limb pain and hyperesthesia, are common
- bladder and bowel involvement may occasionally be seen, but is *never* present at onset and *never* persistent (if so, think of spinal cord disorder)
- CSF protein level and nerve conduction studies *may be normal* in the first week of illness.
- clinical variants of GBS include:
  - Miller Fisher syndrome, characterised by ophthalmoplegia, pupillary dilatation, ataxia and areflexia
  - Pharyngo-Cervico-Branchial (PCB) syndrome, characterised by facial, bulbar (swallowing) and neck weakness
  - Autonomic GBS, which presents with motor weakness and prominent autonomic symptoms, such as dilated cardiomyopathy, postural hypotension and diarrhoea

## Management

The principle of management is to establish the diagnosis and anticipate / pre-empt major complications.

- a **clinical** diagnosis can be made by a history of progressive weakness (< 4 weeks) with areflexia, and an elevated cerebrospinal fluid protein level and normal cell count ("protein-cellular dissociation")
- nerve conduction study is **confirmatory**

## Anticipated complications and management

- **Respiratory compromise**
  - monitor PEFR regularly
  - give oxygen, keep NBM breathless
  - provide respiratory support early with either BiPAP or mechanical ventilation.
- **Progressive severe weakness**

**Table 2. Hughes Functional scale for GBS**

- |   |   |
|---|---|
| 0 | - normal  |
| 1 | - minor symptoms, capable of running                                |
| 2 | - able to walk up to 10 meters without assistance but unable to run |
| 3 | - able to walk 10 meters with assistance of one person, or a walker |
| 4 | - unable to walk  |
| 5 | - requires assisted ventilation                                     |

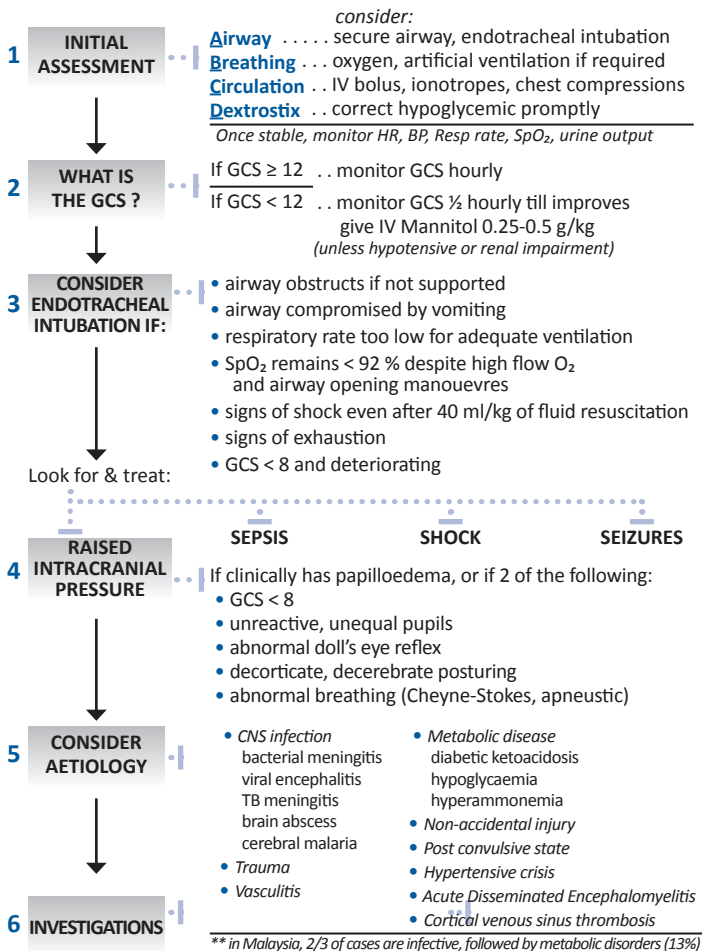
## Specific measures

- Intravenous Immunoglobulins (IVIG) 2 gm/kg total over 2 - 5 days in the first 2 weeks of illness has been shown to :
  - reduce disease severity (by 1 functional level)
  - shorten time on a ventilator
  - shorten time taken to reach functional level 2
- IVIG is as efficacious as Plasma exchange in both children and adults, and is safer and technically simpler
- 10 % of children with GBS may suffer a relapse of symptoms in the first weeks after improvement from IVIG. In these children, there is anecdotal evidence of benefit from a second dose of IVIG.

## General measures

- prophylaxis for deep vein thrombosis should be considered for patients ventilated for GBS, especially if recovery is slow
- liberal pain relief, with either paracetamol, NSAIDs, gabapentin or opiates.

## APPROACH TO A CHILD WITH ALTERED CONSCIOUSNESS



*\*\* in Malaysia, 2/3 of cases are infective, followed by metabolic disorders (13%)*

### Recommended

FBC, urea & electrolytes, glucose  
Liver function tests  
Serum ammonia, blood gas  
Blood cultures  
Urinalysis

### Lumbar Puncture

### Sample when ILL:

1-2 ml plasma/serum: separated, frozen & saved  
10-20 ml urine: frozen & saved

### Optional

Vasculitis screen  
Tandem Mass Spectrometry (IEM screen)  
Blood film for malaria parasite

**Neuroimaging:** CT Brain should be considered for all children with  $\uparrow$  ICP, or if cause of coma is uncertain despite the above; If a brain tumour or ADEM is suspected, then an MRI is more useful.

## 7 MANAGEMENT

### Management of Raised ICP

- Nursing
  - elevate head up to 30°
  - avoid unnecessary suction, procedures
- Fluid balance
  - keep patient well hydrated
  - avoid hypo-osmolar fluid, plain dextrose solutions
  - care with sodium homeostasis:

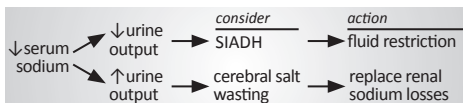


Fig 1: Hyponatremia in children with coma

- Maintain cerebral blood flow
  - keep CPP > 40 mmHg
  - If ↑ BP: do not lower unless hypertensive crisis, e.g. acute glomerulonephritis

$$\text{Cerebral (CPP) Perfusion Pressure} = \text{Mean (MAP) Arterial Pressure} - \text{Intracranial (ICP) Pressure}$$

Fig 2: calculating cerebral perfusion pressure

- Use of IV Mannitol
  - regular doses at 0.25 - 0.5 g/kg q.i.d. if required
  - a CT scan to exclude intracranial bleeding is recommended
- PaO<sub>2</sub> , PaCO<sub>2</sub> level
  - maintain good oxygenation, normocapnoea  
i.e. PaCO<sub>2</sub> 4.0 - 4.6 kPa / 35 - 40 mmHg
- Surgical decompression
  - if medical measures fail, surgical decompression may be indicated (ie. external ventricular drainage, decompressive hemicraniectomy)

### Treatment of Infection

- *Antibiotics*: in all children, unless alternate cause of coma is evident
- *Aciclovir*: in children with encephalitis, until CSF PCR results known
- *Others*: anti-tuberculous therapy, anti-malarials

### Treatment of Metabolic Encephalopathy

.... refer section on Metabolic disease in children

## 8 OUTCOME

### General rules

- outcome depends on the underlying cause:  
1/3 die, 1/3 recover with deficits, 1/3 recover completely
- acute complications improve with time.  
e.g. cortical blindness, motor deficits
- continue anticonvulsants for 6 weeks,  
or longer if seizures persist
- metabolic causes may require long term dietary management



## BRAIN DEATH

### Definition

Brain death is a state when the function of the brain as a whole, including the brain stem is irreversibly lost. A person certified to be brain dead is dead.

### Diagnosis of brain death (All to be fulfilled)

*Preconditions:*

- patient is in deep coma, apnoeic and on ventilator
- cause of coma fully established and sufficient to explain the status of patient
- there is irremediable structural brain damage

*Exclusions:*

- coma due to metabolic or endocrine disturbance, drug intoxication and primary hypothermia (defined as a core temperature of 32 °C or lower).
- certain neurological disorders namely Guillain Barre Syndrome, Miller Fisher syndrome and Locked-in Syndrome
- coma of undetermined cause
- preterm neonates

### Diagnostic Criteria ( All to be fulfilled )

- deep coma, unresponsive and unreceptive, Glasgow scale 3 / 15
- apnoeic, confirmed by apnoea test
- absent brain stem reflexes confirmed by the following tests:-
  1. Pupillary light reflex.
  2. Oculocephalic reflex.
  3. Motor response in cranial nerve distribution
  4. Corneal reflex
  5. Vestibulo-ocular reflex (caloric test)
  6. Oro-pharyngeal reflex
  7. Tracheo-bronchial reflex

### Test

*(All conditions and exclusions fulfilled before proceeding to examine and test for brain death)*

1. *Pupillary light reflex.*  
No response to bright light in both eyes.
2. *Oculocephalic reflex. (Doll's eye response)*  
Testing is done only when no fracture or instability of the cervical spine is apparent. The oculocephalic response is elicited by fast, vigorous turning of the head from middle position to 90° on both sides.
3. *Corneal reflex.*  
No blinking response seen when tested with a cotton swab.
4. *Motor response in cranial nerve distribution.*  
No grimacing seen when pressure stimulus applied to the supraorbital nerve, deep pressure on both condyles at level of the temporo-mandibular joint or on nail bed
5. *Vestibulo-ocular reflex (Caloric test).*  
The test *should not* be performed if there is a perforated tympanic membrane. The head is elevated to 30° during irrigation of the tympanum on each side with 50 ml of ice water. Allow 1 minute after injection and at least 5 minutes between testing on each side. Tonic deviation of the eyes in the direction of cold stimulus is absent.

## 6. Oropharyngeal reflex.

Absent gag response when the posterior pharynx is stimulated.

## 7. Tracheo-bronchial reflex.

A suction catheter is passed down through the endotracheal tube to the level of the carina or beyond. Lack of cough response to bronchial suctioning should be demonstrated.

## 8. Apnoea test.

- prerequisites: the patient must be in stable cardiovascular and respiratory state.
- adjust ventilator to maintain  $\text{PaCO}_2$  at or around 40 mmHg
- pre-oxygenate with 100%  $\text{O}_2$  for 10 minutes
- disconnect from ventilator
- deliver 100%  $\text{O}_2$  via tracheal catheter at 6 L/min
- monitor  $\text{O}_2$  saturation with pulse oximetry
- measure  $\text{PaCO}_2$  after 5 minutes and again after around 8 minutes if  $\text{PaCO}_2$  has not exceeded 60 mm Hg
- re-connect to ventilator after the test
- the disconnection of the ventilator shall not exceed 10 minutes at any one time
- the apnoea test is **positive** when there is no respiratory effort with a  $\text{PaCO}_2$  of  $\geq 60$  mmHg
- if during apnoea testing, there is significant hypotension, marked desaturation or cardiac arrhythmias immediately draw an arterial blood sample, re-connect to ventilator and analyse ABG. Should the  $\text{PaCO}_2 < 60$  mmHg, the result is indeterminate. It is left to the discretion of the paediatrician to decide whether to repeat the test or to depend on an ancillary test to finalise the clinical diagnosis of brain death.

*Note: For patients with chronic lung disease, the baseline  $\text{PaCO}_2$  may already be above 40 mmHg. The apnoea test is then considered positive if there is no respiratory effort at a  $\text{PaCO}_2$  of 20 mmHg above the baseline  $\text{PaCO}_2$*

## Additional criteria for children

It is generally assumed that the young child's brain may be more resilient to certain forms of injury, although this issue is controversial. The *newborn* is difficult to evaluate after perinatal insults. This relates to many factors including difficulties of clinical examination, determination of the cause of coma, and certainty of the validity of laboratory tests. Hence *no recommendation can be made for preterm infants and newborn less than 7 days old*. Beyond this period, the brain death criteria apply but the interval between two examinations is lengthened depending on the age of the child, and an ancillary test (EEG) is recommended for those less than one year old.

Table 1. Time criteria and ancillary testing in children

Age	Interval between assessments	Recommended no. of EEGs
7 days – 2 mths	48 hours	2
2 mths – 1 year	24 hours	2
> 1 year <sup>1</sup>	12 hours	Not needed

Footnote: 1. If hypoxic ischaemic encephalopathy is present, observation for at least 24 hours is recommended. This interval may be reduced if an EEG shows electrocerebral silence.

## Assessment and Certification

- Two specialists who are competent (at least 3 years of postgraduate clinical experience and trained in brain death assessment) in diagnosing brain death are qualified to certify brain death. They should preferably be paediatricians, anaesthesiologists, neurologists and neurosurgeons. Doctors involved in organ transplantation are not allowed to certify brain death.
- A repeat assessment and certification must be carried out after the first (with interval between the 2 examinations depending on the age of the child), not necessarily by the same pair of specialists.
- The 'Brain Death Certification' form is filled up by the first set of doctors (Doctor A and B) and completed by the 2nd set of doctors (Doctor C and D) or Doctor A and B if the same doctors are performing the repeat test. The time of death will then be declared by the doctors performing the repeat test.
- The time of death is at the time of the 2nd testing. Should the patient's heart stop before the repeat test, that will be taken as the time of death.
- Brain death certification must only be done in areas of the hospital with full facilities for intensive cardiopulmonary care of the comatose patients.

## Pitfalls in diagnosis

- may occur in patients with
  - severe facial trauma
  - pre-existing pupillary abnormalities
  - sleep apnoea or severe pulmonary disease resulting in chronic retention of CO<sub>2</sub>
  - toxic levels of any sedative drugs, aminoglycosides, tricyclic antidepressants, anticonvulsants, chemotherapeutic drugs, neuromuscular blocking agents.
- drug levels are useful if they can be quantified. If the drug level is below the therapeutic range, brain death can be declared.
- when the drug or poison cannot be quantified, observe the patients for at least 4 times the elimination half-life, provided the elimination of the drug or toxin is not interfered with, by other drugs or organ dysfunction.
- when the drug unknown but suspicion of its presence is high, observe the patients for 48 hours for a change in brainstem reflexes and motor response; if none are observed, perform an ancillary test (EEG) for brain death.
- determination of brain death should be deferred in the presence of severe acidosis or alkalosis as this may point to certain intoxication and potentially reversible medical illness or endocrine crisis.
- spontaneous and reflex movements have been observed in patients with brain death. The most common are finger jerks, toe flexion sign and persistent Babinski response. These movements are spinal in origin and do not occur spontaneously. They do not preclude the diagnosis of brain death.

Table 2. Common CNS depressants and pharmacodynamics

Drugs	Elimination T <sub>1/2</sub>	Therapeutic Range
Midazolam	2 – 5 hours	50 – 150 ng/ml
Diazepam	40 hours	0.2 – 0.8 ug/ml
Carbamazepine	10 – 60 hours	2 – 10 ug/ml
Phenobarbitone	100 hours	20 – 40 ug/ml
Pentobarbitone	10 hours	1 – 5 ug/ml
Thiopentone	10 hours	6 – 35 ug/ml
Morphine	2 – 3 hours	70-450 ng/ml
Amitriptyline	10 - 24 hours	75 – 200 ng/ml

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### Approach to coma in children

1. Consen

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# ENDOCRINOLOGY

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- 56 Ambiguous Genitalia



## APPROACH TO CHILDREN WITH SHORT STATURE

Short stature can be a sign of disease, disability and social stigma causing psychological stress. It is important to have early diagnosis and treatment.

### Definition

Height  $\leq$  -2 SD or height < 3rd percentile.

Serial heights should be measured to assess the growth pattern and height velocity.

Average height velocity at different phases:

- prenatal growth : 1.2 -1.5 cm / week
- infancy : 23 - 28 cm / year
- childhood : 5 - 6.5 cm / year
- puberty : 8.3 cm / year (girls), 9.5 cm / year (boys)

Definitions of growth failure:

- height below 3rd percentile (-2SD for age and gender)
- height significantly below genetic potentials (-2SD below mid-parental target)
- abnormally slow growth velocity
- downwardly crossing percentile channels on growth chart (> 18 months age)

**Table 1. Differential diagnosis of short stature and growth failure**

<i>Healthy but short children</i>	<i>Endocrinopathies</i>
familial short stature	hypothyroidism
constitutional growth delay	hypopituitarism
<i>Intrinsic short stature</i>	heredity, sporadic, idiopathic
small for gestational age	isolated GH deficiency
genetic syndromes	birth injury
Down syndrome, Turner syndrome	craniopharyngioma
Prader-Willi syndrome	cranial irradiation
skeletal dysplasia	brain tumours
achondroplasia, hypochondroplasia	midline defects
<i>Systemic diseases</i>	haemosiderosis
infectious	GH insensitivity (Laron syndrome)
HIV, tuberculosis	glucocorticoid excess
cardiac disease	Cushing syndrome, exogenous steroids
renal disease	poorly controlled diabetes mellitus
renal tubular acidosis	precocious puberty
chronic renal insufficiency	pseudohypoparathyroidism
gastrointestinal	pseudopseudohypoparathyroidism
cystic fibrosis	<i>Nonorganic aetiologies</i>
inflammatory bowel disease	psychosocial deprivation
central nervous system disease	nutritional dwarfing
chronic lung disease	
malignancy	

*Abbreviation. GH, Growth hormone*



Table 1. Differential diagnosis of short stature and growth failure	
History	Physical Examination
<p><i>Antenatal</i></p> <p>complications of pregnancy, pre-eclampsia, hypertension</p> <p>maternal history of smoking, alcohol, infections</p> <p><i>Birth</i></p> <p>gestational age</p> <p>birth weight and length</p> <p>mode of delivery (breech, forceps)</p> <p>Apgar score</p> <p>neonatal complications</p> <p><i>Nutrition</i></p> <p>general well being: appetite, energy, sleep, and bowel habits.</p> <p>pattern of growth from birth</p> <p><i>Developmental milestones</i></p> <p><i>Maternal and child relationship</i></p> <p><i>Medical history</i></p> <p>underlying illness, drug intake, irradiation</p> <p><i>Family History</i></p> <p>short stature (3 generations).</p> <p>age of onset of puberty in family members of the same sex.</p> <p>diseases in the family.</p>	<p><i>Anthropometry</i></p> <p>height, weight, head circumference</p> <p>height velocity</p> <p>arm span</p> <p>ratios of upper to lower segments</p> <p>1.7 in neonates to slightly &lt;1.0 in adults</p> <p><i>General appearance and behaviour</i></p> <p>dysmorphism</p> <p>pubertal staging</p> <p><i>Family Measurements</i></p> <p>measure height of parents for mid-parental height (MPH)</p> <p>Boys : <math>\frac{\text{Father's height} + (\text{mother's height} +13)}{2}</math></p> <p>Girls : <math>\frac{\text{Mother's height} + (\text{father's height} -13)}{2}</math></p>

Initial screening evaluation of growth failure

- general tests
  - FBC with differentials, renal profile, liver function test, ESR, Urinalysis
- chromosomal analysis in every short girl
- endocrine tests
  - thyroid function tests
  - growth factors: IGF-1, IGFBP-3
  - growth hormone stimulation tests if growth hormone deficiency is strongly suspected. (Refer to Paediatric Endocrine Centre)
- imaging studies
  - bone age : anteroposterior radiograph of left hand and wrist
  - CT / MRI brain ( if hypopituitarism is suspected)
- other investigations depends on clinical suspicion
  - blood gas analysis
  - radiograph of the spine

## Management

- treat underlying cause (hypothyroidism, uncontrolled diabetes mellitus, chronic illnesses)
- for children suspected to be GH deficient, refer to Paediatric Endocrinologist for initiation of GH.
- psychological support for non-treatable causes (genetic / familial short stature; constitutional delay of growth and puberty)

FDA approved indications for GH treatment in Children:

- paediatric GH deficiency
- Turner syndrome
- small for gestational age
- chronic renal insufficiency
- idiopathic short stature
- Prader–Willi syndrome (also improves linear growth)
- AIDS cachexia

## GH Treatment

- GH should be initiated by a Paediatric Endocrinologist.
- GH dose: 0.025 - 0.05 mg/kg/day (0.5 - 1.0 units/kg/wk) SC daily at night.
- GH treatment should start with low doses and be titrated according to clinical response, side effects, and growth factor levels.
- during GH treatment, patients should be monitored at 3-month intervals (may be more frequent at initiation and during dose titration) with a clinical assessment (growth parameters, compliance) and an evaluation for adverse effects (e.g. impaired glucose tolerance, carpal tunnel syndrome), IGF-1 level, and other parameters of GH response.
- other biochemical evaluations:
  - thyroid function
  - HbA1c
  - lipid profile
  - fasting blood glucose
- continue treatment till child reaches near final height, defined as a height velocity of < 2cm / year over at least 9 months (or bone age >13 years in girls and >14 years in boys).
- treat other pituitary hormone deficiencies such as hypothyroidism, hypogonadism, hypocortisolism and diabetes insipidus.

# CONGENITAL HYPOTHYROIDISM

## Introduction

The incidence of congenital hypothyroidism worldwide is 1 in 2500 - 4000 live births. In Malaysia, it is reported as 1 in 3666. It is the commonest preventable cause of mental retardation in children.

Thyroid hormones are crucial for: -

- normal growth and development of the brain and intellectual function, during the prenatal and early postnatal period
- maturation of the foetal lungs and bones

## Clinical diagnosis

Most infants are asymptomatic at birth.

Subtle clinical features include :

- prolonged neonatal jaundice
- constipation
- a quiet baby
- enlarged fontanelle
- respiratory distress with feeding
- absence of one or both epiphyses on X-ray of left knee (lateral view)

If left untreated, overt clinical signs will appear by 3 - 6 months: coarse facies, dry skin, macroglossia, hoarse cry, umbilical hernia, lethargy, slow movement, hypotonia and delayed developmental milestones.

Most infants with the disease have no obvious clinical manifestations at birth, therefore neonatal screening of thyroid function should be performed on all newborns.

## Treatment

### Timing

- should begin immediately after diagnosis is established. If features of hypothyroidism are present, treatment is started urgently.

### Duration

- treatment is life long except in children suspected of having transient hypothyroidism where re-evaluation is done at 3 years of age.

### Preparation

- there are currently no approved liquid preparations
- only L-thyroxine *tablets* should be used. The L-thyroxine tablet should be crushed, mixed with breast milk, formula, or water and fed to the infant.
- the tablets should not be mixed with soy formulas or any preparation containing iron (formulas or vitamins), both of which reduce the absorption of T4

Table 1. Doses of L- thyroxine by age

Age	mcg/kg/dose, daily
0 - 3 months	10 - 15
3 - 6 months	8 - 10
6 - 12 months	6 - 8
1 - 5 yr	5 - 6
6 - 12 yr	4 - 5
> 12 yr	2 - 3

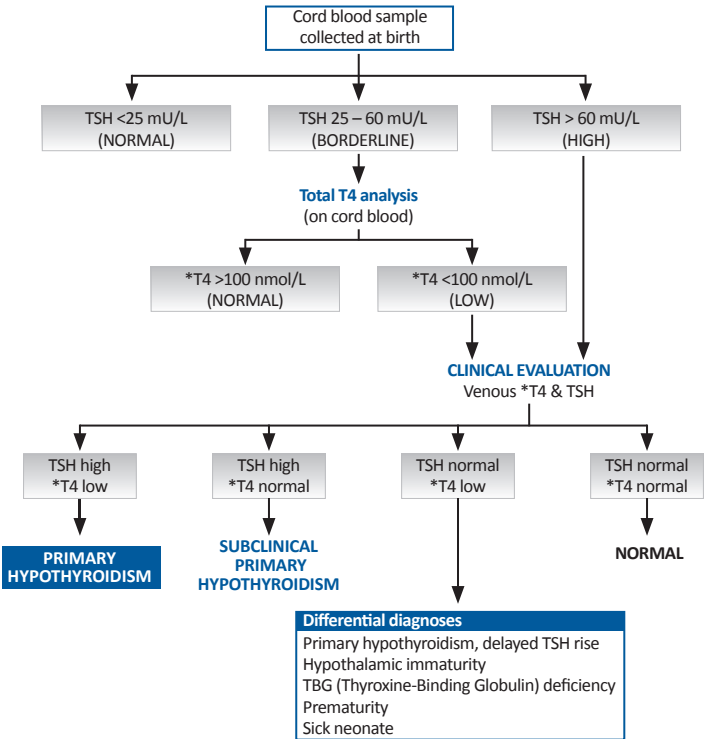
Note:

- average adult dose is 1.6 mcg /kg/day in a 70-kg adult (wide range of dose from 50 - 200 mcg/day).
- L-thyroxine can be given at different doses on alternate days, e.g. 50 mcg given on even days and 75 mcg on odd days will give an average dose of 62.5 mcg/day.

Table 1. Aetiology

<i>Thyroid dysgenesis</i> (85%)
athyreosis (30%)
hypoplasia (10%)
ectopic thyroid (60%)
<i>Other causes</i> (15%)
inborn error of thyroid
hormone synthesis (1:30,000)
hypothalamo-pituitary
defect (1:100,000)
peripheral resistance to
thyroid hormone (very rare)
transient neonatal
hypothyroidism (1:100 - 50,000)
endemic cretinism

Figure 1. Screening for congenital hypothyroidism



Interpretation of the results should take into account the physiological variations of the hormone levels during the neonatal period.

\*Free thyroxine level if available is preferable to total thyroxine level.

### Goals of therapy

- to restore the euthyroid state by maintaining a normal serum T4/ FT4 level at the upper half of the normal age-related reference range. Ideally, serum TSH levels should be between 0.5-2.0 mU/L.
- serum T4/ FT4 level usually normalized within 1-2 weeks, and then TSH usually become normal after 1 month of treatment
- some infants may continue to have high serum TSH concentration (10 - 20 mU/L) despite normal serum T4 values due to resetting of the pituitary-thyroid feedback threshold

Table 2. Goals of therapy in the first year of life

Adequate treatment		Inadequate treatment	
T4	10 -16 mcg/dL (130 - 206 nmol/L)	T4	< 10 mcg/dL (<103 nmol/L)
FT4	1.4 – 2.3 ng/dL (18 - 30 pmol/L)		
TSH	< 5 mU/L	TSH	>15 mU/L more than once in first year

### Follow-up

Monitor growth parameters and developmental assessment.

The recommended measurements of serum T4 / FT4 and TSH by American Academy of Pediatrics are according to the following schedules: -

- at 2 and 4 weeks after initiation of T4 treatment
- every 1 to 2 months during the first 6 months of life
- every 3 to 4 months between 6 months and 3 years of age
- every 6 to 12 months thereafter until growth is completed
- after 4 weeks if medication is adjusted
- at more frequent interval when compliance is questioned or abnormal values are obtained
- ongoing counseling of parents is important because of the serious consequences of poor compliance

### Re-evaluation of patients likely having transient hypothyroidism

This is best done at age 3 years as most thyroid dependent brain growth is completed at this age.

- stop L-thyroxine for 4 weeks then repeat thyroid function test: T4 / FT4, TSH
- imaging studies: Thyroid scan, Ultrasound of the thyroid
- if the FT4 is low and the TSH value is elevated, permanent hypothyroidism is confirmed and L-thyroxine therapy should be re-instituted

### Babies born to mothers with thyroid disorders

All newborns of mothers with thyroid diseases should be evaluated for thyroid dysfunction, followed up and treated if necessary.

## DIABETES MELLITUS

Diabetes in children is almost invariably type I diabetes mellitus. The incidence of type II diabetes mellitus is on the increasing trend among young people due to obesity.

**Table 1. Sign and symptoms of diabetes mellitus**

Early	Late
polydipsia	vomiting
polyuria	dehydration
weight loss	abdominal pain
enuresis (secondary)	hyperventilation due to acidosis
	drowsiness
	coma

**Table 2. Criteria for diagnosis of diabetes mellitus**

- Symptoms of diabetes + casual plasma glucose concentration  $\geq 11.1$  mmol/L ( $\geq 200$  mg/dL).<sup>1</sup>  
Casual is defined as any time of day without regard to time since the last meal.

or

- Fasting plasma glucose  $\geq 7.0$  mmol/L ( $\geq 126$  mg/dL).<sup>2</sup>  
Fasting is defined as no caloric intake for at least 8 h.

OR

- 2-h postload glucose  $\geq 11.1$  mmol/L ( $\geq 200$  mg/dL) during an oral glucose tolerance test (OGTT).  
Using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water or 1.75 g/kg of body weight to a maximum of 75 g. (WHO).

footnote:

1. Corresponding values (mmol/L) are  $\geq 10.0$  for venous whole blood and  $\geq 11.1$  for capillary whole blood.

2. Corresponding values are  $\geq 6.3$  mmol/L for both venous and capillary whole blood.

### Management

#### Principles of insulin therapy

- daily insulin dosage
  - daily insulin dosage varies greatly between individuals and changes over time
  - the correct dose of insulin for any individual is the dose that achieves the best glycemic control without causing obvious hypoglycemia problems, and achieving normal growth (height and weight)
  - dosage depends on many factors such as: age, weight, stage of puberty, duration and phase of diabetes, state of injection sites, nutritional intake and distribution, exercise patterns, daily routine, results of blood glucose monitoring (BGM) and intercurrent illness.
- guidelines on dosage:
  - during the partial remission phase, total daily insulin dose is usually 0.5 IU/kg/day
  - prepubertal children (outside the partial remission phase) usually require insulin of 0.7–1.0 IU/kg/day
  - during puberty, requirements may rise above 1 and even up to 2 IU/kg/day

The total daily dose of insulin is distributed across the day depending on the daily pattern of blood glucose and the regimens that are used.

Table 3. Types of insulin

Types of Insulin	Examples	Onset of Action	Peak	Duration
Rapid-acting insulin	NovoRapid, Humalog	5-15 min	30-60 min	3-5 hours
Short-acting insulin (regular)	Actrapid, Humilin R	30 min	2-3 hours	3-6 hours
Intermediate-acting insulin	Insulatard (NPH) Humulin N	2-4 hours	4-12 hours	12-18 hours
Long-acting insulin	Levemir	<i>Determir</i>	<i>Determir</i>	<i>Determir</i>
	(Detemir), Lantus (Glargine)	1-2 hours <i>Glargine</i> 1 hour	6-8 hours <i>Glargine</i> no peak	6-23 hours <i>Glargine</i> 24 hours

- Frequently used regimens:

#### *Twice Daily Regimens*

- 2 daily injections of a mixture of a short or rapid insulin with and intermediate-acting insulins (before breakfast and the main evening meal)
- approximately 1/3 of the total daily insulin dose is short acting insulin and 2/3 intermediate-acting insulin
- about 2/3 of the total daily dose is given in the morning and 1/3 in the evening

#### *Three injections daily*

- a mixture of short- or rapid- and intermediate-acting insulins before breakfast;
- a rapid-acting analogue or regular insulin alone before afternoon snack or the main evening meal
- and an intermediate- acting insulin before bed

#### *Basal-bolus Regimen*

depending on whether rapid-acting or regular insulin is used:

- Rapid-acting insulin: about 50 % of total daily dose of insulin is given as rapid-acting insulin divided up between 3 – 4 premeal boluses. The rest (about 50%) given as basal nighttime intermediate-acting insulin
- Regular insulin: about 70 % of total daily dose of insulin is given as regular insulin divided up as 3-4 premeal boluses and the rest (about 30% ) given as basal night time intermediate-acting insulin. The proportion of basal insulin is less because regular insulin provides some basal effect
- if using regular insulin: inject 20–30 min before each main meal (breakfast, lunch; and main evening meal); if using rapid-acting insulin analogue inject immediately before or after each main meal (e.g. breakfast, lunch; and the main evening meal).
- basal cover is usually given once daily at bedtime. However sometimes it may be needed to be given twice daily (the other dose usually before breakfast)
- insulin pump regimens are regaining popularity with a fixed or a variable basal dose and bolus doses with meals.

Some notes on converting from intermediate acting insulin to long acting insulin analogues:

- *Insulin Glargine*

- usually given once a day. However if needed, it can be given twice a day.
- when converting from NPH to Glargine, the total dose of basal insulin needs to be reduced by approximately 20% to avoid hypoglycemia. After that, the dose should be individually tailored.

- *Insulin Detemir*

- is most commonly given twice daily in children
- when changing to detemir from NPH, the same doses can be used to start with.

### Monitoring of glycemic control

#### *Self-monitoring of blood glucose (SMBG)*

The frequency of SMBG is associated with improved HbA1c in patients with type 1 diabetes.

- timing of SMBG.
  - at different times in the day to show levels of BG
  - to confirm hypoglycemia and to monitor recovery; and
  - during intercurrent illness to prevent hyperglycemic crises.
- the number and regularity of SMBG should be individualized depending on
  - availability of equipment;
  - type of insulin regimen; and
  - ability of the child to identify hypoglycemia

Note:

- successful application of intensified diabetes management with multiple injection therapy or insulin infusion therapy requires frequent SMBG (four to six times a day) and regular, frequent review of the results to identify patterns requiring adjustment to the diabetes treatment plan.

*Table 4. Target indicators of glycaemic control*

Level of control	Ideal (non-diabetic)	Optimal (diabetic)
<i>Clinical assessment</i>		
Raised BG <sup>1</sup>	not raised	no symptoms
Low BG	not low	few mild, no severe hypoglycaemias
<i>Biochemical assessment</i>		
• SBGM values (mmol/L)		
AM fasting or preprandial	3.6 - 5.6	5.0 - 8.0
• PG <sup>2</sup> in mmol/L		
Postprandial PG	4.5 - 7.0	5.0 - 10.0
Bedtime PG	4.0 - 5.6	6.7 - 10.0
Nocturnal PG	3.6 - 5.6	4.5 - 9.0
• HbA1c (%) <sup>3</sup>	< 6.05	< 7.5

*footnote: 1. BG, , blood glucose; 2. PG, plasma glucose; 3. Diabetes Control and Complications Trial Standard*



- however, each child should have their targets individually determined with the goal of achieving a value as close to normal as possible while avoiding severe hypoglycemia as well as frequent mild to moderate hypoglycemia

**Monitoring of urinary or blood ketones**

- urine or blood ketone measurement should be monitored during episodes of uncontrolled hyperglycemia, insulin deficiency, intercurrent illness (sick days), and impending ketoacidosis.

*Urine ketone testing*

- tablets or urine testing strips (detect increased levels of urinary acetoacetate)

Reading (in mmol/L)	Corresponding
0.5	Trace amounts
1.5	Small amounts
4	Moderate amounts
> 8	Large amounts

*Interpretation of urine ketone testing*

- moderate or large urinary ketone levels in the presence of hyperglycemia indicate insulin deficiency and risk for metabolic decompensation leading to ketoacidosis.
- the presence of vomiting with hyperglycemia and large urinary ketones must be assumed to be because of systemic acidosis and requires further evaluation.
- urine, in contrast to blood ketone testing, is not helpful in ruling out or diagnosing DKA.

*Blood ketone determination.*

- because of cost many centres limit the determination of blood ketone to
  - young children (difficult to obtain a urine specimen),
  - and for any individual if the urine ketone measurement is large – i.e., .4–8 mmol/L.
- blood ketone testing is especially important for patients on pumps as they have a much smaller subcutaneous (s.c.) insulin depot
- determination of blood ketone levels can guide management, e.g., if more intensive treatment is required to avert severe ketoacidosis

*When should we test for ketones?*

- illness with fever and/or vomiting
- persistent blood glucose levels > 14 mmol/L (250 mg/dL), in an unwell child, in a young child, an insulin pump user, or patient with a history of prior episodes of DKA
- persistent polyuria with elevated blood or urine glucose
- episodes of drowsiness
- abdominal pain or rapid breathing

**Recommendations for HbA1c measurement**

- ideally, in younger children, 4 - 6 times per year. In older children, 3 - 4 times per year
- adolescents with stable type 2 diabetes should have 2 - 4 measurements per year because they can rapidly become insulin requiring (compared to adults).
- HbA1c target range for all age-groups of: < 7.5%
  - if hypoglycemia unawareness is present, glycemic targets must be increased until hypoglycemia awareness is restored
  - in children < 6 yr, be particularly vigilant for unrecognized hypoglycemia.

## Diet

- a balance and healthy diet for age is required with dietician involvement

## Exercise

- no restriction.
- eat fast-acting carbohydrates frequently during strenuous exercise
- plan injection sites according to activity e.g. inject insulin in the arm if cycling

## Diabetic Education

At diagnosis: survival skills

- explanation of how the diagnosis has been made and reasons for symptoms
- simple explanation of the uncertain cause of diabetes. No cause for blame.
- the need for immediate insulin and how it will work
- what is glucose? Normal blood glucose (BG) levels and glucose targets
- practical skills: insulin injections; blood and/or urine testing, reasons for monitoring
- basic dietetic advice
- simple explanation of hypoglycemia
- diabetes during illnesses. Advice not to omit insulin – prevent diabetic ketoacidosis
- diabetes at home or at school including the effects of exercise
- psychological adjustment to the diagnosis
- details of emergency telephone contacts

## Medic alert

- wear the medic alert at all times as this may be life saving in an emergency situation.  
A form to request for a medic alert can be obtained from the local diabetes educator.

## Diabetes support group

- Persatuan Diabetes Malaysia (PDM) or Malaysian Diabetes Association, Diabetes Resource Centre at the regional centre or the respective hospital
- encourage patient and family members to enroll as members of diabetes associations and participate in their activities

## School

- the school teachers should be informed about children having diabetes so that some flexibility can be allowed for insulin injections and mealtimes
- symptoms and treatment of hypoglycaemia should be informed so that some emergency measures can be commenced at school

## Other complications and associated conditions

- monitoring of growth and physical development.
- screening of thyroid function at diagnosis of diabetes. Then every second year if asymptomatic, no goitre or thyroid autoantibodies negative. More frequent assessment is indicated otherwise.
- in areas of high prevalence for coeliac disease, screening for coeliac disease should be carried out at the time of diagnosis and every second year thereafter. More frequent assessment if there is clinical suspicion of coeliac disease or coeliac disease in first-degree relative.
- routine clinical examination for skin and joint changes. Regular laboratory or radiological screening is not recommended. There is no established therapeutic intervention for lipodystrophy, necrobiosis lipoidica or limited joint movement.

Table 7. Screening, risk factors, and interventions for vascular complications: the levels of evidence for risk factors and interventions pertaining to adult studies, except for improved glycemic control.

Retinopathy	Nephropathy	Neuropathy	Macrovascular disease
<b>When to commence screening?</b>			
annually from age 11 yr if 2 yrs diabetes duration and from age 9 yrs with 5 yr of duration (E)	annually from age 11 yr if 2 yrs diabetes duration and from age 9 yrs with 5 yr of duration (E)	unclear	after age 12 yrs (E)
<b>Screening methods</b>			
fundal microphotograph or mydriatic ophthalmoscopy (less sensitive) (E)	urine albumin:creatinine ratio or first morning albumin concentration (E)	history and physical examination	lipid profile every 5 yr blood pressure annually (E)
<b>Risk factors</b>			
hyperglycaemia (A) high blood pressure (B) lipid abnormalities (B) higher BMI (C)	high blood pressure (B) lipid abnormalities (B) smoking (B)	hyperglycaemia (A) higher BMI (C)	hyperglycaemia (A) high blood pressure (A) lipid abnormalities (B) smoking (B) higher BMI (B)
<b>Potential intervention</b>			
improved glycemic control (A) laser therapy (A)	improved glycemic control (A) ACEI and AIIRA (A) blood pressure lowering (B)	improved glycemic control (A)	improved glycemic control (A) blood pressure control (B) statins (A)

Abbreviations. BMI, body mass index; ACEI, angiotensin converting enzyme inhibitor; AIIRA, angiotensin II receptor antagonists

Table 6. Target levels for different parameters to reduce the risk of microvascular and cardiovascular diseases in children and adolescents with type 1 diabetes; the level of evidence are from adult studies.

Parameter	Target level	Evidence grade
haemoglobin A1c ( <i>Diabetes Control and Complication Trials Standard</i> )	< 7.5 % without severe hypoglycaemia	A
low density lipoprotein cholesterol	<2.6 mmol/l	A
high density lipoprotein cholesterol	>1.1 mmol/l	C
triglycerides	<1.7 mmol/l	C
blood pressure	<90th percentile by age, sex, height	C/B
body mass index	<95th percentile (non obese)	E
smoking	none	A
physical activity	>1 h of moderate physical activity daily	B
sedentary activities	<2 h daily	B
healthy diet	caloric intake appropriate for age and normal growth fat < 30% of caloric intake and saturated fat < 10 % caloric intake fiber intake 25-35 g daily increased intake of fresh fruit and vegetables	E

## DIABETIC KETOACIDOSIS

### Diabetic Ketoacidosis (DKA)

The biochemical criteria for the diagnosis of DKA are :

- hyperglycaemia: blood glucose > 11 mmol/L ( > 200 mg/dL)
- venous pH < 7.3 or bicarbonate <15 mmol/L
- ketonaemia and ketonuria

### Goals of therapy

- correct dehydration
- correct acidosis and reverse ketosis
- restore blood glucose to near normal
- avoid complications of therapy
- identify and treat any precipitating event

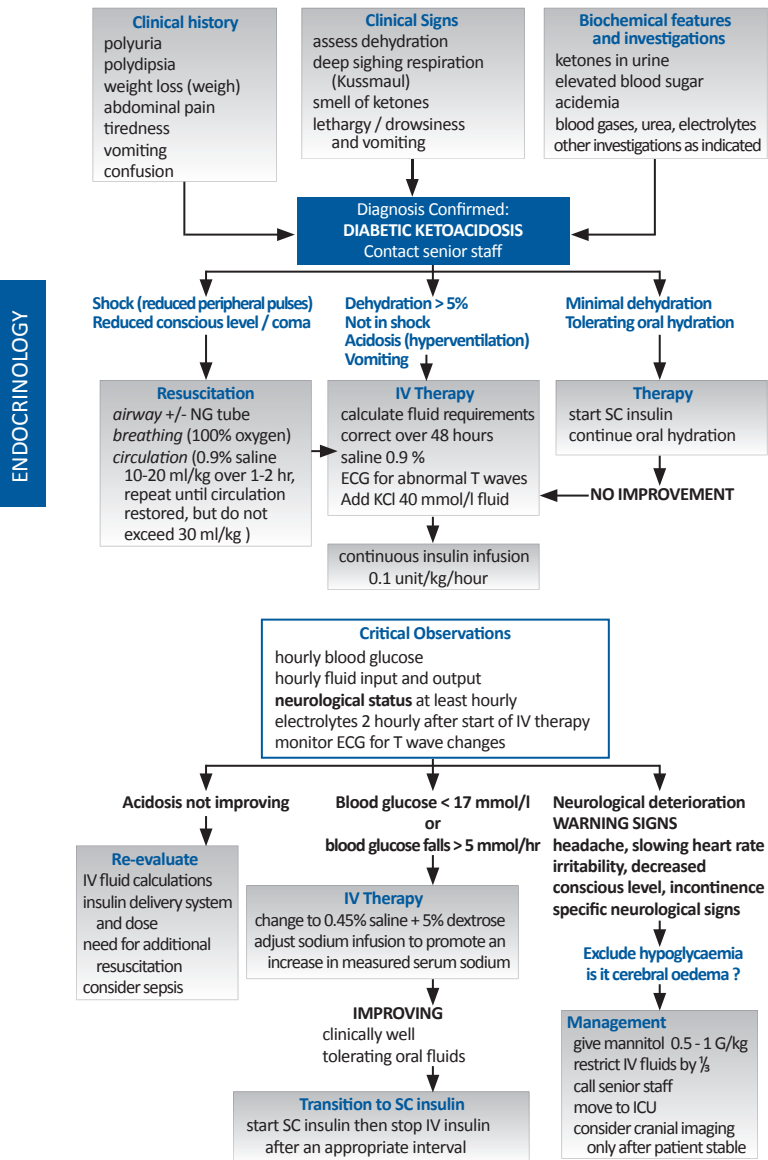
### Emergency management

- bedside confirmation of the diagnosis and determine its cause
- look for evidence of infection
- weigh the patient. This weight should be used for calculations and not the weight from a previous hospital record.
- assess clinical severity of dehydration
- assess level of consciousness [Glasgow coma scale (GCS) ]
- obtain a blood sample for laboratory measurement of:
  - serum or plasma glucose
  - electrolytes, blood urea nitrogen, creatinine, osmolality
  - venous blood gas (or arterial in critically ill patient)
  - full blood count
  - calcium, phosphorus and magnesium concentrations (if possible)
  - HbA1c
  - blood ketone (useful to confirm ketoacidosis; monitor response to treatment)
- urine for ketones
- appropriate cultures (blood, urine, throat), if there is evidence of infection
- if laboratory measurement of serum potassium is delayed, perform an electrocardiogram (ECG) for baseline evaluation of potassium status.

### Supportive measures

- secure the airway and give oxygen
- empty the stomach via a nasogastric tube
- a peripheral intravenous catheter or an arterial catheter (in ICU) for painless repetitive blood sampling
- continuous cardiac monitoring to assess T waves for evidence of hyper- or hypokalaemia
- antibiotics for febrile patients after cultures
- catheterization if the child is unconscious or unable to void on demand (e.g. in infants and very ill young children)

Figure 1. Algorithm for the immediate assessment and management of diabetic ketoacidosis (DKA)



## Clinical and biochemical monitoring

- monitoring should include the following:
  - hourly (or more frequently as indicated) vital signs (heart rate, respiratory rate, blood pressure), head chart, accurate fluid I/O (including all oral fluid).
  - amount of administered insulin
  - hourly capillary blood glucose (must be cross checked against laboratory venous glucose)
  - 2-4 hourly (or more frequent in more severe cases): BUSE, glucose, calcium, magnesium, phosphorus, hematocrit and blood gases
  - 2 hourly urine ketones until cleared or blood b-hydroxybutyrate (BOHB) concentrations (if available)

### Calculations

1. Anion gap =  $(\text{Na} + \text{K}) - (\text{Cl} + \text{HCO}_3)$ 
  - normal value: 12 +/- 2 mmol/L
  - in DKA the anion gap is typically 20–30 mmol/L
  - an anion gap > 35 mmol/L suggests concomitant lactic acidosis
2. Corrected sodium (mmol/L) =  $\text{measured Na} + \frac{2 \times (\text{plasma glucose} - 5.6)}{5.6}$
3. Effective osmolality (mOsm/kg) =  $2 \times (\text{Na} + \text{K}) + \text{plasma glucose} + \text{urea}$

## Fluids and Salt

### Principles of water and salt replacement

- begin with fluid replacement before insulin therapy.
- fluid bolus (resuscitation) required **ONLY** if needed to restore peripheral circulation
- subsequent fluid administration (including oral fluids) should rehydrate evenly over 48 hrs at a rate rarely in excess of 1.5–2 times the usual daily maintenance

### Acute Resuscitation

- if child is in shock, fluid resuscitation is needed to restore peripheral circulation, fluid boluses 10–20 mL/kg over 1–2 hrs of 0.9% saline is used. Boluses may be repeated, if necessary. There is no evidence that the use of colloids is better.

### Replacement of water and salt deficits

- patients with DKA have a deficit in extracellular fluid (ECF) volume. Clinical estimates of the volume deficit are subjective and inaccurate; therefore in
  - moderate DKA use 5–7% deficit
  - severe DKA use 7–10% dehydration
- the rate of fluid (IV, oral) should be calculated to *rehydrate evenly over 48 hours*
  - as a guide fluid infused each day usually < 1.5 - 2 times usual daily maintenance
  - IV or oral fluids given in another facility before assessment should be factored into calculation of deficit and repair.
- replacement should begin with 0.9% saline or Ringer's lactate for at least 4–6 h. Thereafter, use a solution that has a tonicity equal to or greater than 0.45% saline with added potassium chloride (see below under potassium replacement)
- urinary losses should not routinely be added to the calculation of replacement fluid, but may be necessary in rare circumstances
- calculate the corrected sodium (formula as above) and monitor changes:
  - as plasma glucose decreases after IV fluids and insulin, the serum sodium should increase: this does not indicate a worsening of the hypertonic state

- a failure of sodium levels to *rise* or a further decline in sodium levels with therapy may signal impending cerebral oedema: may need to increase sodium in IV fluids
- the use of large amounts of 0.9% saline has been associated with the development of hyperchloraemic metabolic acidosis

### Insulin therapy

- *DKA is caused by either relative or absolute insulin deficiency.*
- *start insulin infusion 1–2 h AFTER starting fluid replacement therapy*
- correction of insulin deficiency
  - dose: 0.1 unit/kg/h IV infusion. (one method is to dilute 50 units regular insulin in 50 ml normal saline, 1 unit = 1 ml)
  - *an initial IV bolus of insulin is not necessary*, and may increase the risk of cerebral oedema and should not be given
- *the dose of insulin should usually remain at 0.1 unit/kg/h at least until resolution of DKA* (evidenced by pH > 7.30, HCO<sub>3</sub> > 15 mmol/L and/or closure of the anion gap), which takes longer than normalization of blood glucose concentrations.
- if the patient as a marked sensitivity to insulin (e.g. young children with DKA, patients with Hyperglycemic Hyperosmolar State (HHS), and older children with established diabetes), the dose may be decreased to 0.05 unit/kg/h, or less, provided that metabolic acidosis continues to resolve.
- during initial volume expansion the plasma glucose concentration falls steeply. After commencing insulin therapy, the plasma glucose concentration typically decreases at a rate of 2–5 mmol/L/h.
- to prevent an unduly rapid decrease in plasma glucose concentration and hypoglycemia, *add 5% glucose to the IV fluid (e.g., 5% glucose in 0.45% saline) when plasma glucose falls to 14–17 mmol/L, or sooner if the rate of fall is rapid*
  - it may be necessary to use 10% or even 12.5% dextrose to prevent hypoglycemia while continuing to infuse insulin to correct the metabolic acidosis.
- if blood glucose falls very rapidly (>5 mmol/L/h) after initial fluid expansion add glucose even before plasma glucose has decreased to 17 mmol/L.
- if biochemical parameters of DKA (pH, anion gap) do not improve, reassess the patient, review insulin therapy, and consider other possible causes of impaired response to insulin; e.g. infection, errors in insulin preparation.
- if continuous IV insulin is not possible, hourly / 2-hourly subcutaneous (SC) or IM administration of a short or rapid-acting insulin analog (insulin lispro or insulin aspart) is safe / effective. (do not use in patients with impaired peripheral circulation)
  - initial dose SC: 0.3 unit/kg, followed 1 h later at SC 0.1 unit/kg every hour, or 0.15–0.20 units/kg every 2 h
  - if blood glucose falls to <14 mmol/L before DKA has resolved (pH still <7.30), add 5% glucose and continue with insulin as above
  - when DKA has resolved and blood glucose is < 14 mmol/L, reduce SC insulin to 0.05 unit/kg/h to keep blood glucose around 11 mmol/L

#### Important

If the blood glucose concentration decreases too quickly or too low before DKA has resolved:

- increase the amount of glucose administered
- Do not decrease the insulin infusion

## Potassium replacement

- *there is always a deficit of total body of potassium (3-6 mmol/kg) even with normal or high levels of serum potassium at presentation. Replacement therapy is therefore required.*
  - if the patient is hypokalemic at presentation, start potassium replacement at the time of initial volume expansion and before starting insulin therapy, at a concentration of 20 mmol/L (0.75 g KCl per pint)
  - if patient is normokalemic, start replacing potassium after initial volume expansion and concurrent with starting insulin therapy. The starting potassium concentration in the infusate should be 40 mmol/L (1.5 g KCl/pint)
  - if the patient is hyperkalaemic ( $K^+ > 5.5$  mmol/L), defer potassium replacement therapy until urine output is documented
  - if immediate serum potassium measurements are unavailable, an ECG may help to determine whether the child has hyper- or hypokalemia
- subsequent potassium replacement therapy should be based on serum potassium measurements
- potassium replacement should continue throughout IV fluid therapy
- the maximum recommended rate of IV potassium replacement is 0.5 mmol/kg/h
- if hypokalemia persists despite maximum rate of potassium replacement, then the rate of insulin infusion can be reduced

## Phosphate

- depletion of intracellular phosphate occurs in DKA
- severe hypophosphatemia, with unexplained weakness, should be treated
- potassium phosphate salts may be safely used as an alternative to or combined with potassium chloride or acetate, provided that careful monitoring of serum calcium is performed as administration of phosphate may induce hypocalcaemia

## Acidosis

- *severe acidosis is reversible by fluid and insulin replacement.*
- *there is no evidence that bicarbonate is either necessary or safe in DKA.* Bicarbonate therapy may cause paradoxical CNS acidosis; hypokalaemia and increasing osmolality.
- used only in selected patients:
  - severe acidaemia (arterial pH < 7.3) in whom decreased cardiac contractility and peripheral vasodilatation can further impair tissue perfusion,
  - life-threatening hyperkalaemia.
  - cautiously give 1–2 mmol/kg over 60 min.

## Introduction of oral fluids and transition to SC insulin injections

- oral fluids should be introduced only with substantial clinical improvement (mild acidosis/ketosis may still be present).
- when oral fluid is tolerated, IV fluid should be reduced.
- when ketoacidosis has resolved (pH > 7.3;  $HCO_3^- > 15$  mmol/L), oral intake is tolerated, and the change to SC insulin is planned, the most convenient time to change to SC insulin is just before a mealtime. E.g. SC regular insulin 0.25 u/kg given before meals (pre-breakfast, pre-lunch, pre-dinner), SC intermediate insulin 0.25 u before bedtime. Total insulin dose is about 1u/kg/day.



- to prevent rebound hyperglycemia, the first SC injection is given 15 - 30 min (with rapid acting insulin) or 1–2 h (with regular insulin) before stopping the insulin infusion to allow sufficient time for the insulin to be absorbed.
- the dose of soluble insulin is titrated against capillary blood glucose.
- convert to long-term insulin regime when stabilized. Multiple dose injections 4 times per day are preferable to conventional (twice daily) injections.

**Morbidity and mortality**

- in national population studies, mortality rate from DKA in children is 0.15–0.30%
- cerebral oedema accounts for 60–90% of all DKA deaths
- 10% to 25% of survivors of cerebral edema have significant residual morbidity

Other rare causes of morbidity and mortality include: hypokalemia, hyperkalemia, severe hypophosphataemia; hypoglycaemia; sepsis; aspiration pneumonia; pulmonary oedema; adult respiratory distress syndrome (ARDS); rhabdomyolysis; acute renal failure and acute pancreatitis.

**Cerebral oedema**

- clinically significant cerebral oedema usually develops 4 -12 h after treatment has started, but may occur before treatment or rarely, as late as 24 - 48 h later

**Table 1. Diagnosis of cerebral oedema in children with diabetic ketoacidosis**

<b>Diagnostic criteria for cerebral oedema</b> abnormal motor or verbal response to pain decorticate or decerebrate posture cranial nerve palsy (especially III, IV, and VI) abnormal neurogenic respiratory pattern (e.g., grunting, tachypnea, Cheyne-Stokes respiration, apneusis)	
Major criteria	Minor criteria
altered mentation / fluctuating level of consciousness sustained HR deceleration (decrease > 20 bpm), not attributable to improved intravascular volume or sleep state age-inappropriate incontinence	vomiting headache lethargy or not easily arousable diastolic blood pressure >90 mmHg age <5 years

*Note: 1 diagnostic criteria, or 2 major criteria, or 1 major and 2 minor criteria have a sensitivity of 92% and a false positive rate of only 4%.*

**Treatment of cerebral oedema**

- initiate treatment as soon as the condition is suspected.
- give mannitol 0.5 - 1 g/kg IV over 20 min and repeat if there is no initial response in 30 minutes to 2 hours
- reduce the rate of fluid administration by one-third.
- hypertonic saline (3%), 5 - 10 ml/kg over 30 min, may be an alternative to mannitol, especially if there is no initial response to mannitol
- elevate the head of the bed.
- intubation may be necessary for the patient with impending respiratory failure. Maintain normocapnia. (PaCO<sub>2</sub> within normal range).
- after treatment for cerebral oedema has been started, a cranial CT scan should be done to rule out other possible intracerebral causes of neurologic deterioration

## AMBIGUOUS GENITALIA

### Introduction

Ambiguous genitalia (AG) of the newborn is the paradigm of a disorder of sex development. This includes infants with bilateral cryptorchidism, perineal hypospadias with bifid scrotum, clitoromegaly, posterior labial fusion, phenotypic female appearance with palpable gonad (with or without inguinal hernia), and infants with discordant genitalia and sex chromosomes.

The word intersex has been in use for some time, but is not favored by many families with AG. The Chicago Consensus in 2006 recommended nomenclature to replace intersex with the umbrella terminology 'disorders of sex development' (DSD). This is defined as a congenital condition in which development of chromosomal, gonadal, or anatomical sex is atypical. Below is a summary of the components of the revised nomenclature

*Table 1. Nomenclature relating to disorders of sex development (DSDs)*

Previous	Proposed
Intersex	DSD
Male pseudohermaphrodite, undervirilization of an XY male, and undermasculinization of an XY male	46, XY DSD
Female pseudohermaphrodite, overvirilization of an XX female, and masculinization of an XX female	46, XX DSD
True hermaphrodite	Ovotesticular DSD
XX male or XX sex reversal	46, XX testicular DSD
XY sex reversal	46, XY complete gonadal dysgenesis

### **Ambiguous Genitalia is a neonatal emergency**

The commonest cause of AG is congenital adrenal hyperplasia (CAH).

*Major concerns are :-*

- underlying medical issues
  - dehydration, salt loss (adrenal crisis)
  - urinary tract infection
  - bowel obstruction
- decision on sex of rearing
  - avoid wrong sex assignment
  - prevent gender confusion
- psychosocial issues

### General concepts of care

- *gender assignment* must be avoided before expert evaluation in newborns.
- evaluation and long-term management must be performed at a center with an experienced multidisciplinary team (Paediatric Subspecialists in endocrinology, surgery, and/or urology, psychology/ psychiatry, gynaecology, genetics, neonatology, and if available, social work, nursing and medical ethics.)
- all individuals should receive a gender assignment
- open communication with patients and family is essential, and participation in decision making is encouraged
- Patients and family concerns (eg, social and culture) should be respected and

## EVALUATION

Ideally, baby/child with parents should be brought to a competent multidisciplinary team.

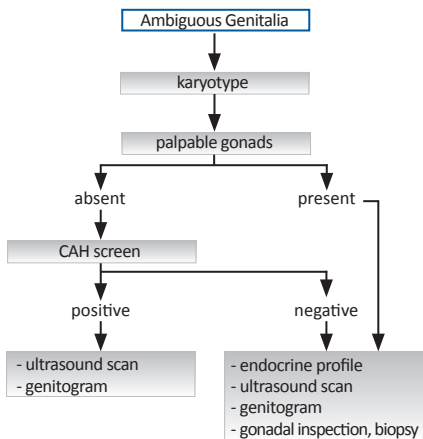
HISTORY - exclude CAH in all neonates

- parental consanguinity.
- obstetric : previous abortions, stillbirths, neonatal deaths.
- antenatal : drugs taken, exogenous androgens, endocrine disturbances.
- family History: Unexplained neonatal deaths in siblings and close relatives
  - infertility, genital anomalies in the family
  - abnormal pubertal development
  - infertile aunts
- symptoms of salt wasting in the first few days to weeks of life.
- increasing pigmentation
- progressive virilisation

### Physical examination

- dysmorphism (Turner phenotype, congenital abnormalities)
- cloacal anomaly
- signs of systemic illness
- hyperpigmentation
- blood pressure
- psychosocial behaviour (older children)
- appearance of external genitalia
  - size of phallus, erectile tissue
  - position of urethral opening (degree of virilisation)
  - labial fusion / appearance of scrotum
  - presence / absence of palpable gonads
  - presence / absence of cervix (per rectal examination)
  - position & patency of anus

Figure 1. Approach to ambiguous genitalia



### Investigations

- chromosome study, karyotyping with X- and Y-specific probe detection
- abdominopelvic ultrasound
- genitogram
- exclude salt losing CAH
- serial BUSE in the neonatal period
- serum 17-hydroxyprogesterone (taken after the first day of life)
- cortisol, testosterone, renin
- testosterone, LH, FSH
- anti mullerian hormone (depending on indication and availability)

### Additional investigations as indicated:

- LHRH stimulation test
- hCG stimulation tests (testosterone, dihydrotestosterone (DHT) at Day 1 & 4)
- urinary steroid analysis
- androgen receptor study (may not be available)
- DNA analysis for SRY gene (sex-determining region on the Y chromosome)
- imaging studies
- biopsy of gonadal material in selected cases.
- currently, molecular diagnosis is limited by cost, accessibility and quality control.
- trial of testosterone enanthate 25 mg IM monthly 3x doses
  - this can be done to demonstrate adequate growth of the phallus and is essential before a final decision is made to raise an ambiguous child as a male.

Table 2. Differential diagnosis

Uterus present	Uterus absent
46,XX DSD virilising CAH foetal exposure to excessive androgens	46, XY DSD androgen insensitivity syndrome 5-alpha reductase deficiency defect in testosterone synthesis
46, XY DSD 46,XY gonadal dysgenesis	
Sex chromosome DSD 45, XO/46, XY gonadal dysgenesis	
Ovotesticular DSD true hermaphroditism	

Table 3. Key features to aid diagnosis

Hyperpigmentation	+	-	-	-
Palpable gonad(s)	-	+	+	+
Uterus present	+	+	-	-
Dysmorphism	-	+ / -	-	-
Systemic illness	+	-	-	-
Diagnosis	21-Hydroxylase deficiency	Gonadal dysgenesis	Partial androgen insensitivity syndrome	Testosterone biosynthesis defect
Karyotype	46, XX	XO/XY 46, XY; 46, XX	46, XY	46, XY

## Management

### Goals

- preserve fertility
- ensure normal sexual function
- phenotype and psychosocial outcome concordant with the assigned sex

### General considerations

- admit to hospital. Salt losing CAH which is life threatening must be excluded.
- urgent diagnosis
- do not register the child until final decision is reached
- protect privacy of parents and child pending diagnosis
- counseling of parents that DSD conditions are biologically understandable.
- encourage bonding

### Gender Assignment

Gender assignment and sex of rearing should be based upon the most probable adult gender identity and potential for adult function. Factors to be considered in this decision include :-

- diagnosis
- fertility potential
- adequacy of the external genitalia for normal sexual function. Adequate phallic size when considering male sex of rearing
- endocrine function of gonads. Capacity to respond to exogenous androgen.
- parents' socio-cultural background, expectations and acceptance
- psychosocial development in older children
- decision about sex of rearing should only be made by an informed family after careful evaluation, documentation, and consultation

*Gender reinforcement*

- appropriate name
- upbringing, dressing
- treatment and control of underlying disease e.g. CAH
- surgical correction of the external genitalia as soon as possible

*Assigned female*

- remove all testicular tissue
- vaginoplasty after puberty
- no place for vaginal dilatation in childhood

*Assigned male*

- orchidopexy
- remove all Mullerian structures
- surgical repair of hypospadias
- gonadectomy to be considered if dysgenetic gonads

*Surgical management*

- the goals of surgery are:
  - genital appearance compatible with gender
  - unobstructed urinary emptying without incontinence or infections
  - good adult sexual and reproductive function
- the surgeon has the responsibility to outline the surgical sequence and subsequent consequences from infancy to adulthood. Only surgeons with the expertise in the care of children and specific training in the surgery of DSD should perform these procedures
- early genitoplasty is feasible only if the precise cause of DSD has been established and gender assignment has been based on certain knowledge of post pubertal sexual outcome. Other wise surgery should be postponed, as genitoplasty involves irreversible procedures such as castration and phallic reduction in individuals raised females and resection of utero-vaginal tissue in those raised male.
- the procedure should be anatomically based to preserve erectile function and the innervations of the clitoris
- emphasis in functional outcome rather than a strictly cosmetic appearance.
- timing of surgery: it is felt that surgery that is performed for cosmetic reasons in the first year of life relieves parental distress and improves attachment between the child and the parents; the systematic evidence for this is lacking.

**CONGENITAL ADRENAL HYPERPLASIA (CAH)****Neonatal diagnosis and treatment**

- the newborn female with CAH and ambiguous external genitalia requires urgent expert medical attention
- the ambiguity is highly distressing to the family; therefore, immediate comprehensive evaluation is needed by referral to a pediatric endocrinologist
- ensure parents develop a positive relationship with their child

**Clinical evaluation in term and premature neonates**

- every newborn with ambiguous genitalia, a suspected diagnosis of CAH, or an abnormal result in a newborn screen for 17-hydroxyprogesterone (17OHP) should be evaluated by a pediatric endocrinologist
- the evaluation of an infant with ambiguous genitalia have been discussed above.

## Newborn screening for CAH

- neonatal mass screening for 21-hydroxylase deficiency identifies both male and female affected infants, prevents incorrect sex assignment, and decreases mortality and morbidity. However, it has not been started in Malaysia yet.

## Clinical presentation

### Neonatal period

- ambiguous genitalia
- salt loss (75%)
- family history of previous unexplained neonatal death
- hyperpigmentation (90%) - both sexes
- boy with precocious puberty but small testis (volume <4 ml)
- virilisation of a girl
- hypertension

## Diagnosis of salt-wasting CAH

- may not be apparent in the first days/weeks after birth by electrolyte measurements
- salt wasters may be differentiated from simple virilizers by :
  - serial serum/plasma and/or urine electrolytes
  - plasma renin activity (PRA) or direct renin
  - results of CYP21 molecular analysis

## Management of salt losing crisis

- for patient in shock: normal saline (0.9%) bolus : 10-20 ml/kg
- correct hypoglycemia if present : 2-4 mg/kg of 10% glucose
- correct hyperkalaemia with administration of glucose and insulin if necessary.
- rehydrate using  $\frac{1}{2}$  NS 5% dextrose
- monitor hydration status, BP, HR, glucose

*Note: Hypotonic saline or 5% dextrose should not be used because it can worsen hyponatraemia*

## Treatment considerations in patients with CAH

### Optimal glucocorticoid dosing

- aim to replace deficient steroids, minimize adrenal sex hormone and glucocorticoid excess: thus preventing virilization, optimizing growth, and protecting potential fertility
- during infancy, initial reduction of markedly elevated adrenal sex hormones may require hydrocortisone (HC) up to 25 mg/m<sup>2</sup>/d, but typical dosing is 10–15 mg/m<sup>2</sup>/d in 3 divided doses. Divided or crushed tablets of HC should be used in growing children
- excessive doses, especially in infancy, may cause persistent growth suppression, obesity, and other Cushingoid features. Therefore, avoid complete adrenal suppression.
- whereas HC is preferred in infancy and childhood, long-acting glucocorticoids may be used at or near the completion of linear growth. Prednisolone needs to be given twice daily. (at 2–4 mg/m<sup>2</sup>/d). Dexamethasone dose is 0.25–0.375 mg/m<sup>2</sup>/d, given once daily.
- in children with advanced bone age and central precocious puberty, treatment with a GnRH agonist may be required

### Mineralocorticoid use

- all classic CAH patients should receive fludrocortisone at diagnosis in the newborn period
- dosage requirements in early infancy range from 0.05–0.30 mg/d, whereas typical maintenance doses are 0.05–0.2 mg/d, depending on the sodium intake

- therapy will reduce vasopressin, ACTH levels and lower dosage of glucocorticoid required
- the need for continuing mineralocorticoids should be assessed based on PRA and BP.
- sodium chloride supplements are often needed in infancy, at 1-3 g/day (17-51 mEq/day), distributed in several feedings.

### Monitoring treatment for classic CAH

- monitoring may be accomplished based on physical and hormonal findings suggestive of excessive or inadequate steroid therapy
- laboratory measurements may include serum/plasma electrolytes, serum 17OHP, cortisol, and/or testosterone, and PRA or direct renin, every 3 months during infancy and every 4–12 months thereafter
- the time from the last glucocorticoid dose should be noted; the diurnal rhythm of the adrenal axis should be taken into account. Patients receiving adequate replacement therapy may have cortisol levels above the normal range.
- ideally, laboratory data will indicate a need for dose adjustments before physical changes, growth, and skeletal maturation indicates inadequate or excessive dosing.
- patients should carry medical identification and information concerning their medical condition and therapy

### Treatment with glucocorticoids during stress

- parents must be given clear instruction on stress dosing
- because circulating levels of cortisol increase during stress, patients should be given increased doses of glucocorticoids during febrile illness ( $>38.5^{\circ}\text{C}$ ), when vomiting or poor oral intake, after trauma and before surgery
- participation in endurance sports may also require additional steroid dosing
- mental and emotional stress, such as school examinations, does not require increased dosing
- stress dosing should be 2–3 times the maintenance glucocorticoid dose for patients able to take oral medications
- surgical and trauma patients and those unable to take oral steroids require parenteral hydrocortisone
  - below 3 years old: to give 25mg, followed by 25-30mg/day
  - 3-12 years old: to give 50mg, followed by 50-60 mg/day
  - >12 years old: to give 100mg, followed by 100mg/day
- glucose concentrations should be monitored, and intravenous sodium and glucose replacement may be required.

### Genital surgery

- the decision for surgery and the timing should be made by the parents, together with the endocrinologist and the paediatric surgical team, after complete disclosure of all relevant clinical information and all available options have been discussed and after informed consent has been obtained.
- general principals of surgery for AG has been outlined in the preceding section on AG.
- it is recognized that 46,XX children with significant virilization may present at a later age. Consideration for sex reassignment must be undertaken only after thorough psychological evaluation of patient and family. Surgery appropriate to gender assignment should be undertaken after a period of endocrine treatment.



## Psychological issues

- females with CAH show behavioral masculinization, most pronounced in gender role behavior, less so in sexual orientation, and rarely in gender identity.
- even in females with psychosexual problems, general psychological adjustment seems to be similar to that of females without CAH.
- currently, there is insufficient evidence to support rearing a 46,XX infant at Prader stage 5 as male.
- decisions concerning sex assignment and associated genital surgery must consider the culture in which a child and her/his family are embedded.

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# NEPHROLOGY

- 57 Acute Glomerulonephritis
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- 60 Acute Peritoneal Dialysis
- 61 Neurogenic Bladder
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- 63 Antenatal Hydronephrosis



## POST INFECTIOUS ACUTE GLOMERULONEPHRITIS

### Introduction

Acute glomerulonephritis (AGN) implies that it is of abrupt onset and associated with one or more features of what is known as acute nephritic syndrome.

### Acute nephritic syndrome

- oedema e.g. facial puffiness
- decreased urine output (oliguria)
- microscopic /macroscopic haematuria
- hypertension
- (urine: tea-coloured or smoky)
- azotemia

Table 1. Aetiology

Causes of nephritis
post streptococcal AGN
post-infectious acute glomerulonephritis (other than group A $\beta$ -haemolytic streptococci)
subacute bacterial endocarditis
Henoch-Schoenlein purpura
IgA nephropathy
hereditary nephritis
systemic lupus erythematosus
systemic vasculitis

Table 2. Post Streptococcal AGN

Presenting features
acute nephritic syndrome (most common)
nephrotic syndrome
rapidly progressive glomerulonephritis
hypertensive encephalopathy
pulmonary oedema
subclinical (detected on routine examination)

In children, the commonest cause of an acute nephritic syndrome is post infectious AGN, the majority of which is due to post-streptococcal infection of the pharynx or skin. Post streptococcal AGN is commonest in the 6 – 10 year age group.

### Investigation findings in Post-streptococcal AGN

- urinalysis and culture
  - haematuria – present in all patients
  - proteinuria (trace to 2+, but may be in the nephrotic range;  
usually associated with more severe disease.)
  - red blood cell casts (pathognomonic of acute glomerulonephritis)
  - other cellular casts
  - pyuria may also be present
- bacteriological and serological evidence of an antecedent streptococcal infection
  - raised ASOT ( > 200 IU/ml )
  - increased anti-DNAse B (if available) – a better serological marker of  
preceding streptococcal skin infection
  - throat swab or skin swab
- renal function test
  - blood urea, electrolytes and serum creatinine
- full blood count
  - anaemia (mainly dilutional)
  - leucocytosis may be present
- complement levels
  - C3 level – low at onset of symptoms, normalises by 6 weeks.
  - C4 is usually within normal limits in post-streptococcal AGN.
- ultrasound of the kidneys
  - not necessary if patient has clear cut acute nephritic syndrome

## Management

- strict monitoring – fluid intake, urine output, daily weight, BP (nephrotic chart)
- Penicillin V for 10 days to eliminate  $\beta$  - haemolytic streptococcal infection (give erythromycin if penicillin is contraindicated)
- fluid restriction to control oedema and circulatory overload during oliguric phase until child diureses and blood pressure is controlled
  - day 1 : up to 400 mls/m<sup>2</sup>/day. Do not administer intravenous or oral fluids if child has pulmonary oedema.
  - day 2 : till patient diureses – 400 mls/m<sup>2</sup>/day  
(as long as patient remains in circulatory overload)
  - when child is in diuresis – free fluid is allowed
- diuretic (e.g. frusemide) should be given in children with pulmonary oedema. It is also usually needed for treatment of hypertension
- diet – no added salt to diet. Protein restriction is unnecessary
- look out for complications of post-streptococcal AGN:
  - hypertensive encephalopathy usually presenting with seizures
  - pulmonary oedema (acute left ventricular failure)
  - acute renal failure

## Management of severe complications of post-streptococcal AGN

### Hypertension

- significant hypertension but asymptomatic
  - bed rest and recheck BP ½ hour later
  - If BP still high, give oral nifedipine 0.25 - 0.5 mg/kg. Recheck BP ½ hour later.
  - monitor BP hourly x 4 hours then 4 hourly if stable.
  - oral nifedipine can be repeated if necessary on 4 hourly basis.
  - may consider regular oral nifedipine (6 – 8 hourly) if BP persistently high.
  - add frusemide 1 mg/kg/dose if BP still not well controlled.
  - other anti-hypertensives if BP still not under control:
    - captopril (0.1-0.5 mg/kg q8 hourly), metoprolol 1-4 mg/kg 12 hourly
- symptomatic, severe hypertension or hypertensive emergency / encephalopathy
  - symptom / signs: headache, vomiting, loss of vision, convulsions, papilloedema
  - emergency management indicated to reduce BP sufficiently to avoid hypertensive complications and yet maintain it at a level that permits antiregulatory mechanism of vital organs to function
  - target of BP control:
    - reduce BP to <90th percentile of BP for age, gender and height percentile
    - total BP to be reduced = observed mean BP – desired mean BP
    - reduce BP by 25% of target BP over 3 – 12 hours
    - the next 75% reduction is achieved over 48 hours

### Pulmonary oedema

- give oxygen, prop patient up; ventilatory support if necessary
- IV frusemide 2 mg/kg/dose stat; double this dose 4 hours later if poor response
- fluid restriction – withhold fluids for 24 hours if possible
- consider dialysis if no response to diuretics.

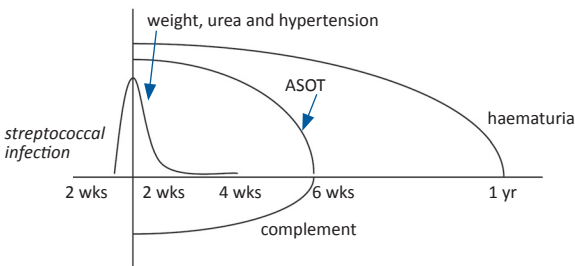
Acute renal failure

- mild renal impairment is common;
- severe persistent oliguria or anuria with azotaemia is uncommon
- management of severe acute renal failure – refer section on acute renal failure

Table 3. Antihypertensive drugs used for hypertensive emergencies in children

Drug	Dose
Nifedipine	0.25 – 0.5 mg/kg/dose oral may be repeated twice if no response
Sodium nitroprusside	0.5 – 1.0 mcg/kg/min, iv infusion may increased stepwise to 8.0 mcg/kg/min maximum <b>Needs to be given in an ICU setting</b> <i>Caution: in liver and renal failure</i>
Labetolol	0.2 – 1.0 mg/kg/dose by repeated iv boluses or 0.25 – 2.0 mg/kg/hour by iv infusion
Hydralazine	0.2 – 0.4 mg/kg/dose by iv bolus may be repeated twice if no response

Figure 1. Natural history of acute post-streptococcal glomerulonephritis



Follow-up

- for at least 1 year.
- monitor BP at every visit
- do urinalysis and renal function to evaluate recovery.
- repeat C3 levels 6 weeks later if not already normalised by time of discharge

Table 4. Indications for renal biopsy

- severe acute renal failure requiring dialysis.
- features suggesting non post-infectious AGN as the cause of acute nephritis.
- delayed resolution
  - oliguria > 2 weeks
  - azotaemia > 3 weeks
  - gross haematuria > 3 weeks
  - persistent proteinuria > 6 months

Outcome

- short term outcome: excellent, mortality <0.5%.
- long term outcome: 1.8% of children develop chronic kidney disease following post streptococcal AGN. These children should be referred to the paediatric nephrologists for further evaluation and management.

## IDIOPATHIC NEPHROTIC SYNDROME

### Diagnosis

Nephrotic syndrome is a clinical syndrome of massive proteinuria defined by

- oedema
  - proteinuria  $> 40 \text{ mg/m}^2/\text{hour}$  ( $> 1 \text{ g/m}^2/\text{day}$ )
  - or an early morning urine protein creatinine index of  $> 200 \text{ mg/mmol}$  ( $> 3.5 \text{ mg/mg}$ )
- hypoalbuminaemia of  $< 25 \text{ g/l}$   
hypercholesterolaemia

### Aetiology

*Primary or idiopathic* (of unknown cause) nephrotic syndrome is the commonest type of nephrotic syndrome in children.

*Secondary* causes of nephrotic syndrome include post-streptococcal glomerulonephritis and systemic lupus erythematosus (SLE). This chapter outlines the management of idiopathic nephrotic syndrome. Management of secondary forms of nephrotic syndrome follows the management of the primary condition.

### Investigations at initial presentation

- full blood count
- renal profile
  - urea, electrolyte, creatinine
- quantitative urinary protein excretion (*spot urine protein: creatinine ratio or 24 hour urine protein*)
- serum cholesterol
- liver function tests
  - particularly serum albumin
- urinalysis, urine culture

*Other investigations* would depend on the age of the patient, associated renal impairment, hematuria, hypertension or features to suggest an underlying *secondary* cause for the nephrotic syndrome.

These tests include:

- antinuclear factor / anti-dsDNA to exclude SLE
- serum complement (C3, C4) level to exclude SLE and post infectious glomerulonephritis
- ASOT titres to exclude post streptococcal glomerulonephritis.
- other tests as indicated.

### Renal biopsy

A renal biopsy is not needed prior to starting corticosteroid or cyclophosphamide therapy. This is because 80% of children with idiopathic nephrotic syndrome have minimal change steroid responsive disease.

The main indication for renal biopsy is steroid resistant nephrotic syndrome, defined as *failure to achieve remission despite 4 weeks of adequate corticosteroid therapy*.

Other indications are features that suggest non-minimal change nephrotic syndrome:

- persistent hypertension, renal impairment, and/or gross haematuria.

### Management

- confirm that patient has nephrotic syndrome by ensuring that the patient fulfills the criteria above
- exclude other causes of nephrotic syndrome. If none, then the child probably has idiopathic nephrotic syndrome

### General management

- a normal protein diet with adequate calories is recommended.
- no added salt to the diet when child has oedema.
- Penicillin V 125 mg BD (1-5 years age), 250 mg BD (6-12 years), 500 mg BD (>12 years) is recommended at diagnosis and during relapses, particularly in the presence of gross oedema
- careful assessment of the haemodynamic status.
  - check for signs and symptoms which may indicate  
*hypovolaemia*: abdominal pain, cold peripheries, poor capillary refill, poor pulse volume with or without low blood pressure; *OR*  
*hypervolaemia*: basal lung crepitations, rhonchi, hepatomegaly, hypertension
  - fluid restriction - not recommended except in chronic oedematous states
- diuretics (e.g. frusemide) is not necessary in steroid responsive nephrotic syndrome but if required, use with caution as it can precipitate hypovolaemia
- human albumin (20-25%) at 0.5 - 1.0 g/kg can be used in symptomatic grossly oedematous states together with IV frusemide at 1-2 mg/kg to produce a diuresis  
*Caution: fluid overload and pulmonary oedema can occur with albumin infusion especially in those with impaired renal function. Urine output and blood pressure should be closely monitored*

### General advice

- counsel patient and parents about the disease particularly with regards to the high probability (85-95%) of relapse
- home urine albumin monitoring: once daily dipstick testing of the first morning urine specimen. The patient is advised to consult the doctor if albuminuria > 2+ for 3 consecutive days, or 3 out of 7 days.
- the child is also advised to consult the doctor should he/she become oedematous regardless of the urine dipstick result.
- children on systemic corticosteroids or other immunosuppressive agents should be advised and cautioned about contact with chickenpox and measles, and if exposed should be treated like any immunocompromised child who has come into contact with these diseases.
- immunisation:
  - while the child is on corticosteroid treatment and within 6 weeks after its cessation, only killed vaccines may safely be administered to the child. Live vaccines can be given 6 weeks after cessation of corticosteroid therapy.
  - pneumococcal vaccine should be administered to all children with nephrotic syndrome. If possible, give when the child is in remission.
- *acute adrenal crisis*  
 this may be seen in children who have been on long term corticosteroid therapy (equivalent to 18 mg/m<sup>2</sup> of cortisone daily) when they undergo situations of stress. Hydrocortisone at 2-4 mg/kg/dose TDS or prednisolone at 1 mg/kg/day should be given.



## Management of the complications of nephrotic syndrome

### *Hypovolaemia.*

- clinical features: abdominal pain, cold peripheries, poor pulse volume, hypotension, and haemoconcentration.
- treatment: infuse human albumin at 0.5 to 1.0 g/kg/dose fast.  
If human albumin is not available, other volume expanders like human plasma can be used. Do not give frusemide.

### *Primary Peritonitis*

- clinical features: fever, abdominal pain and tenderness in children with newly diagnosed or relapse nephrotic syndrome.
- investigations: Blood culture, peritoneal fluid culture (not usually done)
- treatment: parenteral penicillin and a third generation cephalosporin

### *Thrombosis*

- thorough investigation and adequate treatment with anticoagulation is usually needed. Please consult the paediatric nephrologists.

## Corticosteroid therapy

Corticosteroids are effective in inducing remission of idiopathic nephrotic syndrome.

### *Initial treatment*

- once a diagnosis of idiopathic nephrotic syndrome has been established, oral prednisolone should be started at:
  - 60 mg / m<sup>2</sup> / day ( maximum 80 mg / day ) for 4 weeks followed by
  - 40 mg / m<sup>2</sup> / every alternate morning (EOD) (maximum 60 mg) for 4 weeks.then reduce prednisolone dose by 25% monthly over next 4 months.
- with this corticosteroid regime, 80% of children will achieve remission (defined as urine dipstix trace or nil for 3 consecutive days) within 28 days.
- children with *steroid resistant* nephrotic syndrome, defined by failure to achieve response to an initial 4 weeks treatment with prednisolone 60 mg/m<sup>2</sup>/ day, should be referred to a nephrologist for further management, which usually includes renal biopsy.

## Treatment of relapses

- the majority of children with nephrotic syndrome will relapse.  
A relapse is defined by *urine albumin excretion > 40 mg/m<sup>2</sup>/hour or urine dipstix of  $\geq 2+$  for 3 consecutive days.*
- these children do not need admission unless they are grossly oedematous or have any of the complications of nephrotic syndrome.
- induction of relapse is with oral prednisolone as follows:
  - 60 mg / m<sup>2</sup> / day ( maximum 80 mg / day ) *until remission* followed by
  - 40 mg / m<sup>2</sup> / EOD (maximum 60 mg) for 4 weeks only

*Breakthrough proteinuria* may occur with intercurrent infection and usually does not require corticosteroid induction if the child has no oedema, remains well and the proteinuria remits with resolution of the infection.

However, if proteinuria persists, treat as a relapse.

### Treatment of frequent relapses

- defined as  $\geq 2$  relapses within 6 months of initial diagnosis or  $\geq 4$  relapses within any 12 month period.

#### Treatment

- induction of relapse is with oral prednisolone as follows:
  - 60 mg / m<sup>2</sup> / day ( maximum 80 mg / day ) until remission followed by
  - 40 mg / m<sup>2</sup> / EOD (maximum 60 mg) for 4 weeks only
- taper prednisolone dose every 2 weeks and keep on as low an alternate day dose as possible for 6 months. Should a child relapse while on low dose alternate day prednisolone, the child should be re-induced with prednisolone as for relapse.

### Treatment of steroid dependent nephrotic syndrome

- defined as  $\geq 2$  consecutive relapses occurring during steroid taper or within 14 days of the cessation of steroids.

#### Treatment

- if the child is not steroid toxic, re-induce with steroids and maintain on as low a dose of alternate day prednisolone as possible. If the child is steroid toxic (short stature, striae, cataracts, glaucoma, severe cushingoid features) consider cyclophosphamide therapy

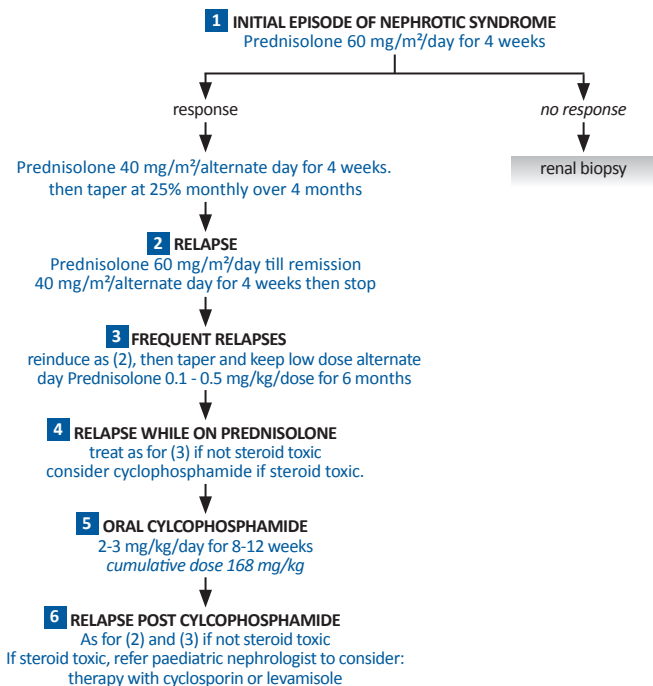
#### Cyclophosphamide therapy

- indicated for the treatment of steroid dependent nephrotic syndrome with signs of steroid toxicity; begin therapy when in remission after induction with corticosteroids
- parents should be counseled about the effectiveness and side effects of cyclophosphamide therapy (leucopenia, alopecia, haemorrhagic cystitis, gonadal toxicity).
  - dose: 2-3 mg/kg/day for 8-12 weeks (cumulative dose 168 mg/kg)
  - monitor full blood count and urinalysis 2 weekly

#### Relapses post cyclophosphamide

- relapses after a course of cyclophosphamide are treated as for relapses following the initial diagnosis of nephrotic syndrome, if the child does not have signs of steroid toxicity
- should the relapse occur soon after a course of cyclophosphamide when the child is still steroid toxic, or if the child again becomes steroid toxic after multiple relapses, then a paediatric nephrology opinion should be sought. The treatment options available include cyclosporine and levamisole.

Figure 1. Summary of treatment of nephrotic



### Steroid resistant nephrotic syndrome

Refer for renal biopsy. Specific treatment will depend on the histopathology.

General management of the nephrotic state

- control of edema:
  - restriction of dietary sodium.
  - diuretics e.g. frusemide, spironolactone.
- ACE inhibitor e.g. captopril or angiotensin II receptor blocker (AII RB) e.g. losartan, irbesartan, to reduce proteinuria  
*monitor BP and renal profile 1-2 weeks after initiation of ACE inhibitor or AII RB*
- control of hypertension – antihypertensive of choice – ACE inhibitor/AII RB
- penicillin prophylaxis.
- monitor renal function.
- nutrition: normal dietary protein content, salt-restricted diet
- evaluate calcium and phosphate metabolism.

## ACUTE RENAL FAILURE

### Definition

Abrupt rise in serum creatinine level and decreased glomerular filtration rate resulting in inability of the kidneys to regulate fluid and electrolyte balance. Acute renal failure (ARF) is also known as acute kidney injury (AKI).

### Clinical features

- of underlying cause.
- oliguria ( $< 300 \text{ ml/m}^2/\text{day}$  in children;  $< 1 \text{ ml/kg/hour}$  in neonates)
- non-oliguric.
- clinical features arising from complications of ARF  
e.g. seizures, acute pulmonary oedema

Table 1. Common causes of acute renal failure

Pre-renal	Renal, or intrinsic
<i>hypovolaemia</i> dehydration, bleeding, <i>third space loss</i> nephrotic syndrome, burns <i>distributive shock</i> dengue shock, sepsis syndrome <i>cardiac</i> congestive heart failure cardiac tamponade	<i>glomerular</i> infection related systemic lupus erythematosus acute glomerulonephritis <i>tubulointerstitial</i> acute tubular necrosis from - hypoxic-ischaemic injury - drugs e.g. aminoglycosides, chemotherapy toxins e.g. myoglobin, haemoglobin venom e.g. bee sting tumour lysis, uric acid nephropathy infection, pyelonephritis <i>vascular</i> ACE-inhibitors, vascular lesions
<b>Post-renal</b> posterior urethral valves acute bilateral ureteric obstruction acute obstruction in solitary kidney	
<i>footnote:</i> - important to consider pre-renal failure as a cause of oliguria. - In pre-renal failure, the kidney is intrinsically normal and the tubules are working to conserve water and sodium appropriately. - In acute tubular necrosis (ATN) the damaged tubules are unable to conserve sodium appropriately	

## MANAGEMENT

### Fluid balance

#### In Hypovolaemia

- fluid resuscitation regardless of oliguric / anuric state
- give crystalloids e.g. isotonic 0.9% saline / Ringer's lactate 20 ml/kg fast (in  $< 20$  minutes) after obtaining vascular access.
- transfuse blood if haemorrhage is the cause of shock.
- hydrate to normal volume status.
- if urine output increases, continue fluid replacement.
- if there is no urine output after 4 hours (confirm with urinary catheterization),
- monitor central venous pressure to assess fluid status

Refer to section on shock for details of management.

### *In Hypervolaemia / Fluid overload*

Features of volume overload include hypertension, raised JVP, displaced apex beat, basal crepitations, hepatomegaly and increasing ventilatory requirements.

- if necessary to give fluid, restrict to insensible loss ( $400 \text{ ml/m}^2/\text{day}$  or  $30 \text{ ml/kg}$  in neonates depending on ambient conditions)
- IV frusemide  $2 \text{ mg/kg/dose}$  (over 10-15 minutes), maximum of  $5 \text{ mg/kg/dose}$  or IV frusemide infusion  $0.5 \text{ mg/kg/hour}$
- dialysis if no response or if volume overload is life-threatening

### *Euvolaemia*

- once normal volume status is achieved, give insensible loss plus obvious losses (urine / extrarenal)
- monitor fluid status: weight, BP, heart rate, nutritional needs, intake/output.

### **Hypertension**

- usually related to fluid overload and/or alteration in vascular tone
- choice of anti-hypertensive drugs depends on degree of BP elevation, presence of CNS symptoms of hypertension and cause of renal failure. A diuretic is usually needed

*For further details on drug therapy, refer to section on hypertension in 'post-infectious acute glomerulonephritis'.*

### **Metabolic acidosis**

- treat if  $\text{pH} < 7.2$  or symptomatic or contributing to hyperkalaemia
- $\text{bicarbonate deficit} = 0.3 \times \text{body weight (kg)} \times \text{base excess (BE)}$
- ensure that patient's serum calcium is  $> 1.8 \text{ mmol/L}$  to prevent hypocalcaemic seizures with sodium bicarbonate therapy.
- replace half the deficit with IV 8.4% sodium bicarbonate (1:1 dilution) if indicated
- monitor blood gases

### **Electrolyte abnormalities**

#### *Hyperkalaemia*

- definition: serum  $\text{K}^+ > 6.0 \text{ mmol/l}$  (neonates) and  $> 5.5 \text{ mmol/l}$  (children).
- cardiac toxicity generally develops when plasma potassium  $> 7 \text{ mmol/l}$
- regardless of degree of hyperkalaemia, treatment should be initiated in patients with ECG abnormalities from hyperkalaemia

*Table 2. Recommended investigations*

#### *Blood*

full blood count  
urea, electrolytes, creatinine  
blood gas  
serum albumin, calcium, phosphate

#### *Urine*

biochemistry, microscopy

#### *Imaging*

renal ultrasound scan  
(urgent if cause unknown)

#### *Other investigations*

as determined by cause

*Table 3. ECG changes in hyperkalemia*

- tall peaked T waves
- prolonged PR interval
- widened QRS complex
- flattened P wave
- sine wave (QRS complex merges with peaked T waves)
- VF or asystole

### Treatment

- do 12-lead ECG and look for hyperkalaemic changes
  - if ECG is abnormal or plasma  $K^+$  > 7 mmol/l, connect patient to cardiac monitor and give the following in sequence:
    - IV 10% calcium gluconate 0.5 – 1.0 ml/kg (1:1 dilution) over 5 – 15 mins  
(immediate onset of action)
    - IV dextrose 0.5 g/kg (2 ml/kg of 25%) over 15 – 30 mins
    - ± IV insulin 0.1 unit/kg  
(onset of action 30 mins)
    - IV 8.4% sodium bicarbonate 1 ml/kg (1:1 dilution) over 10 – 30 mins  
(onset of action 15 – 30 mins)
    - Nebulized 0.5% salbutamol 2.5 – 5 mg  
(0.5 – 1 ml : 3 ml 0.9% sodium chloride)  
(onset of action 30 mins)
    - Calcium polystyrene sulphonate 0.25g/kg oral or rectally 4 times/day (max 10g/dose)  
(Calcium Resonium / Kalimate)

[give rectally (NOT orally) in neonates 0.125 – 0.25g/kg 4 times/day]

OR

- Sodium polystyrene sulphonate 1g/kg oral or rectally 4 times/day (max 15g/dose) (Resonium)
- in patients with serum potassium between 5.5 - 7 mmol/L *without* ECG changes, give calcium or sodium polystyrene sulphonate
  - dialyse if poor or no response to the above measures

### Hyponatraemia

- usually dilutional from fluid overload
- if asymptomatic, fluid restrict
- dialyse if symptomatic or the above measures fail

### Hypocalcaemia

- treat if symptomatic (usually serum  $Ca^{2+}$  < 1.8 mmol/L), and if sodium bicarbonate is required for hyperkalaemia, with IV 10% calcium gluconate 0.5 ml/kg, given over 10 – 20 minutes, with ECG monitoring

### Hyperphosphataemia

- phosphate binders e.g. calcium carbonate or aluminium hydroxide orally with main meals

### Nutrition

Optimal intake in ARF is influenced by nature of disease causing it, extent of catabolism, modality and frequency of renal replacement therapy.

Generally, the principles of nutritional requirement apply except for:

- avoiding excessive protein intake
- minimizing phosphorus and potassium intake
- avoiding excessive fluid intake (if applicable)
- if the gastro-intestinal tract is intact and functional, start enteral feeds as soon as possible
- total parenteral nutrition via central line if enteral feeding is not possible; use concentrated dextrose (25%), lipids (10 – 20%), protein (1.0 – 2.0g/kg/day)
- if oliguric and caloric intake is insufficient because of fluid restriction, start dialysis earlier

Table 4. Dosage adjustment in renal failure for some common antimicrobials

drug	creatinine clearance <sup>1</sup>	dose	dose interval
Crystalline/benzylpenicillin	10 – 50	Nil	8 – 12
	< 10	Nil	12
Cloxacillin	< 10	Nil	8
Amoxicillin/clavulanic acid (Augmentin)	10 – 30	Normal dose initially then half-dose 12-hourly.	
	< 10	Normal dose initially then half-dose 24-hourly.	
Ampicillin/sulbactam (Unasyn)	15 – 29	Nil	12
	5 - 14	Nil	24
Cefotaxime	< 5	Normal dose initially, then 1/2 dose, same frequency	
Cefuroxime	> 20	Nil	8
	10 – 20	Nil	12
	< 10	Nil	24
Ceftriaxone	< 10	Dose not > 40mg/kg (maximum 2g)/day	
Ceftazidime	30 – 50	50-100%	12
	15 – 30	50-100%	24
	5 – 15	25-50%	24
	< 5	25–50%	48
Cefepime	30 – 50	50mg/kg	12
	11 – 29	50mg/kg	24
	< 10	25mg/kg	24
Imipenem	40	75%	8
	10	25%	12
	anuric	15%	24
Meropenem	25 – 50	100%	12
	10 – 25	50%	12
	< 10	50%	24
Ciprofloxacin	40	Nil	12
	10	50%	24
	anuric	33%	24
Metronidazole	< 10	Nil	12
Acyclovir (iv infusion)	25 – 50	Nil	12
	10 - 25	Nil	24
Acyclovir (oral)	10 – 25	Nil	8
	< 10	Nil	12
Erythromycin	< 10	60%	Nil
Gentamicin	Avoid if possible. If needed, give 5mg/kg, check trough level 24 hours later, and peak 1 hour post-dose.		
Amikacin	Avoid if possible, If needed, give initial dose, take trough sample immediately before next dose, and peak 1 hour post-dose.		
Vancomycin	Give initial / loading dose, take trough sample immediately before next dose and peak, 1 hour after completion of infusion		

<sup>1</sup>Note:

It is difficult to estimate GFR from the serum creatinine levels in ARF. A rough estimate can be calculated using the formula below once the serum creatinine level remains constant for at least 2 days.

$$\text{Calculated creatinine clearance (ml/min/1.73m}^2\text{)} = \frac{\text{height (cm)} \times 40}{\text{serum creatinine (micromol/l)}}$$

Assume creatinine clearance of < 10ml/min/1.73m<sup>2</sup> if patient is on dialysis or anuric.

## Dialysis

Dialysis is indicated if there are life-threatening complications like:

- fluid overload manifesting as
  - pulmonary oedema
  - congestive cardiac failure or
  - refractory hypertension
- electrolyte / acid-base imbalances:
  - hyperkalaemia ( $K^+ > 7.0$ )
  - symptomatic hypo- or hypernatraemia or
  - refractory metabolic acidosis
- symptomatic uraemia
- oliguria preventing adequate nutrition
- oliguria following recent cardiac surgery

The choice of dialysis modality depends on:

- experience with the modality
- patient's haemodynamic stability
- contraindications to peritoneal dialysis e.g. recent abdominal surgery

Refer to section on 'acute peritoneal dialysis' for further details.

## Medications

Avoid nephrotoxic drugs if possible; if still needed, monitor drug levels and potential adverse effects. Check dosage adjustment for all drugs used.

# ACUTE PERITONEAL DIALYSIS

## Introduction

The purpose of dialysis is

- to remove endogenous and exogenous toxins and
- to maintain fluid, electrolyte and acid-base equilibrium until renal function returns

*Peritoneal dialysis (PD)* is the simpler modality in infants and children as it is technically simpler and easily accessible even in centers without paediatric nephrologists.

## Contraindications to Acute PD

- abdominal wall defects or infection
- bowel distension, perforation, adhesion or resection
- communication between the chest and abdominal cavities

## Types of Catheter Access

- a *soft PD catheter* implanted percutaneously or surgically (preferred)
- a *straight rigid catheter* if a soft PD catheter is not available

Table 1. Indications for dialysis

### Acute renal failure

- pulmonary oedema
- refractory hypertension
- oliguria following recent heart surgery
- symptomatic electrolyte or acid-base imbalance
  - hyperkalaemia ( $K^+ > 7.0$ )
  - hypo- or hypernatraemia
  - acidosis ( $pH < 7.2$ , or  $< 7.3$  with hyperkalaemia)
- uraemia

### Inborn errors of metabolism

- encephalopathy
- hyperammonaemia
- severe metabolic acidosis



### Site of insertion

- commonest site is at the midline infra-umbilical position 1 inch below the umbilicus
- in small children, where the space below the umbilicus is limited, alternative sites include insertion lateral to the inferior epigastric artery as shown in the dotted lines in the diagram, two-thirds of the distance from the umbilicus to the left last rib (just lateral to the border of rectus muscle)
- ensure that the catheter is inserted way below any enlarged spleen or liver.

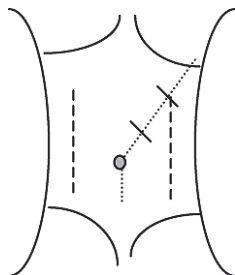


Fig 1. Site of insertion and direction of catheter introduction

### Procedure of PD catheter insertion

1. consent for first peritoneal dialysis
2. bladder must be emptied; catheterise the bladder in unconscious, ill patients
3. the procedure must be done under aseptic technique
4. prepare the set of PD lines and spike the PD fluids
5. clean the area with povidone iodine and drape the patient
6. infiltrate insertion site with lignocaine; additional IV sedation may be needed
7. for small infants or patients with very scaphoid abdomen, infiltrating the abdominal cavity with 10 – 15 ml/kg PD fluid using 20G or larger branula prior to catheter insertion will help prevent traumatic puncture of underlying viscus
8. for technique of catheter insertion - see boxes 2 and 3
9. connect the catheter to the PD line via the connector provided in the set.
10. bleeding from the insertion site can be stopped by a purse-string suture.

Table 2. Technique of insertion of different PD catheters

#### Acute stiff PD catheter

1. check catheter for any breakages (by withdrawing the stylette) before insertion.
2. make a small skin incision (slightly smaller than the diameter of the catheter) using a sharp pointed blade. Do not cut the muscle layer
3. introduce the catheter with the stylette perpendicular to the abdominal wall while controlling the length with the dominant hand, until the peritoneum is pierced. The stylette is then withdrawn and the catheter gently pushed in, directing it towards either iliac fossa until all the perforations are well within the peritoneal cavity

#### Soft PD catheter (Seldinger technique)

1. Cooke's set 15F
2. advance the needle provided in the set connected to a syringe perpendicularly until peritoneum is breached (a give is felt)
3. thread and advance the guide wire through the needle aiming for either iliac fossa
4. remove the needle. Using the guide wire, introduce the dilator and sheath through a skin nick into the abdominal cavity
5. remove the dilator and guide wire while retaining the sheath in the abdomen
6. introduce the soft PD catheter through the sheath into the abdominal cavity directing it to either iliac fossa until the external cuff fits snugly at the skin
7. peel off the sheath and secure the catheter via taping or a skin stitch

**Table 3. The PD Prescription****Exchange volume**

Start at 20 ml/kg and observe for discomfort, cardiorespiratory changes or leakage at catheter site  
The volume can be increased to a maximum of 50ml/kg or 1000 -1200ml/m<sup>2</sup> body surface area.

**Cycle Duration**

First 6 cycles are rapid cycles i.e. no dwell time. The cycle duration depends on needs of the patient. However, the standard prescription usually last an hour:

- 5-10 minutes to instill (depending on exchange volume)
- 30-40 minutes dwell
- 10-15 minutes to drain (depending on exchange volume)

The cycles can be done manually or with an automated cycler machine if available.

**PD Fluids**

Type of PD fluids:

- 1.5%, and 4.25% dextrose (standard commercially available)
- Bicarbonate dialysate<sup>1</sup>, useful if lactic acidosis is a significant problem

PD is usually initiated with 1.5% - if more rapid ultrafiltration is required higher glucose concentration by mixing various combinations of 1.5 and 4.25% solutions can be used. Watch for hyperglycaemia.

**Duration of PD**

The duration of PD depends on the needs of the patient

The usual practice is 60 cycles but at times more cycles may be needed based on biochemical markers or clinical needs. Peritonitis is frequent when dialysis is prolonged or when acute catheters are used for more than 3 to 4 days.

<sup>1</sup>Note: In centers with continuous renal replacement therapy, the bicarbonate solution used for CRRT (Continuous Renal Replacement Therapy) can be used. In centers where this is not available, the assistance of the pharmacist is required to constitute a physiological dialysis solution. The contents and concentrations are Table 4.

**Monitoring while on PD**

- oversee the first 3 cycles of dialysis to ensure good flow.
- check for turbidity, leakage and ultrafiltration every two hours.
- input / output chart, vital signs and PD chart should be kept up-to-date. Turbid effluent must be noted to the doctor.
- send PD fluid for cell count and culture and sensitivity at start and end of PD and when the effluent is turbid.
- blood urea, serum electrolytes and creatinine should be requested according to patients needs. In stable patients, once daily should be more than sufficient.
- blood urea and electrolyte results to be reviewed by the doctor and potassium chloride to be added into dialysate if necessary.

(1 g of potassium chloride in 10 ml ampoule is equivalent to 13.3 mmol of potassium.  
Hence adding 3 ml to 1 litre would result in dialysate with 4.0 mmol/l of potassium)

**Common Complications**

- poor drainage (omental obstruction, kinking)  
for temporary PD cannulas
  - re-position
  - reinsert catheter if above unsuccessful
- for surgically implanted catheters
  - irrigation
  - add heparin (500 units/ litre) into PD fluids

**Table 4. Pharmacy constituted PD-Bicarbonate solution 1.5% dextrose 3000ml / bag**

Content	Quantity (ml)
NaCl 0.9%	1374.00
NaCl 20%	13.23
Sodium Bicarbonate 8.4%	120.00
Magnesium Sulphate 49.3%	1.11
Dextrose 50%	90.00
Water for injection	1401.66

- peritonitis  
*diagnostic criteria :*
  - abdominal pain, fever, cloudy PD effluent, PD effluent cell count > 100 WBC/mm<sup>2</sup>*treatment:*
  - intraperitoneal antibiotics (empirical Cloxacillin + Ceftazidime) for 7 to 14 days
  - adjust antibiotics once culture results known (dosage as given in the table)
- exit site infection
  - send swab for culture
  - remove PD catheter that is not surgically implanted
  - systemic antibiotics may be considered
- leaking dialysate
  - at exit site – resuture immediately
  - leakage from tubings – change dialysis set, empiric intraperitoneal antibiotics for one to two days may be needed
- blood stained effluent
  - if mild observe. It should clear with successive cycles.
  - if heavy, but vital signs stable, run rapid cycles.  
 transfuse cryoprecipitate. consider blood transfusion and DDAVP.  
 if bleeding does not stop after the first few cycles, stop the dialysis.
  - if heavy, patient in shock, resuscitate as for patient with hypovolaemic shock.  
*stop dialysis and refer surgeon immediately.*

Table 4. Guidelines for intraperitoneal antibiotic use

Paediatric Antibiotic Dosing Recommendations			
Administration should be via intraperitoneal route unless specified otherwise.			
	continuous therapy		intermittent therapy
	loading dose	maintenance dose	
<i>Glycopeptides</i>			
Vancomycin	500 mg/L	30 mg/L	30 mg/kg q 5-7 days
<i>Cephalosporins</i>			
Cephazolin/cephalothin	250 mg/L	125 mg/L	15 mg/kg q 24 hrs
Cefuroxime	200 mg/L	125 mg/L	15 mg/kg q 24 hrs
Cefotaxime	500 mg/L	250 mg/L	30 mg/kg q 24 hrs
Ceftazidime	250 mg/L	125 mg/L	15 mg/kg q 24 hrs
<i>Antifungals</i>			
Amphotericin B	1 mg/kg IV	1 mg/kg/day IV	---
Fluconazole	---	---	3-6 mg/kg IP, IV, or PO q 24-48 hrs (max 200 mg)
<i>Aminoglycosides</i>			
Amikacin	25 mg/L	12 mg/L	
Gentamicin	8 mg/L	4 mg/L	
Netilmycin	8 mg/L	4 mg/L	
<i>Penicillins</i>			
Amoxicillin	250 -500 mg/L	50 mg/L	
<i>Combinations</i>			
Ampicillin/Sulbactam	1000 mg/L	100 mg/L	
Imipenem/Cilastatin	500 mg/L	200 mg/L	

## NEUROGENIC BLADDER

### Introduction

Neurogenic bladder can develop as a result of a lesion at any level in the nervous system, i.e. cerebral cortex, spinal cord, or peripheral nervous system. However, the commonest cause of neurogenic bladder is spinal cord abnormalities.

### Multi-disciplinary approach

Children with spinal dysraphism require care from a multidisciplinary team consisting of neurosurgeon, neurologist, orthopedic surgeon, rehabilitation specialist, neonatologist, nephrologists, urologist and other allied medical specialists.

Long-term follow-up is necessary since renal or bladder function can still deteriorate after childhood.

Children with the conditions listed in table 1 can present with various patterns of detrusor sphincter dysfunction within a wide range of severity, not predicted by the level of the spinal cord defect.

Table 1. Causes of neurogenic bladder

open spinal dysraphism (meningocele, myelomeningocele and lipomyelomeningocele)
occult spinal dysraphism (spinal bifida occulta)
anorectal agenesis, sacral agenesis
spinal trauma
spinal cord tumors
transverse myelitis

The commonest cause of neurogenic bladder is lumbosacral myelomeningocele. At birth, the majority of patients with lumbosacral myelomeningocele have normal upper urinary tracts, but nearly 60% of them develop upper tract deterioration due to infections, bladder changes and reflux by 3 years of age. Progressive renal damage is due to high detrusor pressures both throughout the filling phase (poor compliance bladder) as well as superimposed detrusor contractions against a closed sphincter (detrusor sphincter dyssynergia).

### Aims of management:

- preserve upper renal tracts and renal function
- achieve urinary continence
- develop sense of autonomy and better self esteem

### Open spinal dysraphism

Early management with clean intermittent catheterization (CIC):

- aim is to create a low-pressure reservoir and ensuring complete and safe
- bladder emptying with clean intermittent catheterization.
- CIC should be started once the myelomeningocele is repaired  
starting CIC in early infancy has led to easier acceptance by parents and children  
and reduced upper tract deterioration and improvement in continence

### Timing of urodynamic study

Urodynamic study is indicated in *all* children with neurogenic bladder. However due to limited availability, urodynamic study should be carried out in children with neurogenic bladder with the following:

- recurrent UTI
- thickened bladder wall
- hydronephrosis
- raised serum creatinine
- incontinence despite CIC

In infants with lumbosacral myelomeningocele with any of the above conditions and who have been started on CIC, anti-cholinergic e.g. oxybutinin (0.3-0.6 mg/kg/day in 2 to 3 divided dose) should be started even if urodynamic study is not available.

#### *Clean intermittent catheterisation*

- children, as young as 5, have learnt to do self-catheterization
- patients are taught catheterisation in hospital by trained nurse/doctor
- the rationale and benefits of intermittent catheterisation are explained, and the patient is reassured that it should be neither painful nor dangerous
- patients are taught to catheterise themselves lying down, standing up, or sitting on a lavatory, chair, or wheelchair

#### *Complications of CIC*

Urethral trauma with creation of false passages, urethral strictures and bacteriuria.

*Table 2. Clean intermittent catheterisation*

#### **Technique of clean intermittent catheterisation**

##### *Procedure*

1. assemble all equipment: catheter,  $\pm$  lubricant, drainage receptacle, adjustable mirror
2. wash hands with soap and water
3. clean the urethral orifice with clean water.

##### *In boys:*

1. lift penis with one hand to straighten out urethra.
2. lubricate the catheter, with local anaesthetic gel (lignocaine) or K-Y jelly.
3. use the other hand to insert the catheter into the urethra. There may be some resistance as the catheter tip reaches the bladder neck.
4. continue to advance the catheter slowly using gentle, firm pressure until the sphincter relaxes.

##### *In girls:*

1. the labia are separated and the catheter inserted through the urethral meatus into the bladder.

##### *For both males and females*

1. the catheter is inserted gently until the urine flows.
2. the urine is collected in a jug or bottle or is directed into the lavatory.
3. once the urine has stopped flowing the catheter should be rotated and then, if no urine drains, slowly withdrawn.
4. wash hands on completion of catheterization
5. catheterise at the prescribed time with the best available measures

##### *Size of catheters*

Small babies: 6F

Children: 8-10F

Adolescence: 12-14F

##### *How Often to Catheterise*

Infants: 6 times a day

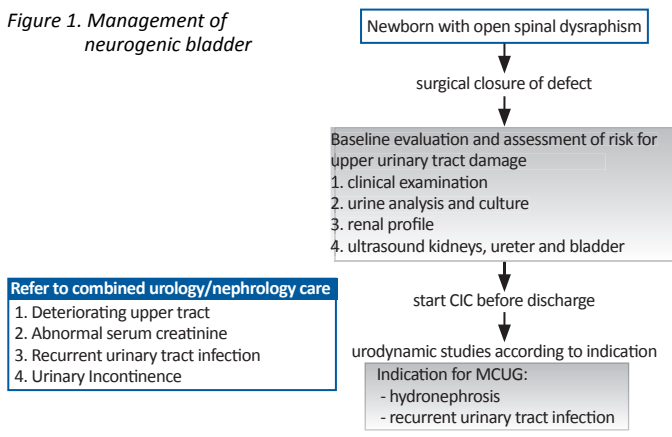
children: 4-5 times a day, more frequently in patients with a high fluid intake, and in patients with a small capacity bladder.

##### *Reuse of catheters*

1. catheters can be re-used for 2 to 4 weeks
2. after using the catheter, wash in soapy water, rinse well under running tap water, hang to air dry and store in clean container.

*Note: In infants with myelomeningocele, management is directed at creating a low-pressure reservoir and ensuring complete and safe bladder emptying with clean intermittent catheterization. CIC should be started once the myelomeningocele is repaired. Starting CIC in early infancy has led to easier acceptance by parents and children and reduced upper tract deterioration and improvement in continence.*

**Figure 1. Management of neurogenic bladder**



### *Recurrent urinary tract infection (UTI) and antibiotics*

- prophylactic antibacterial therapy is not recommended as therapy *does not decrease* the incidence of clinical infections
- asymptomatic bacteriuria are common but does not require treatment
- all febrile UTIs should be treated with antibiotics as soon as possible
- children with recurrent symptomatic UTI should be given prophylactic antibiotics and may benefit from circumcision

### *Management of bowel incontinence*

- laxatives: mineral oil, lactulose, enema
- aim to achieve regular and efficient bowel emptying regimen

### *Follow up assessment*

- voiding chart: timing of daytime and night-time voiding, volume of each void, and incontinence and urge episodes
- constipation and fecal incontinence
- monitoring of blood pressure, urinalysis, renal profile
- urine culture in suspected febrile UTI or symptomatic UTI
- serial ultrasound imaging at regular intervals depending on the age and baseline ultrasound findings. Infants and younger children require more frequent ultrasound scans up to 3 to 6 monthly

### **Occult spinal dysraphism**

- may present with cutaneous stigmata (hairy tufts, skin tags, lumbosacral subcutaneous masses and haemangiomas)
- spinal ultrasound can be used in neonates and infants, optimally before 6 months of age, when ossification of posterior elements prevents an acoustic window. After 6 months of age, the imaging modality is MRI of spine.

### **Other conditions that lead to neurogenic bladder**

- start CIC in patients with acquired neurogenic bladder with urinary retention, recurrent urinary tract infection and/or hydronephrosis

## URINARY TRACT INFECTION

### Introduction

Urinary tract infection (UTI) comprises 5% of febrile illnesses in early childhood. 2.1% of girls and 2.2% of boys will have had a UTI before the age of 2 years. UTI is an important risk factor for the development of hypertension, renal failure and end stage renal disease.

### Definition

- *urinary tract infection* is growth of bacteria in the urinary tract or combination of clinical features and presence of bacteria in the urine
- *significant bacteriuria* is defined as the presence of > 105 colony forming units (cfu) of a single organism per ml of freshly voided urine (Kass)
- *acute pyelonephritis* is bacteriuria presenting clinically with fever > 38°C and/or loin pain and tenderness. It carries a higher risk of renal scarring
- *acute cystitis* is infection limited to the lower urinary tract presenting clinically with acute voiding symptoms: dysuria, urgency, frequency, suprapubic pain or incontinence
- *asymptomatic bacteriuria* is presence of bacteriuria in the urine in an otherwise asymptomatic child

### Clinical Presentation

Symptoms depend on the age of the child and the site of infection.

In infants and toddlers: signs and symptoms are non-specific e.g. fever, irritability, jaundice and failure to thrive. The presence of UTI should be considered in children with unexplained fever. Symptoms of lower UTI such as pain with micturition and frequency are often not recognized before the age of two.

### Physical Examination

- general examination, growth, blood pressure
- abdominal examination for distended bladder, ballotable kidneys, other masses, genitalia, and anal tone
- examine the back for any spinal lesion
- look for lower limb deformities or wasting (suggests a neurogenic bladder)

### Diagnosis

Accurate diagnosis is extremely important as false diagnosis of UTI would lead to unnecessary interventions that are costly and potentially harmful.

*The quality of the urine sample is of crucial importance (see table 1).*

#### *Urine specimen transport*

If collected urine cannot be cultured within 4 hours; the specimen should be refrigerated at 4°C or a bacteriostatic agent e.g. boric acid (1.8%) added. Fill the specimen container pre-filled with boric acid with urine to the required level.

#### *Urine testing*

Rapid diagnosis of UTI can be made by examining the fresh urine with urinary dipstick and microscopy. However, where possible, a fresh specimen of urine should be sent for culture and sensitivity.

**Table 1. Collection of urine****Bag urine specimen**

- high contamination rate of up to 70%
- negative culture excludes UTI in untreated children
- positive culture should be confirmed with a clean catch or suprapubic aspiration specimen (SPA)

**Clean catch specimen**

- recommended in a child who is bladder trained

**Catheterisation**

- sensitivity 95%, specificity 99%, as compared to SPA
- low risk of introducing infection.

**Suprapubic aspiration (SPA)**

- the best technique ("gold standard") of obtaining an uncontaminated urine sample
- any gram negative growth is significant.
- technique:
  - lie the child in a supine position
  - thin needle with syringe is inserted vertically in the midline, 1 - 2 cm above symphysis pubis.
  - urine is obtained at a depth of 2 to 3 cm
  - usually done in infants < 1 year; also applicable in children aged 4 - 5 years if bladder is palpable above the symphysis pubis.
  - success rate is 98% with ultrasound guidance.

*Note: When it is not possible to collect urine by non-invasive methods, catheterization or SPA should be used.*

**Management**

All infants with febrile UTI should be admitted and intravenous antibiotics started as for acute pyelonephritis. In patients with high risk of serious illness, it is preferable that urine sample should be obtained first; however treatment should be started if urine sample is unobtainable.

**Antibiotic prophylaxis**

Previous guidelines have recommended routine antibiotic prophylaxis for all children below 5 years of age prior to radiological imaging. However recent evidence has not supported this practice. Hence, antibiotic prophylaxis may be considered in the following:

- infants and children with recurrent symptomatic UTI
- infants and children with vesico-ureteric reflux grades of at least grade III

**Measures to reduce risk of further infections**

- **Dysfunctional elimination syndrome (DES)** or dysfunctional voiding is defined as an abnormal pattern of voiding of unknown aetiology characterised by faecal and/or urinary incontinence and withholding of both urine and faeces. treatment of DES includes high fibre diet, use of laxatives, timed frequent voiding, and regular bowel movement. if condition persists, referral to a paediatric urologist/nephrologist is needed.

**Table 2. Sensitivity and specificity of various tests for UTI**

test	sensitivity % (range)	specificity % (range)
leucocyte esterase (LE)	78 (64-92)	83 (67-94)
nitrite	98 (90-100)	53(15-82)
LE or nitrite positive	72 (58-91)	93 (90-100)
pyuria	81 (45-98)	73 (32-100)
bacteria	83 (11-100)	81(16-99)
any positive test	70 (60-90)	99.8 (99-100)

*Note: The presence of bacteria, positive nitrite ± positive leucocyte esterase is suggestive of UTI and antibiotic should be started after sending a urine sample for culture.*



Table 3. Antibiotic treatment of UTI

Type of Infection	Preferred Treatment	Alternative Treatment
<b>UTI (Acute cystitis)</b> - <i>E.coli.</i> - <i>Proteus spp</i>	PO Trimethoprim 4mg/kg/dose bd (max 300mg daily) for 1 week	PO Trimethoprim/sulphamethazole 4mg/kg/dose (TMP) bd x1 week
<i>Note: - cephalexin, cefuroxime can also be used especially in children who had prior antibiotics. - single dose of antibiotic therapy not recommended.</i>		
<b>Upper UTI (Acute pyelonephritis)</b> - <i>E.coli.</i> - <i>Proteus spp</i>	IV cefotaxime 100mg/kg/day q8h for 10-14 days	IV cefuroxime 100mg/kg/d q8h or IV Gentamicin 5-7mg/kg/day daily
<i>Note: - repeat culture within 48hours if poor response - antibiotic may need to be changed according to sensitivity.</i>		
<b>Asymptomatic bacteriuria</b>		
No treatment recommended		

Table 4. Antibiotic prophylaxis for UTI

Indication	Preferred Treatment	Alternative Treatment
<b>UTI prophylaxis</b>	PO Trimethoprim 1-2mg/kg ON	Nitrofurantoin 1-2mg/kg ON or Cephalexin 5mg/kg ON
<i>Note: - antibiotic prophylaxis should not be routinely recommended in children with UTI. - prophylactic antibiotics should be given for 3 days with MCUG done on the second day - if a child develops an infection while on prophylactic medication, treatment should be with a different antibiotic and not a higher dose of the same prophylactic antibiotic.</i>		

## Recommendations for imaging

Previous guidelines have recommended routine radiological imaging for all children with UTI. Current evidence has narrowed the indications for imaging as summarized below:

### Ultrasound

Recommended in

- all children less than 3 years of age
- children above 3 years of age with poor urinary stream, seriously ill with UTI, palpable abdominal masses, raised serum creatinine, non E coli UTI, febrile after 48 hours of antibiotic treatment, or recurrent UTI

### DMSA scan

Recommended in infants and children with UTI with any of the following features:

- seriously ill with UTI
- poor urine flow
- abdominal or bladder mass
- raised creatinine
- septicaemia
- failure to respond to treatment with suitable antibiotics within 48 hours
- infection with non-E. coli organisms

### Micturating cystourethrogram (MCUG)

Should be considered in:

- infants with recurrent UTI
- infants with UTI and the following features: poor urinary stream, seriously ill with UTI, palpable abdominal masses, raised serum creatinine, non E coli UTI, febrile after 48 hours of antibiotic treatment
- children less than 3 years old with the following features:
  - dilatation on ultrasound
  - poor urine flow
  - non E coli infection
  - family history of VUR

Other radiological investigations e.g. DTPA scan, MCUG in older children would depend on the ultrasound findings.

### Further Management

This depends upon the results of investigation.

#### Normal renal tracts

- prophylactic antibiotic not required.
- urine culture during any febrile illness or if the child is unwell.

#### No VUR but renal scarring present.

- repeat urine culture only if symptomatic.
- assessment includes height, weight, blood pressure and routine tests for proteinuria
- children with a minor, unilateral renal scarring do not need long-term follow-up unless recurrent UTI or family history or lifestyle risk factors for hypertension
- children with bilateral renal abnormalities, impaired renal function, raised blood pressure and or proteinuria should be managed by a nephrologist.
- close follow up during pregnancy

### Vesicoureteric reflux

#### Definition

Vesicoureteral reflux (VUR) is defined as the retrograde flow of urine from the bladder into the ureter and collecting system. In most individuals VUR results from a congenital anomaly of ureterovesical junction (primary VUR), whereas in others it results from high pressure voiding secondary to posterior urethral valve, neuropathic bladder or voiding dysfunction (secondary VUR).

#### Significance of VUR

- commonest radiological abnormality in children with UTI (30 – 40%).
- children with VUR thought to be at risk for further episodes of pyelonephritis with potential for increasing renal scarring and renal impairment

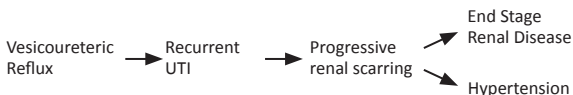
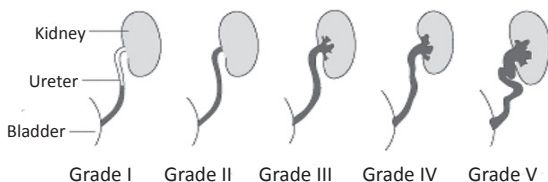


Figure 2. Natural history of vesicoureteric reflux

Classification of VUR according to the International Reflux Study Committee.



## Management

*Antibiotic prophylaxis* – refer to antibiotic prophylaxis section above

*Surgical management* is considered if the child has recurrent breakthrough febrile UTI

*Posterior urethral valve*

refer to paediatric urologist/surgeon/nephrologist.

*Renal dysplasia, hypoplasia or moderate to severe hydronephrosis*

- may need further imaging to evaluate function or drainage in the case of hydronephrosis
- refer surgeon if obstruction is confirmed.
- monitor renal function, BP and growth parameters

## Summary

- all children less than 2 years of age with unexplained fever should have urine tested for UTI.
- greater emphasis on earlier diagnosis & prompt treatment of UTI
- diagnosis of UTI should be unequivocally established before a child is subjected to invasive & expensive radiological studies

## ANTENATAL HYDRONEPHOSIS

### Definition

The most generally accepted definition is the maximum antero-posterior diameter of the renal pelvis of at least 5mm on antenatal ultrasound of the fetus.

### Advantages of prenatal detection

Has allowed identification of conditions that require immediate treatment and which otherwise would go unrecognized until symptoms arose postnatally.

### Timing of antenatal detection

- 90% detection rate after 18 weeks of gestation
- 95% by 22 weeks gestation

### Grading

The two classifications commonly used by perinatal specialists and radiologists are reproduced below:

*Table 1. The Society of Fetal Urology (SFU) has developed the following classification system*

SFU Grade 0	Intact central renal complex (renal pelvis)
SFU Grade I	Mild splitting of central renal complex
SFU Grade II	Pelviectasis but no calyctasis*
SFU Grade III	A markedly split pelvis with uniformly dilated calyces, but normal renal parenchyma
SFU Grade IV	SFU Grade IV Characteristics of grade III with thinning of renal parenchyma

\*Pelviectasis: dilatation of pelvis; Calyctasis: dilatation of calyx

*Table 2. Another system of grading looked at the length of renal pelvis diameter (RPD)*

5 - 8 mm	Mild hydronephrosis
8 - 12 mm	Moderate hydronephrosis
> 12 mm	Severe hydronephrosis

*Sensitivity and specificity: An 8mm pelvic diameter has a sensitivity of 91% and specificity of 72%*

Marked hydronephrosis is frequently seen in pelvic ureteric junction obstruction whereas mild hydronephrosis is associated with vesicoureteric reflux

### Epidemiology

#### *Incidence*

- 1 in 150-700 of livebirths
- increased frequency of up to 8% with positive family history of renal agenesis, multicystic kidney, reflux nephropathy and polycystic kidneys
- male to female ratio is 2:1.
- bilateral in 20 to 40 %

*Table 3. Causes of antenatal hydronephrosis*

Frequency (%)	Abnormality
48	Transient
15	Physiologic
11	Pelvic ureteric junction obstruction
4	Vesicoureteric reflux
4	Megaureter, obstructed or non-obstructed
2	Multicystic kidneys
2	Ureterocoeles
1	Posterior urethral valves

*from Woodward M. BJU International 2002; 89:149*

## Transient and physiologic hydronephrosis

60% of antenatal hydronephrosis is physiological. This will resolve before the end of pregnancy or within the first year of life.

Fetal urine flow is four to six times greater than neonatal urine production. This is due to differences in renovascular resistances, GFR and concentrating ability before and after birth. These differences may contribute to ureteric dilatation in-utero in the absence of functionally significant obstruction.

## Antenatal Management

In general antenatal interventions are not required except for watchful monitoring. Pregnancy should be allowed to proceed to term and normal delivery can be allowed in the absence of other complications like severe oligohydramnios or other fetal abnormalities.

## Postnatal management

### *Physical examination*

Certain clinical features may suggest specific underlying causes:

- abdominal mass: enlarged kidney due to pelvic-ureteric junction obstruction or multicystic dysplastic kidneys.
- palpable bladder and/or poor stream and dribbling: posterior urethral valves in a male infant.
- deficient abdominal wall with undescended testes: Prune Belly syndrome.
- abnormalities in the spine and lower limb with patulous anus: neurogenic bladder

Examination for other anomalies should also be carried out.

## Unilateral hydronephrosis

- in babies who are normal on physical examination, a repeat ultrasound should be done after birth; subsequent management will depend on the ultrasound findings.
- the ultrasound should be repeated one month later if initial postnatal US is normal or show only mild hydronephrosis. The patient can be discharged if the repeat ultrasound is also normal.

## Bilateral Hydronephrosis

These babies need a full examination and investigation after birth.

- ultrasound of the kidneys and urinary tracts should be repeated.
- urine output should be monitored.
- renal profile should be done on day 2 of life.
- the child should be monitored closely for UTI and a second-generation cephalosporin started if there is any suggestion of UTI.

In boys, detailed ultrasound scan should be done by an experienced radiologist to detect thickened bladder wall and dilated posterior urethra suggestive of posterior urethral valves. Any suggestion of posterior urethral valve or renal failure warrants an urgent MCU.

Urgent referral to a paediatric nephrologist and/or urologist is needed if the newborn has renal failure, or confirmed or suspected posterior urethral valves.

Other radiological investigations

99mDTPA/Mag 3 SCAN

DTPA or Mag 3 scans are required when there is moderate or gross hydronephrosis on postnatal ultrasound. These scans detect differential function of both kidneys as well as the presence of significant obstruction in the urinary tract. In Malaysia, only DTPA scan is available in most radionuclear centers. It is best done after one month of life.

Intravenous Urogram (IVU)

With the availability of DTPA /Mag3 scan, IVU is no more indicated.

Antibiotics

Antibiotic prophylaxis is started in infants with antenatal hydronephrosis.

Table 4. Commonly used prophylactic antibiotics

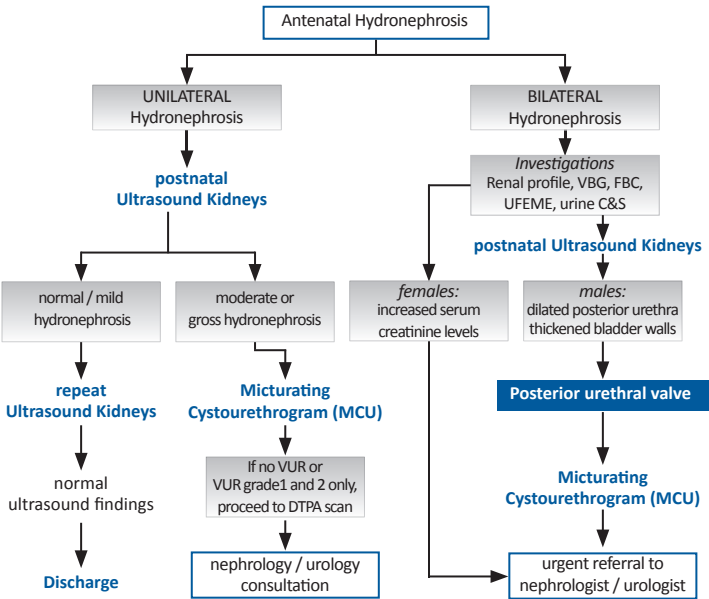
Trimethoprim	1-2mg/kg at night
Cephalexin	5mg/kg at night

Paediatric Formulary Guy's, St. Thomas' and Lewisham Hospital 4th edition.1998

Follow up Care

All children with significant hydronephrosis should be referred to paediatric nephrologists / urologist after relevant radiological investigations have been completed.

Figure 1. Algorithm for the management of antenatally diagnosed hydronephrosis



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# HAEMATOLOGY AND ONCOLOGY

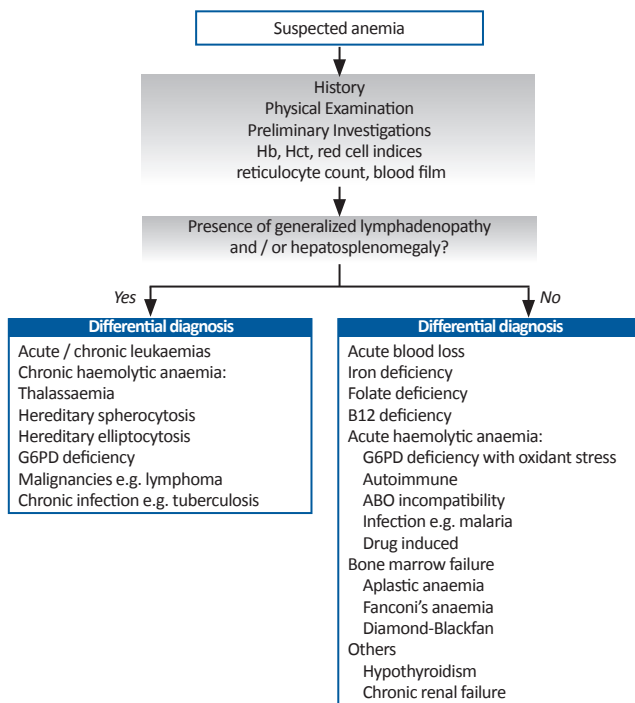
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Maintenance Therapy





## APPROACH TO A CHILD WITH ANAEMIA

Figure 1. Approach to children with anaemia



### IRON DEFICIENCY ANAEMIA

#### Laboratory findings

red cell indices : Low MCV, Low MCH  
low serum ferritin

Table 1. Causes of IDA

Chronic blood loss
Increase demand
prematurity
growth
Malabsorption
worm infestation
Poor diet

Table 2. Variation in FBC indices with age

Age	Hb (g/dl)	RBC ( $\times 10^{12}/l$ )	MCV (fl)
Birth	14.9 – 23.7	3.7-6.5	100-135
2 mon	9.4-13.0	3.1-4.3	84-105
12 mon	11.3-14.1	4.1-5.3	71-85
2-6 yr	11.5-13.5	3.9-5.3	75-87
6-12 yr	11.5-15.5	4.0-5.2	77-95
12-18 yr girls	12.0-16.0	4.1-5.1	78-95
12-18 yr boys	13.0-16.0	4.5-5.3	78-95

Hb, haemoglobin; RBC, red blood cell count; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin

## Treatment

### Nutritional counseling

- maintain breastfeeding
- use iron fortified cereals

### Oral iron medication

- give 6 mg/kg/day of elemental iron in 3 divided doses,
- continue for 6-8 weeks after haemoglobin level is restored to normal.
- Syr FAC (Ferrous ammonium citrate): 1 mg elemental iron per ml
- Tab. Ferrous fumarate 200 mg elemental iron per tablet.

### Consider the following if failure to response to oral iron:

- non – compliance
- inadequate iron dosage
- unrecognized blood loss
- incorrect diagnosis
- impaired GI absorption

### Blood transfusion

- no transfusion required in chronic anemia unless signs of decompensation (e.g. cardiac dysfunction) and the patient is otherwise debilitated.
- in severe anaemia (Hb < 4 g/dL) give low volume packed red cells (< 5mls/kg) if necessary over 4-6 hours with i.v. frusemide (1mg/kg) midway.

## HEREDITARY SPHEROCYTOSIS

### Pathogenesis

A defective structural protein (spectrin) in the RBC membrane producing spheroidal shaped and osmotically fragile RBCs that are trapped & destroyed in the spleen, resulting in shortened RBC life span. The degree of clinical severity is proportional to the severity of RBC membrane defect.

Inheritance is autosomal dominant in 2/3; recessive or *de novo* in 1/3 of children.

### Clinical features – mild, moderate & severe

- anaemia
- splenomegaly
- intermittent jaundice
- splenomegaly
- pigmented gallstones – adolescents & young adults
- aplastic crises with Parvovirus B19 infections
- haemolytic crises
- megaloblastic crises
- all patients should receive folate supplement

### Rare manifestations

- leg ulcers, spinocerebellar ataxia, myopathy
- extramedullary haematopoietic tumours,

Table 3. Investigations in children with suspected spherocytosis

Reticulocytosis
Microspherocytes in peripheral blood film
Osmotic fragility is increased
Elevated MCHC
Normal direct antiglobulin test
Autohaemolysis is increased and corrected by glucose

## Treatment

- splenectomy to be delayed as long as possible
- in mild cases – avoid splenectomy unless gallstones developed
- folic acid supplements – 1 mg day

### Note:

*Splenectomy is avoided for patients < 5 years because of the increased risk of postsplenectomy sepsis. Give pneumococcal, haemophilus & meningococcal vaccination 4-6 weeks prior to splenectomy & prophylactic oral penicillin to be given post splenectomy.*

## Introduction

$\beta$ -Thalassaemia major is an inherited blood disorder presenting with anaemia at 4 - 6 months of age. Common presenting symptoms are lethargy, failure to thrive and hepatosplenomegaly.

In Malaysia, the  $\beta$ -thalassaemia carrier rate is estimated at 3-5%, most of whom are unaware of their carrier / thalassaemia minor status.

**Baseline investigations** to be done for all new patients: -

- full blood count, peripheral blood film (In typical cases, the Hb is about 7g/dl)
- haemoglobin analysis by electrophoresis / HPLC:
  - typical finding: HbA decreased or absent, HbF increased, HbA2 variable
- serum ferritin
- red cell phenotyping (ideal) before first transfusion.
- DNA analysis (optional)
  - for confirmation of difficult cases, used in prenatal diagnosis and detection of  $\alpha$ - carrier (limited availability upon request at IMR, HUKM, UMMC and USM)
- liver function test
- infection screen – HIV, Hepatitis B & C, VDRL screen (before first transfusion)
- HLA typing (for all patient with unaffected sblings)
  - *all nuclear family members must be investigated by Hb Analysis for genetic counseling.*
  - *1st degree and 2nd degree relatives should also be encouraged to be screened & counseled (cascade screening).*

## Management

Regular maintenance blood transfusion and iron chelation therapy is the mainstay of treatment in patients with transfusion dependent thalassaemia.

## Maintenance Blood Transfusion

*Beta thalassaemia major*

- when to start blood transfusion?
  - after completing blood investigations for confirmation of diagnosis.
  - Hb < 7g/dl on 2 occasions > 2 weeks apart (in absence other factors e.g. infection)
  - Hb > 7g/dl if impaired growth, bone changes, enlarging liver and spleen.
- transfusion targets?
  - maintain pre transfusion Hb level at 9 -10 g/dl
  - keep mean post-transfusion Hb at 13.5-15.5g/dl (not advisable > 15.5 g/dl)
  - current recommendation: keep mean Hb 12 - 12.5g/dl
    - This allows for normal physical activity and growth, abolishes chronic hypoxaemia and reduce compensatory marrow hyperplasia which causes irreversible facial bone changes*
- transfusion interval?
  - usually 4 weekly interval (usual rate of Hb decline is at 1g/dl/week). Interval varies from individual patients (range: 2 - 6 weekly)
  - volume: 15 - 20mls/kg (maximum) packed red cells over 4 hours
  - round-up to the nearest pint of cross-matched blood provided.
    - i.e. if calculated volume is just > 1 pint of blood, give 1 pint, or if calculated volume is just < 2 pints, give 2 pints. This strategy would minimize the number of exposure to immunologically different units of blood product and avoid wastage of donated blood.*

Note:

- In the presence of cardiac failure or Hb < 5g/dl, use low volume red packed cells (< 5ml/kg) at slow infusion rate over > 4 hours with furosemide 1 mg/kg (20 mg maximum dose).
- It is recommended for patients to use leucodepleted (pre-storage, post storage or bedside leucocyte filters) packed cells < 2 weeks old. Leucodepletion would minimize non-haemolytic febrile reactions and alloimmunization by removing the white cells.
- **Aim for a pre transfusion Hb of 9 g/dl**

#### *Beta thalassaemia intermedia*

Late onset and milder form of  $\beta$ -thalassaemia, usually presenting > 2 years age with Hb 8g/dl or more. Severity of patients is heterogeneous from being symptomatic at presentation to being asymptomatic until later adult life. If they require regular transfusion, then follow a  $\beta$ -thalassaemia major transfusion regime

#### *Alpha thalassaemia (Hb H disease)*

Transfuse only if Hb persistently < 7g/dl and/or symptomatic.

### **Iron Chelation Therapy**

This is essential to prevent iron overload. Current effective medication readily available throughout the country and approved for use in all children is **Desferrioxamine** (Desferal®). Compliance to treatment is directly related to superior survival outcome.

- when to start?
  - usually when the child is > 2 years old and when the serum ferritin reaches 1000ng/ml. This usually occurs after 10-20 blood transfusions.
- dosage and route
  - average daily dose is 20 – 60mg/kg/day by subcutaneous (s.c.) continuous infusion using a portable pump over 8-10 hours daily, 5 - 7 nights a week.
  - aim to maintain serum ferritin level below 1000 ng/ml.
  - vitamin C augments iron excretion with Desferal®.
  - severely iron loaded patients require longer or continuous s.c. or i.v. (via portacath) infusion of Desferal®.

#### *Complications of Desferal®*

- local skin reactions usually due to inadequately diluted Desferal®.
- Yersinia infection: presents with fever, abdominal pain & diarrhoea.  
*Stop Desferal® and treat with cotrimoxazole, aminoglycoside or 3rd generation cephalosporin.*
- severe allergy (rare)
- Desferal® toxicity (high doses > 50mg/kg/day in presence of low serum ferritin)
- ocular toxicity: reduced vision, visual fields, night blindness; reversible
- auditory toxicity: high tone deafness. Not usually reversible
- growth retardation
- skeletal lesions: pseudo rickets, metaphyseal changes, vertebral growth retardation

#### *Complications of chronic iron overload in thalassaemics over 10 years*

- endocrine: growth retardation, pubertal delay, hypothyroidism, hypoparathyroidism & diabetes mellitus
- cardiac: arrhythmias, pericarditis, cardiac failure
- hepatic: liver cirrhosis

### Oral iron chelator

**Deferiprone / L1** (Kelfer® / Ferriprox®) is an alternative if iron chelation is ineffective or inadequate despite optimal Desferal® use, or if Desferal® use is contraindicated. (However, there is no formal evaluation in children < 10 years of age)

Deferiprone is given 75 – 100 mg/kg/day in 3 divided doses. It can also be used in combination with Desferal®, using a lower dose of 50mg/kg/day.

There is a small risk of reversible agranulocytosis, arthritis, or gastrointestinal disturbance. Weekly full blood counts are advised. Stop if neutropaenic ( $<1,500/\text{mm}^3$ ).

**Deferasirox** (Exjade®) is recently approved for use in transfusional iron overload in patients 2 years or older. The dose is 20-30 mg/kg/day in liquid dispersible table, taken once daily. There is a small risk of transient skin rash, GI disturbance and a reversible rise in serum creatinine below upper limit of normal (ULN) in some patients. Monthly monitoring of renal function is required.

### Monitoring of patients

*During each admission for blood transfusion*, the following should be done:

- clinical assessment – height, weight, liver & spleen size assessment
- pre transfusion Hb, platelet count, post transfusion Hb (half hour post transfusion)
- volume of blood transfused: volume of *pure RBC* (PRBC) based on haematocrit (HCT) of packed red cells given (usually > 50 - 55%)  
i.e. volume of PRBC = volume blood given x HCT of blood given (e.g. 600 mls x 0.55 = 330 mls)
- other medications

*Every 3- 6 months*

- evaluate growth and development
- serum ferritin
- liver function test

*Every year or more frequent if indicated*

- evaluate growth and development
- endocrine assessment - RBS, T4/TSH, Ca, PO4 (If Ca low - check PTH & Vit. D)
- pubertal and sexual development from 10 years onwards
- Tanner stage of breast and genitalia
- follicle stimulating hormone (FSH), luteinizing hormone (LH) levels, oestradiol or testosterone levels
- infection screen (6 monthly) – Hepatitis B and C, HIV, VDRL
- calculate transfusion indices (*Volume of Pure red blood cell transfused / median weight*)
- evaluate iron balance
- bone – osteoporosis & skeletal abnormalities

*Cardiac assessment* at variable intervals and especially after 10 years of age

- yearly ECG
- annual cardiac echocardiography
- cardiac T2\* MRI (available in Hospital Sentosa, Kuala Lumpur)

*Liver iron assessment*

- liver biopsy for liver iron concentration and the assessment of hepatitis, fibrosis or cirrhosis in selected cases and prior to bone marrow transplant.

## Splenectomy

### Indications

- blood consumption volume of PRBC > 1.5X normal or >200-220 ml/kg/year in those > 5 years of age to maintain average haemoglobin levels.
- evidence of hypersplenism.

### Note:

- give pneumococcal and HIB vaccinations 4-6 weeks prior to splenectomy
- meningococcal vaccine required in endemic areas
- penicillin prophylaxis for life after splenectomy
- low dose aspirin (75 mg daily) if thrombocytosis > 800,000/mm<sup>3</sup> after splenectomy

### Diet and supplements

- oral folate at minimum 1 mg daily may benefit most patients.
- low dose Vitamin C at 3 mg/kg augment iron excretion for those on Desferal.
  - dose: <10 years, 50mg daily; >10yrs, 100mg daily given only on deferral days
  - only to be given for patients on Desferal
- avoid iron rich food such as red meat and iron fortified cereals or milk.
- tea may help decrease intestinal iron absorption.
- dairy products are recommended as they are rich in calcium.
- vitamin E as antioxidant.

### Bone marrow transplantation (BMT)

- potential cure option when there is a HLA -compatible sibling.
- classification of patients into 3 risk groups based on presence of hepatomegaly, iron chelation status and presence of liver fibrosis.

Table 4. Survival following BMT (Pesaro group, Lucarelli et al)

Class	No. of risk factors	Survival %	Disease free survival (>10 yrs) %
1	0	92	85
2	1-2	84	80
3	3	61	53

best results if BMT is done at the earliest age possible in Class 1 patients.

*Note: in newly diagnosed cases, the family should be informed of this option and referred to a Paediatrician for counseling & HLA typing of patient and unaffected siblings to identify a potential donor.*

### Antenatal diagnosis

- can be done by chorionic villous sampling at 9-11 weeks period of gestation

### Support groups

- various state and local Thalassaemia Societies are available
- provides support and education for families
- organises fund raising activities and awareness campaigns
- health professionals are welcomed to participate

# IMMUNE THROMBOCYTOPENIC PURPURA

## Definition

Isolated thrombocytopenia with otherwise normal blood counts in a patient with no clinically apparent alternate cause thrombocytopenia (e.g. HIV infection, systemic lupus erythematosus, lymphoproliferative disorders, alloimmune thrombocytopenia, and congenital or hereditary thrombocytopenia).

## Pathogenesis

- increased platelet destruction, likely due to autoantibodies to platelet membrane antigens
- in children, ITP is an acute, self-limiting disorder that resolves spontaneously

## Clinical Manifestation

- onset is usually acute
- cutaneous bleeding
  - especially over the legs
- mucosal bleeding
  - palatal petechiae, epistaxis, haematuria, menorrhagia
  - gastrointestinal bleeding, intracranial haemorrhage
- absence of hepatosplenomegaly or lymphadenopathy
- thrombocytopenia, with normal haemoglobin and white cell count
- peripheral blood picture is normal apart from reduced, larger platelets
- prolonged bleeding time

Table 5. Other causes of thrombocytopenia

Neonatal alloimmune/ isoimmune thrombocytopenia if < 6 months old
Sepsis and infections including HIV infection
Drug-induced thrombocytopenia
Haematological malignancy
e.g. acute leukaemias
Congenital marrow failure syndromes
e.g. Fanconi anaemia, thrombocytopenia with absent radius
Autoimmune disorders
e.g. Systemic lupus erythematosus, Evan syndrome
Primary immunodeficiency syndromes
e.g. Wiskott-Aldrich syndrome

## Diagnosis

- diagnosis is based on history, physical examination, blood counts, and examination of the peripheral blood smear, which should exclude other causes of thrombocytopenia

Threshold for performing a *bone marrow aspiration* is low and is indicated if:

- atypical features:
  - organomegaly, significant lymphadenopathy, abnormal blood counts
  - suspicious peripheral blood picture.
- before starting steroid therapy  
(to avoid partially inducing an undiagnosed acute leukaemia)
- failure to respond to Immunoglobulin therapy
- persistent thrombocytopenia > 6 months
- thrombocytopenia recurs after initial response to treatment

Other tests may be indicated when there is atypical presentation

- Antinuclear factor
- Coomb's test
- ultrasound of abdomen
- HIV testing



## Treatment

*Not all children with diagnosis of acute ITP need hospitalization.*

Hospitalization is indicated if:

- severe life-threatening bleeding (e.g. ICH) regardless of platelet count
- platelet count  $< 20,000/\text{mm}^3$  with evidence of bleeding
- platelet count  $< 20,000/\text{mm}^3$  without bleeding but inaccessible to health care
- parents request for admission

Most children remit spontaneously: 70% achieve a platelet count  $> 50,000/\text{mm}^3$  by the end of the 3rd week.

Careful observation and monitoring of platelet count, without specific treatment, is appropriate for patients with:

- platelet count  $> 20,000/\text{mm}^3$  without bleeding
- platelet count  $> 30,000/\text{mm}^3$  with only cutaneous purpura

Treatment is indicated if there is:

- life threatening bleeding episode (e.g. ICH) regardless of platelet count
- platelet count  $< 20,000/\text{mm}^3$  with mucosal bleeding
- platelet count  $< 10,000$  with any bleeding

Choice of treatment include:

- oral prednisolone 4 mg/kg/day for 7 days, then taper and discontinue at 21 days
- IV Methylprednisolone 30 mg/kg/day for 3 days
- IV Immunoglobulin (IVIG) 0.8 g/kg/dose for 1 day or 250 mg/kg for 2 days.
- IV Anti-Rh(D) immunoglobulin (50 – 75  $\mu\text{g/kg}$ ) in Rhesus positive patients

*Notes regarding treatment:*

- *all are effective in raising platelet count much quicker compared to no treatment, with IVIG being the most effective. However there is no evidence that these treatments reduce bleeding complications or mortality or influence progression to chronic ITP.*
- *side effects of IVIG are common (15 – 75%): fever, flushing, headache, nausea, aseptic meningitis and transmission of Hepatitis C (older preparations).*
- *steroids should not be continued if there is no response or if there is a rapid relapse after withdrawal. The long-term side-effects in a growing child outweigh the benefits of either frequent high-dose pulses or titration of platelet count against a regular lower steroid dose.*
- *treatment should not be directed at increasing the platelet count above a preset level but rather on the clinical status of the patient.*

## Intracranial Haemorrhage

- the most feared complication of ITP with 50% mortality rate
- cumulative risk of ICH in newly diagnosed ITP child within 1st year is  $< 1\%$
- risk of ICH highest with platelet count  $< 20,000/\text{mm}^3$ , history of head trauma,
- aspirin use and presence of cerebral arteriovenous malformation.
- 50% of all ICH occurs after 1 month of presentation, 30% after 6 months
- early treatment with steroid or IVIG may not prevent late onset ICH

Emergency treatment of ITP with ICH (alone or in combination):

- IVIG 1 g/kg/dose/day for 2 days
- IV anti-Rh(D) 50 – 75 microgram/kg
- high dose IV Methylprednisolone 30 mg/kg/day for 3 days

- platelet transfusion
- neurosurgical intervention, if indicated.
- splenectomy if other modalities fail and if craniotomy required.

## CHRONIC ITP

- persistent thrombocytopenia after 6 months of onset (occurs in 20%)
- wide spectrum of manifestations: mild asymptomatic low platelet counts to
- intermittent relapsing symptomatic thrombocytopenia to the rare stubborn and persistent symptomatic and haemorrhagic disease

## Management

- every opportunity should be given for disease to remit spontaneously as the
- majority will do so if given enough time
- revisit diagnosis to exclude other causes of thrombocytopenia (Immunodeficiency, lymphoproliferative or collagen disorders or HIV infection).
- asymptomatic children can be left without therapy and kept under observation.
- symptomatic children may need short course of treatment to tide them over the relapse which include:
  - intermittent pulses of IVIG
  - intermittent anti-Rh(D) antibody treatment for those with Rhesus D positive
  - intermittent pulses of steroids
- care must be taken with any pulse steroid strategy to avoid treatment-related steroid side-effects. Aware of immunosuppression e.g. risk of severe varicella no justification for long-term continuous steroids

## Splenectomy

- is indicated when:
  - persistence of disease after 12 months with
  - bleeding symptoms and
  - platelet count  $< 10,000/\text{mm}^3$  (ages 3 – 12 years) or  $< 10,000/\text{mm}^3$  to  $30,000/\text{mm}^3$  (ages 8 – 12 years)
  - no response or only transient success with intermittent IVIG, anti-D or pulsed steroids
  - no contra-indications to surgery
- operative mortality  $< 1\%$
- over 70% rate of complete remission post-splenectomy
- pre-splenectomy immunization against pneumococci, *haemophilus influenzae* type b and meningococci infection mandatory 2 weeks before surgery
- post-splenectomy penicillin prophylaxis

For post-splenectomy failure or relapse, consider:

- danazol, vincristine, azathioprine, cyclophosphamide, alpha-interferon, staphylococcal protein A immunoabsorption, cyclosporine, cholic acid or dapsone.

# HAEMOPHILIA

## Definition

A group of blood disorders in which there is a defect in the clotting mechanism. Of X-linked recessive inheritance, but in 30% there is no family history as it is a spontaneous new mutation. The most common haemophilias are:

Haemophilia A – Deficiency of factor VIII (85% cases)

Haemophilia B – Deficiency of factor IX (15% cases)

## Clinical Manifestation

bleeding in the neonatal period is unusual.

usually present with easy bruising when crawling and walking (9-12 months age)

haemarthrosis is characteristic of haemophilia. Large joints are usually affected (knee, ankle, elbow); swollen, painful joints are common.

epistaxis, gum bleeding, haematuria also occur

life-threatening intracranial haemorrhages can be life threatening

bleeding may also occur spontaneously or after trauma or operation.

## Diagnostic Investigations

full blood count

coagulation screen: PT, APTT (*in haemophilia: the APTT is prolonged, PT normal*)

specific factor assay: FVIII level (low in Haemophilia A)

specific factor assay: FIX level (low in Haemophilia B)

Table 6. Classification of haemophilia and clinical presentation

Factor level	Classification	Clinical presentation
< 1 %	severe	spontaneous bleeding, risk of intracranial haemorrhage
1-5 %	moderate	bleeding may only occur with
5-25 %	mild	trauma or after surgery

## Further Investigations

- Hepatitis B surface antigen, anti HBS antibody
- Hepatitis C antibody
- HIV serology
- Diagnosis of carrier status for genetic counseling.
  - mother of a newly diagnosed son with haemophilia
  - female siblings of boys with haemophilia
  - daughter of a man with haemophilia

Once a child is diagnosed to have haemophilia, check the viral status at diagnosis and then yearly. This is because treatment carries the risk of acquiring viruses. All haemophiliacs should be immunized against Hepatitis B.

## Treatment

- treatment consists of replacing the missing factor:
- Factor VIII concentrates for haemophilia A; Factor IX concentrates in Haemophilia B.
- avoid Fresh frozen plasma and cryoprecipitate as high risk for viral transmission.
- the dose of factor replacement depends on the type and severity of bleed (refer Table 7)

Table 7. Suggested replacement doses of factor VIII and XI concentrate

Type of bleed	Factor VIII dose	Factor XI dose
Haemarthrosis	20 U/kg	40 U/kg
Soft tissue or muscle bleeds	30-40 U /kg	60-80 U/kg
Intracranial haemorrhage or surgery	50 U/kg	120 U/kg

- alternative formula for calculating dose:
  - units of Factor VIII:  $(\% \text{ rise required}) \times (\text{weight in kg}) \times 0.5$
  - units of Factor IX:  $(\% \text{ rise required}) \times (\text{weight in kg}) \times 1.4$
- the percentage of factor aimed for depends on the type of bleed.
  - for haemarthroses, 30-40 % is adequate.
  - for soft tissue or muscle bleed aim for 40- 50 % level.  
(there is potential to track and cause compression/compartment syndrome)
  - for intracranial bleeds or patients going for surgery, aim for 100%.
- factor VIII is given every 8 – 12 hours. Factor IX is given every 12 – 24 hours.
- duration of treatment depends on type of bleed:
  - haemarthroses 2-3 days
  - soft tissue bleeds 4-5 days
  - intracranial bleeds or surgery 7-10 days.

## Supportive Treatment

### Analgesia

There is rapid pain relief in haemarthroses once missing factor concentrate is infused. If analgesia is required, avoid intramuscular injections. Also do not use aspirin or the non-steroidal anti-inflammatory drugs (NSAIDS) as risk of bleeding.

### Dental care

Good dental hygiene is important as dental caries are a regular source of bleeding. Dental clearance with factor replacement will be required in severe cases.

### Immunisations

These are important and must be given: in this case intramuscular injections are allowed: use the smallest gauge needle to minimise trauma. If a baby has had a haematoma after immunization, give the next injection under factor cover.

## Complications

### Joint destruction

Recurrent haemarthroses into the same joint will destroy the joint causing osteoarthritis and deformity. This can be prevented by prompt and adequate factor replacement.

### Acquisition of viruses

Hepatitis B, C or HIV: immunisation and regular screening is recommended.

### Inhibitors

In 15-25% cases of haemophilia A, patients may develop antibodies to the missing factors. This is suspected when factor replacement does not result in clinical improvement. If a patient is suspected to have inhibitors, the case should be discussed with a haematologist.

## SPECIFIC GUIDELINES FOR MANAGEMENT

### Intracranial haemorrhage (ICH)

- give factor replacement before suspected bleed is confirmed by CT scan
- aim to increase Factor VIII:C level to 100%
- for haemophilia B, aim for 80 % if monoclonal factor IX is used, or 50 % if prothrombin complex concentrate (PCC)
- urgent CT scan:
  - if scan confirms ICH : maintain factor level > 50% , give factor concentrates 6-8 hourly for at least 3-5 days depending on the clinical response, then reduce dose to maintain at 30%, initially 12 hourly and then daily up to a total of 10 -14 days replacement therapy
  - if CT scan show no evidence of ICH, admit 1 day for observation
- lab investigations:
  - full coagulation profile – PT,PTT
  - pre-treatment factor assay level and inhibitor level before starting treatment and to repeat after 3 days of treatment to ensure adequate levels have been achieved and no inhibitor has developed
  - post treatment factor assay level ( ½ hour after infusion ) to ensure required factor level is achieved ( if the level is not achieved , consider development of inhibitors ) and should be repeated after 3 – 5 days
- follow up CT scan after 2 weeks

### Surgery

- pre-op investigations
  - full coagulation profile – PT, PTT
  - pre-factor assay level and inhibitor level
  - blood grouping, full antibody screening and full cross matching if required
- calculate dose
  - ½ hour before operation, infuse patient with appropriate factors.
  - preferable level :
    - 80-100% for factor VIII
    - 70% for monoclonal factor IX
    - 50% if prothrombin complex concentrate (PCC) used
- check post transfusion specific factor level ½ hour later if necessary or after surgery to ensure correct factor level is achieved
- clotting factor level should be maintained above 50% during the operation and 24 hours after surgery.
- repeat pre factor assay and check inhibitor level on day 3 to ensure adequate level and no inhibitors have developed
  - day 3 till day 7 – maintain at 50%
  - day 8 till day 14 – reduce the dose gradually
- replacement therapy is recommended post operatively for at least 10 -14 days
- replacement therapy should be given as long as there is bleeding plus another 5 –10 days after the bleeding stops, until the wound heals

## Illiopsoas bleed

### Investigations

- abdominal ultrasound to assess the size of haemorrhage
- full coagulation profile, pre-factor specific assay and inhibitor screen
- full blood picture
- renal function test

### Management

- complete bed rest
- give factor replacement early - aim for level > 50% for haemophilia A & B
- maintain level > 50% with factor concentrates given 8 hourly for haemophilia A and 12 hourly for haemophilia B for at least 3-5 days. Reduce dose accordingly.
- a minimum of 10 – 14 days replacement therapy is recommended
- physiotherapy – when pain subsides
- repeat abdominal ultrasound 1 week later to assess progress

## Haematuria

### Management

- bed rest
- drink plenty of water (1 ½ maintenance).
- monitor for first 24 hours: UFEME & Urine C&S
- if bleeding persists for > 24 hours, start factor concentrate infusion.
- perform KUB & Ultrasound of the kidneys

*DO NOT give anti-fibrinolytic drugs (tranexamic acid) because this may cause formation of clots in the tubules which may not recanalize.*

## Haemarthroses (Joint haemorrhages)

- episodic replacement therapy is the main stay of treatment
- most spontaneous haemarthroses respond to a single infusion of factor concentrate. Aim for a level of 30 % to 40%.
- if swelling or spasm is present, treatment to level of 50% is required and infusion may have to be repeated at 12-24 hours interval, until pain subsides
- minor haemarthroses may not require immobilization
- elastic bandage or slings and ice may help in pain relief
- in severe haemarthroses:
  - rest, splint in position of comfort, give analgesics if required
  - factor replacement
  - joint rehabilitation to be started as soon as possible

## HAEMOPHILIA SOCIETY

All haemophiliacs should be registered with the Haemophilia Society, and have a medic-alert bracelet/chain which identifies them as haemophiliacs. They usually carry a book in which the diagnosis, classification of severity, types of bleeds and admissions can be recorded.

Address: The Haemophilia Society of Malaysia  
c/o Pusat Perkhidmatan Darah  
Hospital Kuala Lumpur  
Jalan Pahang

# ONCOLOGY EMERGENCIES

## I. METABOLIC EMERGENCIES

### Tumour Lysis Syndrome

#### Introduction

- massive tumour cell death with rapid release of intracellular metabolites, which exceeds the excretory capacity of the kidneys leading to acute renal failure. Can occur before chemotherapy is started.
- more common in lymphoproliferative tumours with abdominal involvement (e.g. B cell/ T cell lymphoma, leukaemias and Burkitt's lymphoma)

#### Tumour lysis syndrome

##### Characterised by:

hyperuricemia  
hyperkalemia  
hyperphosphatemia with  
associated hypocalcemia

#### Hyperuricaemia

- release of intracellular purines increase uric acid

#### Hyperkalaemia

- occurs secondary to tumour cell lysis itself or secondary to renal failure from uric acid nephropathy or hyperphosphataemia.

#### Hyperphosphataemia with associated hypocalcaemia

Most commonly occurs in lymphoproliferative disorders because lymphoblast phosphate content is 4 times higher than normal lymphocytes.

#### Causes:

- tissue damage from  $\text{CaPO}_4$  precipitation. Occurs when  $\text{Ca} \times \text{PO}_4 > 60 \text{ mg/dl}$ . Results in renal failure, pruritis with gangrene, eye and joint inflammation
- hypocalcaemia leading to altered sensorium, photophobia, neuromuscular irritability, seizures, carpopedal spasm and gastrointestinal symptoms

#### Renal failure

##### Multifactorial:

- uric acid, phosphorus and potassium are excreted by kidneys
- the environ of the collecting ducts of the kidney is acidic coupled with lactic acidosis due to high leucocyte associated poor perfusion will cause uric acid crystallization and then uric acid obstructive nephropathy. Usually occur when levels  $> 20 \text{ mg/dl}$ .
- increased phosphorus excretion causing calcium phosphate precipitation (in vivo solubility dependant on  $\text{Ca} \times \text{P} = 58$ ) in microvasculature and tubules.
- risk increases if renal parenchymal is infiltrated by tumour e.g. lymphoma or ureteral/venous obstruction from tumour compression (lymph nodes).

**Table 1. Risk factors for Tumour lysis syndrome**

Bulky disease
Rapid cellular turnover.
Tumour which is exquisitely sensitive to chemotherapy
Elevated LDH / serum uric acid
Depleted volume
Concentrated urine or acidic urine
Poor urine output

### Management (Prevention):

To be instituted in every case of acute leukaemia or lymphoma prior to induction chemotherapy.

- **Hydration:** Double hydration - 125ml/m<sup>2</sup>/hr or 3000ml/m<sup>2</sup>/day. **No added potassium.**
- **Alkalinization of urine:** Adding NaHCO<sub>3</sub> at 150 - 200 mmol/m<sup>2</sup>/day (3 mls/kg/day NaHCO<sub>3</sub> 8.4%) into IV fluids to keep urine pH 7.0 - 7.5. Avoid over alkalinization as this may aggravate hypocalcaemia and cause hypoxanthine and xanthine precipitation. It can also cause precipitation of calcium phosphate if pH >8. Monitor urine pH and VBG 8 hourly. If urine pH < 7.0, consider increasing NaHCO<sub>3</sub> infusion. This can only be done if HCO<sub>3</sub><sup>-</sup> in the blood is below normal range. Otherwise, have to accept that some patients just cannot alkalinise their urine.
- **Allopurinol** 10mg/kg/day, max 300mg/day.
- may have to *delay chemotherapy* until metabolic status stabilizes.
- **Close electrolyte monitoring-** BUSE, Ca<sup>2+</sup>, PO<sub>4</sub>, uric acid, creatinine, bicarbonate
- **Strict I/O charting.** Ensure adequate urine flow once hydrated. Use diuretics with caution.

### Management (Treatment)

- treat hyperkalaemia – resonium, dextrose-insulin, Consider dialysis.
- diuretics
- hypocalcaemia management depends on the phosphate level:
  - if phosphate is raised, then management is directed to correct the high phosphate
  - if phosphate is normal or if child is symptomatic, then give replacement IV calcium
  - if hypocalcaemia is refractory to treatment, exclude associated hypomagnesaemia
- dialysis if indicated. Haemodialysis most efficient at correcting electrolyte abnormalities. Peritoneal dialysis is not effective in removing phosphates.

### Other Metabolic Emergencies:

#### Hyponatraemia

- usually occurs in acute myeloid leukaemia (AML)
- treat as for hyponatraemia.

#### Hypokalaemia

- common in AML
- rapid cellular generation leads to uptake of potassium into cells. (Intracellular potassium 30 - 40 X times higher than extracellular potassium). Therefore may hyperkalaemia may develop after chemotherapy.

#### Hypercalcaemia

- associated with Non Hodgkin lymphoma, Hodgkin lymphoma, alveolar rhabdomyosarcoma, rhabdoid tumours and others.

### Management

- hydration.
- oral phosphate
- IV frusemide (which increases calcium excretion)
- mithramycin



## II. HAEMATOLOGICAL EMERGENCIES

### Hyperleucocytosis

- occurs in acute leukaemia. Defined as TWBC  $> 100\,000 / \text{mm}^3$
- associated
  - in acute lymphoblastic leukaemia (ALL) with high risk of tumour lysis
  - in AML with leucostasis (esp monocytic)
  - affects the lungs due to pulmonary infiltrates. May cause dyspnoea, hypoxaemia and right ventricular failure
  - affects the central nervous system causing headaches, papilloedema, seizures, haemorrhage or infarct.
  - other complications: renal failure, priapism, dactylitis
- mechanism:
  - excessive leukocytes form aggregates and thrombi in small veins causing obstruction; worsens when blood is viscous.
  - excessive leukocytes competes for oxygen; damages vessel wall causing bleeding

#### Management

- hydration
  - to facilitate excretion of toxic metabolites
  - to reduce blood viscosity
- avoid increasing blood viscosity.
  - cautious in use of packed cell transfusion and diuretics.
- during induction in hyperleukocytosis, keep platelet  $>20\,000/\text{mm}^3$  and coagulation profile near normal
- exchange transfusions and leukopheresis should not be used alone as rapid rebound usually occurs. Concurrent drug treatment should therefore be initiated soonest possible.

### Coagulopathy

AML especially M3 is associated with an initial bleeding diathesis from *consumptive coagulopathy* due to release of a tissue factor with procoagulant activity from cells. However the use of all-trans retinoic acid (Atra) has circumvented this complication.

#### Management

- platelet transfusions – 6 units /  $\text{m}^2$  should increase platelets by  $50,000 / \text{mm}^3$
- fresh frozen plasma (FFP) or cryoprecipitate
- vitamin K
- +/- heparin therapy (10u/kg/hr) - controversial

### Other haematological emergencies

- thrombocytopenia
- severe anaemia

### III. SUPERIOR VENA CAVA OBSTRUCTION

#### Superior Vena Cava (SVC) Obstruction

- common in Non Hodgkin Lymphoma / Hodgkin Lymphoma / ALL .
- rarely: malignant teratoma, thymoma, neuroblastoma, rhabdomyosarcoma or Ewing's may present with anterior or middle mediastinal mass and obstruction.
- 50% associated with thrombosis.
- presentation: shortness of breath, facial swelling, syncope.

#### Management

- *recognition of symptoms and signs of SVC obstruction and avoidance of sedation and general anaesthesia*

Tissue diagnosis is important but should be established by the least invasive measure available. Risk of circulatory collapse or respiratory failure may occur with general anesthesia or sedation.

- BMA

- biopsy of superficial lymph node under local anaesthesia.

- measurement of serum markers e.g. alpha-fetoprotein

If tissue diagnosis is not obtainable, empiric treatment may be necessary based on the most likely diagnosis. Both chemotherapy and DXT may render histology uninterpretable within 48 hours, therefore biopsy as soon as possible.

- *avoid upper limb venepunctures*
  - bleeding due to increased intravascular pressure
  - aggravate SVC obstruction.
- primary mode of treatment is with steroids } if pathology due to Non-Hodkin
- chemotherapy. } Lymphoma
- +/- DXT.

### IV. INFECTION

#### Febrile neutropenia

Febrile episodes in oncology patients **must** be treated with urgency especially if associated with neutropenia. Nearly all episodes of bacteraemia or disseminated fungal infections occur when the absolute neutrophil count (ANC)  $<500 /\text{mm}^3$ . Risk increases maximally if ANC  $<100 /\text{mm}^3$  and greatly reduced if the ANC  $>1000 /\text{mm}^3$ .

#### Management (Follow Algorithm in Figure 1)

other considerations:

- if central line is present, culture from central line (both lumens); add anti-Staph cover e.g. cloxacillin
- repeated physical examination to look for new clues, signs and symptoms of possible sources
- close monitoring of patient's well-being
  - vital signs, perfusion, BP, I/O.
- repeat cultures if indicated
- investigative parameters, FBC, CRP, BUSE as per necessary.
- in presence of oral thrush or other evidence of candidal infection, start antifungals.
- try to omit aminoglycoside and vancomycin if on cisplatin - nephrotoxic and ototoxic. If required, monitor renal function closely.

#### Febrile neutropenia

Common organisms

*Staphylococcus aureus*

*Staphylococcus epidermidis*

*Streptococcus pneumonia*

*Escherichia coli*

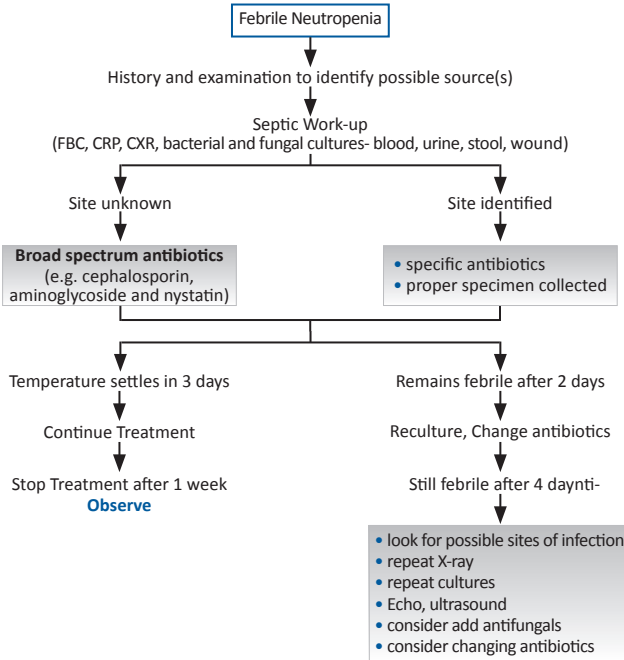
*Pseudomonas spp.*

*Klebsiella spp.*

*Candida spp*

*Aspergillus*

Figure 1. Approach to a patient with febrile neutropenia



Abbreviations. FBC, full blood count; CRP, C-reactive protein; CXR, chest X-ray; CVL, central venous line.

## Typhilitis

- a necrotizing colitis localised to the caecum occurring in neutropenic patients.
- bacterial invasion of mucosa causing inflammation - can lead on to full thickness infarction and perforation
- usual organisms are *Clostridium* and *Pseudomonas*
- X-ray shows non specific thickening of gut wall. At the other end of the spectrum, there can be presence of pneumatosis intestinalis +/- evidence of free gas

## Management

- usually conservative with broad spectrum antibiotics covering gram negative organisms and anaerobes (metronidazole). Mortality 20-100%
- criteria for surgical intervention:
  - persistent gastrointestinal bleeding despite resolution of neutropenia and thrombocytopenia and correction of coagulation abnormalities.
  - evidence of perforation
  - clinical deterioration suggesting uncontrolled sepsis (controversial)

# Shock

Table 2 lists the common causes of shock in child with cancer

Table 2. Common causes of shock in children with cancer		
Distributive	Hypovolaemic	Cardiogenic
<i>Sepsis</i>	<i>Haemorrhage</i>	<i>Myopathy</i>
<i>Anaphylaxis</i>	haemorrhagic cystitis	anthracycline
etoposide	gastrointestinal bleeding	high dose cyclophosphamide
L-asparaginase	ulcers	radiation therapy
anti-thymocyte globulin	typhilitis	<i>Cardiac tamponade</i>
cytosine	massive haemoptysis	intracardiac tumour
carboplatin	<i>Pancreatitis</i>	intracardiac thrombus
blood products	<i>Addisonian crisis</i>	pericardial effusion
amphotericin B	<i>Intractable vomiting</i>	constrictive pericarditis
<i>Veno occlusive disease</i>	<i>Diabetes mellitus</i>	<i>Metabolic</i>
	<i>Diabetes insipidus</i>	hyperkalaemia, hypokalaemia
	<i>Hypercalcaemia</i>	hypocalcaemia
		<i>Myocarditis</i>
		viral, bacterial, fungal

## Management

Ascertain cause and treat accordingly

## V. NEUROLOGICAL COMPLICATIONS

### Spinal Cord Compression

- prolonged compression leads to permanent neurologic sequelae.
- epidural extension: lymphoma, neuroblastoma and soft tissue sarcoma
- intradural: Spinal cord tumour
- Presentation
  - back pain: localized or radicular, aggravated by movement, straight leg raising, neck flexion
  - later: weakness, sensory loss, loss of bladder and bowel continence
- diagnosed by CT myelogram/MRI

## Management

- laminectomy urgent (if deterioration within 72 hours).
- if paralysis present > 72 hours, chemotherapy is the better option if tumour is chemosensitive, e.g. lymphoma, neuroblastoma and Ewing's tumour. This avoids vertebral damage. Onset of action of chemotherapy is similar to radiotherapy.
- prior IV Dexamethasone 0.5mg/kg 6 hourly to reduce oedema
- +/- Radiotherapy

### Increased Intracranial Pressure (ICP) and brain herniation

Cause : Infratentorial tumours causing blockage of the 3rd or 4th ventricles such as medulloblastomas, astrocytomas and ependymomas.

Signs and symptoms vary according to age/site.

- infant - vomiting, lethargy, regression of milestones, seizures, symptoms of obstructive hydrocephalus and increased OFC.
- older - early morning recurrent headaches +/- vomiting, poor school performance
- cerebellar: ipsilateral hypotonia and ataxia

- herniation of cerebellar tonsil – head tilt and neck stiffness
- tumours near 3rd ventricle – craniopharyngioma, germinoma, optic glioma, hypothalamic and pituitary tumours
  - visual loss, increased ICP and hydrocephalus
  - aqueduct of Sylvius obstruction due to pineal tumour: raised ICP, Parinaud's syndrome (impaired upward gaze, convergence nystagmus, altered pupillary response)

#### *Management*

- assessment of vital signs, look for focal neurological deficit,
- look for evidence of raised ICP (bradycardia, hypertension and apnea)
- look for evidence of herniation (respiratory pattern, pupil size and reactivity)
- dexamethasone 0.5 mg/kg QID
- urgent CT to determine cause
- prophylactic antiepileptic agents.
- lumbar puncture is contraindicated
- decompression – i.e. shunting +/- surgery.

#### **Cerebrovascular accident (CVA)**

- can result from direct or metastatic spread of tumour, antineoplastic agent or haematological abnormality
- L-Asparaginase associated with venous or lateral and sagittal sinus thrombosis caused by rebound hypercoagulable state
- AML especially APML is associated with DVC and CVA, due to the release of procoagulant

#### *Management*

- supportive
- use of anticoagulant potentially detrimental
- in L-Asparaginase induced, recommended FFP bd

### **VI. MISCELLANEOUS EMERGENCIES**

#### **Pancreatitis**

Should be considered in patients on L-Asparaginase and steroids and complaining of abdominal pain. Careful examination plus measurement of serum amylase and ultrasound abdomen.

#### **ATRA (all-trans retinoic acid) syndrome**

- characterised by: fever, respiratory distress, respiratory failure, oedema, pleural/pericardial effusion, hypotension
- pathophysiology: respiratory distress due to leukocytosis associated with ATRA induced multiplication and differentiation of leukaemic promyelocytes
- treatment: dexamethasone 0.5 – 1mg/kg/dose bd, maximum dose 20mg bd.

## GENERAL GUIDELINES FOR MAINTENANCE CHEMOTHERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

### General considerations

- check height, weight and calculate surface area ( $m^2$ ) every 3 months and adjust drug dosages accordingly. In the absence of a Normogram to calculate the surface area, use the following formula:  
**SURFACE AREA = SQUARE ROOT of [Height (cm) x Weight (kg) / 3600]**
- check full blood picture every 2 weeks for the next 1- 2 months after starting maintenance chemotherapy and monthly thereafter if stable.
- bone marrow aspiration should be considered if counts are repeatedly low or if there is clinical suspicion of relapse. The majority of relapse ( $>2/3$ ) would occur within the first year of diagnosis.
- central nervous system disease usually presents with headache, vomiting, altered sensorium or hypothalamic symptoms (e.g. hyperphagia, excessive weight gain)

### Managing blood counts

- adjust chemotherapy to maintain absolute neutrophil count (ANC)  $\geq 1 \times 10^9$  /dL.
  - if ANC is  $0.75 - 1.0 \times 10^9$  /L ( $500 - 1000/mm^3$ ) or platelet count  $50-100 \times 10^9$  /L, reduce 6-mercaptopurine (6MP) and methotrexate (MTX) dose by 50%.
  - keep at this dose until counts are above those levels.
  - then increase 6MP and MTX to 75% recommended dose and review in 1 week.
  - if counts are acceptable, then continue at 100% dose,
  - if neutrophil count  $< 0.5 \times 10^9$  /L or platelets  $< 50 \times 10^9$  /L, stop both drugs.
  - restart drugs at 50% dose when ANC  $> 1.0 \times 10^9$  /L, then increase to 75% and 100% as above.
- normally Hb would remain stable but repeated falls in haemoglobin alone may be due to 6MP intolerance; hence reduce dose as above and attempt to increase dose gradually again. MTX should stay at top dose. If counts take longer to recover, consider performing bone marrow aspiration after 2-3 weeks.
- Anaemia occurring early in the course of continuing therapy should be treated with transfusion and the dose of 6MP and MTX maintained. If persistent anaemia occurs (i.e. Hb  $< 8$  gm/dl) despite reducing the dose of 6MP, the MTX dose should be reduced appropriately.
- if counts are persistently low and dose of 6MP/MTX are suboptimal, consider withholding cotrimoxazole. Re-introduce once 6MP or MTX are at  $> 75\%$  of protocol dosage. If neutropenia recurs or if child cannot tolerate at least 75% drug dosage, cotrimoxazole should be stopped. The maintenance of adequate drug dose should take priority over continuing cotrimoxazole. If cotrimoxazole is stopped, it must be remembered that the child is at increased risk of pneumocystis pneumonia and there should be a low threshold for treatment of suspected interstitial pneumonitis.

### Other complications

- in severe diarrhoea and vomiting, stop both drugs. Restart at 50% protocol when better and return to full dose when tolerated.
- severe MTX mucositis; withhold MTX until improvement and restart at full dose.
- initiate supportive treatment with mouthwash, antifungal treatment (Nystatin / Daktarin oral gel) and local anaesthetic e.g. viscous xylocaine.

- in clinically significant liver dysfunction (e.g. jaundice); oral MTX should be stopped until improvement occurs. Restart at reduced dose and increase as tolerated. Investigate for causes of liver dysfunction. Monitor LFT.

## Infections

- *Pneumocystis carinii* pneumonia (PCP) prophylaxis  
Cotrimoxazole is routinely used as prophylaxis against PCP and continued until the end of therapy. In the event of chronic cough or unexplained tachypnoea, a chest X-ray is required. If there is evidence of interstitial pneumonitis, then send off nasopharyngeal secretions for PCP IFT and treat empirically with high dose cotrimoxazole (Bactrim/Septim) (20 mg/kg/day in divided doses) for 2 weeks.
- *Febrile neutropaenia* (ANC <  $1 \times 10^9$  /dL)
  - if there is significant fever (temperature  $\geq 38.5^\circ\text{C} \times 1$  or  $\geq 38^\circ\text{C} \times 2$ , one hour apart), stop all drugs and admit to hospital for IV antibiotics.
  - take appropriate cultures and chest X-rays as indicated; start IV antibiotics immediately, without waiting for specific bacteriological confirmation. Use an aminoglycoside - cephalosporin combination to treat both gram negative and gram positive organisms.
  - if nosocomial infection is suspected, use the appropriate antibiotics according to your hospital's culture-sensitivity pattern. Assume multiresistant bacterial sepsis when dealing with patients presenting with septic shock.
  - early and aggressive therapy will save lives.
- *Antifungal therapy* may be indicated in prolonged neutropenia or if there is no response to antibiotics, or if fungal infection is suspected.
- *Vancomycin* may be indicated if there is a long line in situ or if MRSA or coagulase negative *Staphylococcus* infections are suspected.
- *Chicken Pox/Measles infection*
  - these are life-threatening infections in ill immunocompromised children.
  - always reinforce this information on parents when they come for follow-up.
  - if a patient is significantly/directly exposed (in the same room > 1 hour), including the 3 days prior to clinical presentation, to sibling, classroom contact, enclosed playmate contact or other significant contact, they are at increased risk of developing these infections. **GIVE:**
  - **Measles:** Human broad-spectrum immune globulin IM 0.5ml/kg divided into 2 separate injection sites on the same day.
  - **Chickenpox:** There is no Zoster immune globulin readily *available locally*.  
exposed patients: oral Acyclovir 200mg 3 x/day for 5 days (< age 6 years) and 400 mg 3 x/day if > 6 years for 5 days.  
These patients must be monitored for signs of infections. If a patient develops chickenpox, admit, isolate and treat immediately with IV acyclovir 500 mg/m<sup>2</sup>/dose every 8 hours until no new lesions are noted, followed by oral acyclovir 400mg 5x daily ( children < 2 years old) until the lesions are healed, usually in 10 days. If > 2 years old, 800mg 5x daily.
  - Chemotherapy must be stopped on suspicion of exposure; and if infected and treated: commence chemotherapy at 2-3 weeks after last vesicle has dried up.

## Vaccinations

Children on chemotherapy should not receive any vaccinations until 12 months after cessation of chemotherapy. They may then recommence their immunisation programme continuing from where they left off.

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# GASTROENTEROLOGY

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## ACUTE GASTROENTERITIS

### Introduction

*This guideline is based on the WHO guideline on The Treatment of Diarrhoea in Children and the Integrated Management of Childhood Illness (IMCI) guidelines. However modifications have been made to Treatment Plan C in keeping with the guideline on fluid resuscitation in the Paediatric Advanced Life Support Programme.*

Acute gastroenteritis is a leading cause of childhood morbidity and mortality and is also an important cause of malnutrition. Many diarrhoeal deaths are caused by dehydration from fluid and electrolytes loss. Mild and moderate dehydration can be safely and effectively treated with ORS solution but severe dehydration needs intravenous fluid therapy.

**If you have gone through the PALS course, first assess the state of perfusion of the child: Is the child in shock? If so go straight to treatment Plan C.**

**OR** you can also use the WHO chart below to assess the degree of dehydration and then choose the treatment plan A, B or C, as needed.

<i>Assess</i>			
Look at child's general condition	well, alert	restless or irritable	lethargic or unconscious
Look for sunken eyes	no sunken eyes	sunken eyes	sunken eyes
Offer the child fluid	drinks normally	drinks eagerly, thirsty	not able to drink or drinks poorly
Pinch skin of abdomen	skin goes back immediately	skin goes back slowly	skin goes back very slowly (> 2 seconds)
<i>Classify</i>	<b>no dehydration (&lt; 5 %)</b>	<b>≥ 2 above signs present: some dehydration (5-10%)</b>	<b>≥ 2 above signs present: severe dehydration (&gt; 10%)</b>
<i>Treat</i>	Give fluid and food to treat diarrhoea at home, <b>Treatment Plan A</b>	Give fluid and food for some dehydration, <b>Treatment Plan B</b>	Give fluid for severe dehydration, <b>Treatment Plan C</b>

*Note: Children on treatment Plan C may show signs of shock such as tachycardia, weak peripheral pulses, delayed capillary refill time > 2 seconds, cold peripheries, depressed mental state with or without hypotension.*

### PLAN A: TREAT DIARRHOEA AT HOME

Counsel the mother on the 3 rules of home treatment:

**Give Extra Fluid, Continue Feeding, When to return**

1. *Give Extra Fluids* (as much as the child will take)

- tell the mother:
  - breastfeed frequently and for longer at each feed
  - if the child is exclusively breastfed, give ORS or cooled boiled water in addition to breastmilk
  - if the child is not exclusively breastfed, give one or more of the following: ORS, food-based fluids (soup and rice water) or cooled boiled water
- It is especially important to give ORS at home when:
  - the child has been treated with Plan B or Plan C during this visit
  - the child cannot return to a clinic if the diarrhoea gets worse
- teach the mother how to mix and give ORS. Give the mother 8 packets of ORS to use at home.

- show mother how much ORS to give in addition to the usual fluid intake:
  - Up to 2 years : 50 to 100ml after each loose stool
  - 2 years or more : 100 to 200ml after each loose stool
  - (If weight is available, give 10ml/kg of ORS after each loose stool)
- tell mother to
  - give frequent small sips from a cup or spoon
  - if child vomits, wait 10 minutes, then continue but more slowly
  - continue giving extra fluid until diarrhoea stops

## 2. Continue Feeding

- breastfed infants should continue nursing on demand
- formula fed infants should continue their usual formula immediately on rehydration
- lactose-free or lactose-reduced formula usually are unnecessary
- children receiving semi-solid or solid foods should continue to receive their usual food during the illness
- foods high in simple sugar should be avoided as osmotic load may worsen the diarrhoea

## 3. When to Return (to clinic/hospital)

When child is

- not able to drink or breastfeed or drinking poorly
- becomes sicker
- develops a fever
- has blood in stool

## PLAN B: TREAT SOME DEHYDRATION WITH ORS

Give recommended amount of ORS over 4-hour period:

Table 2. Determining the amount of ORS to give in the first 4 hours

Age <sup>1</sup>	Up to 4 months	4 - 12months	12 months -2 years	2 - 5 years
Weight	<6kg	6- <10kg	10- <12kg	12- 19kg
In ml	200-400	400-700	700-900	900-1400

footnote: 1. Use the child's age only when you do not know the weight. The approximate amount of ORS required (in ml) can be calculated by multiplying the child's weight (in kg) x 75

2. If the patient wants more ORS than shown, give more

Show the mother how to give ORS solution

- give frequent small sips from cup or spoon
- if the child vomits, wait 10 minutes, then continue but more slowly (i.e. 1 spoonful every 2 - 3 minutes).
- continue breastfeeding whenever the child wants

After 4 hours

- reassess the child and classify the child for dehydration
- select the appropriate plan to continue treatment (Plan A, B or C)
- begin feeding the child

*If the mother must leave before completing treatment*

- show her how to prepare ORS solution at home.
- show her how much ORS to give to finish the 4-hour treatment at home.
- give her enough ORS packets to complete rehydration. Also give her 8 packets as recommended in Plan A.
- explain the 3 Rules of Home Treatment (Plan A):
  1. GIVE EXTRA FLUID
  2. CONTINUE FEEDING
  3. WHEN TO RETURN

#### Important

- If possible, observe the child at least 6 hours after re-hydration to be sure the mother can maintain hydration giving the child ORS solution by mouth
- If there is an outbreak of cholera in your area, give an appropriate oral antibiotic after the patient is alert.

### PLAN C: TREAT SEVERE DEHYDRATION QUICKLY

1. *Start intravenous (IV) or intraosseous (IO) fluid immediately.* If patient can drink, give ORS by mouth while the drip is being set up. Give 100 ml/kg Ringers lactate or normal saline divided as follows:-
  - i) first give 20 ml/kg as fast as possible. Repeat fluid boluses as necessary until perfusion has improved.
  - ii) then give the remaining fluid over 5 hours (age  $\leq$  12 months) or 2 1/2 hours (age  $>$  12 months)
- reassess the patient after every bolus and stop the boluses once perfusion improves or when fluid overload is suspected. If the patient does not respond to rapid bolus rehydration, consider the possibility of an underlying disorder e.g. septic shock, toxic shock syndrome, myocarditis, myocardiopathy or pericarditis. Inotropic agents may then be necessary to maintain perfusion
- reassess the child every 1-2 hours during rehydration.
- also give ORS (about 5 ml/kg/hour) as soon as the child can drink, usually after 3 to 4 hours for infants, and 1 to 2 hours for older children.
- reassess an infant after 6 hours and a child after 3 hours. Classify dehydration
- then choose the appropriate plan (A, B, or C) to continue treatment.
2. *If you cannot or fail to set up IV or IO line, arrange for the child to be sent to the nearest centre that can do so immediately.* Meanwhile as arrangements are made to send the child (or as you make further attempts to establish IV or IO access):
  - try to rehydrate the child with ORS orally (if the child can drink) or by orogastric tube. Give ORS 20 ml/kg/hour over 6 hours. Continue to give the ORS along the journey.
  - reassess the child every 1-2 hours
  - if there is repeated vomiting or increasing abdominal distension, give the fluid more slowly.
  - reassess the child after six hours, classify dehydration
  - then choose the most appropriate plan (A, B or C) to continue treatment.

## Indications for intravenous therapy

- severe dehydration
- unconscious child
- continuing rapid stool loss ( > 15-20ml/kg/hour)
- frequent, severe vomiting, drinking poorly
- abdominal distension with paralytic ileus, usually caused by some anti-diarrhoeal drugs ( e.g. codeine, loperamide ) and hypokalaemia
- glucose malabsorption, indicated by marked increase in stool output and large amount of glucose in the stool when ORS solution is given (uncommon)

## Intravenous therapy

Calculation of required therapy is as follows:

### 1. Fluid deficit

- fluid deficit (mls) = percentage dehydration X body weight in grams

### 2. Maintenance fluid therapy

- type of fluid solution:  
1/5 normal saline 5% dextrose solution or 1/2 normal saline 5% dextrose with or without added KCl in the drip.
- volume of fluid required:
  - less than 6 months age: 150 ml/kg/day
  - 6 months to 1 year age: 120 ml/kg/day
  - more than 1 year age: 1st 10 kg = 100 ml/kg  
10-20 kg = 1000 ml for first 10 kg  
+ 50 ml/kg for next 10 subsequent kg  
>20 kg = 1500 ml for first 20kg  
+ 20 ml/kg for any subsequent kg

### 3. Treating metabolic acidosis

- metabolic acidosis usually self corrects with rehydration
- correction only required if pH < 7.1
- formula for calculation of sodium bicarbonate correction:  
 $\text{IV } 8.4\% \text{ NaHCO}_3 \text{ (mEq or ml)} = \frac{1}{3} \times \text{base deficit} \times \text{weight};$   
usually only *half* this volume (1/2 correction) is given
- review with a repeat blood gas

### 4. Electrolyte requirement and replacement formulae

- normal daily requirement of K<sup>+</sup> (potassium) = 2-3 mmol/kg/day x body weight (kg)
- normal daily requirement of Na<sup>+</sup> (sodium) = 2-3 mmol/kg/day x body weight (kg)
- sodium deficit (mmol) = (140 - patient's serum Na level x 0.6 x wt (kg))

## Indications for admission to Hospital

- need for intravenous therapy (as above)
- concern for other possible illness or uncertainty of diagnosis
- patient factors, e.g. young age, unusual irritability/drowsiness, worsening symptoms
- caregivers not able to provide adequate care at home
- social or logistical concerns that may prevent return evaluation if necessary

## Electrolyte disorders

Knowing the levels of serum electrolytes often does not change the management of children with diarrhoea. The disorders described below can often be adequately treated by using ORS solution.

### 1. Hypernatraemia (serum sodium $> 150$ mmol/l)

- clinical presentation is notoriously deceptive
  - shock is late and ominous sign
  - skin has a characteristic doughy feel
  - anterior fontanelle may not be sunken
- Treatment :
  - a. Resuscitation
    - if in shock, give normal saline/Ringer's lactate 20ml/kg intravenously over ½ to 1 hour and repeat as necessary till perfusion improves
  - b. Rehydration
    - reduce serum sodium slowly - dramatic fall results in cerebral oedema, seizures.
    - calculate the fluid deficit and give together with maintenance fluid over at least 48 to 72 hours. If fluid has been given to resuscitate, the amount given should be subtracted from the fluid deficit. This is particularly important in hypernatraemic dehydration to avoid giving too much fluid.
    - reduction in serum sodium should not exceed 10 mmol/L per 24 hours
    - oral rehydration is the method of choice and the safest. Only if this fails is slow IV rehydration necessary.
    - use normal saline 5% dextrose for the duration of the fluid replacement, continue using this fluid until serum sodium is  $< 145$  mmol/l. Then use 1/2 normal saline 5% dextrose or 1/5 normal saline 5% dextrose solution.
    - add KCL when child passes urine and review blood urea and serum electrolytes
    - monitor blood urea serum electrolytes 6 hourly

### 2. Hyponatraemia (serum sodium $< 130$ mmol/l)

- ORS solution is safe and effective therapy for nearly all children with hyponatraemia.

### 3. Hypokalaemia (serum potassium $< 3$ mmol/l)

- hypokalaemia can be prevented, and the potassium deficit corrected, by using ORS solution for rehydration therapy and by giving food rich in potassium during diarrhoea and after it has stopped.

## Acute bloody diarrhoea (Dysentery)

- assess for dehydration and treat accordingly
- consider antimicrobial\* treatment:  
Trimethoprim (TMP) 5 mg/kg /sulfamethoxazole(SMX) 25 mg/kg BD for 5 days  
or  
Ampicillin 25 mg/kg 4 QID for 5 days

*\*check for sensitivities of local strains*



## Other problems associated with diarrhoea

### 1. Fever

- may be due to *another infection or dehydration*
- always search for the source of infection if there is fever, especially if it persists after the child is rehydrated

### 2. Convulsions

- consider:
  - febrile convulsion (assess for possible meningitis)
  - hypoglycaemia
  - hyper – or hyponatraemia

### 3. Lactose intolerance

- usually in formula-fed babies less than 6 months old with infectious diarrhoea
- clinical features:
  - persistent loose/watery stool
  - abdominal distension
  - increased flatus
  - perianal excoriation
- making the diagnosis: compatible history; check stool for reducing sugar
- treatment: If diarrhoea is persistent and watery (over 7-10 days) and there is evidence of lactose intolerance, a lactose free formula may be given. Normal formula can usually be reintroduced after 2–3 weeks

## Pharmacological Agents

### • antimicrobials

Antibiotics should not be used routinely. They are reliably helpful only in children with bloody diarrhoea, probable shigellosis, and suspected cholera with severe dehydration.

### • antidiarrhoeal and anti emetic drugs

Antidiarrhoeal drugs and anti emetics should not be given to young children with diarrhoea or dysentery. They do not prevent dehydration and some have dangerous, sometimes fatal side effects.

### • probiotics

*Lactobacillus* containing compounds are not recommended in the treatment of acute diarrhoea in children. Based on limited scientific evidence, efficacy has not been shown, although toxic effects are not a concern.

### • zinc supplements

It has been shown that zinc supplements during an episode of diarrhoea reduce the duration and severity of the episode and lower the incidence of diarrhoea in the following 2-3 months. WHO recommends zinc supplements as soon as possible after diarrhoea has started. Dose up to 6 months of age is 10 mg/day, and age 6 months and above 20mg/day, for 10-14 days.

## RESUSCITATION PROTOCOL FOR CHILDREN WITH SEVERE MALNUTRITION

This guideline is intended for orang asli and indigenous children who present to District Hospitals and Health Centres with a history of being unwell with fever, diarrhoea, vomiting and poor feeding.

*This protocol is not to be used for a child who does not have malnutrition.*

This guideline is recommended only for those who fulfill the following criteria:

- orang asli or other indigenous ethnic group
- severe malnutrition
- ill
- lethargic or has lost consciousness
- shock

### Initial assessment

- weigh the child (or estimate)
- measure temperature, pulse rate, BP and respiratory rate
- give oxygen
- insert intravenous or intraosseous line
- draw blood for investigations where possible (Blood sugar, FBC, BUSE, Blood culture, BFMP, ABG)



### Resuscitation for shock

- give IV/IO fluid 15ml/kg over 1 hour
- solutions used -1/2NS, Hartmans if 1/2NS not available
- use 1/2NSD5% if hypoglycaemic



### Monitor and stabilise

- measure pulse and breathing rate every 5-10 minutes
- Start antibiotic IV cefotaxime or ceftriaxone (if not available ampicillin+ chloramphenicol)
- monitor blood sugar and prevent hypothermia
- IV Quinine only after discussion with Paediatrician



### If there are signs of improvements (pulse and breathing rates are falling)

- repeat IV/IO bolus 15ml/kg over 1 hour
- initiate ORS (or ReSoMal) per oral 10ml/kg/h
- discuss case with Paediatrician and refer

### If the child deteriorates

- (breathing up by 5 breaths/min or pulse up by 25 beats/min or fails to improve during IV/IO fluid)
- stop infusion as this can worsen child's condition
  - discuss case with Paediatrician immediately and refer

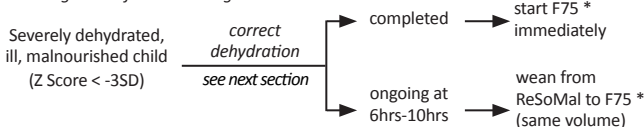
### Reference

1. Management of the child with a serious infection or severe malnutrition (IMCI). Unicef WHO 2000

## RE-FEEDING SEVERELY MALNOURISHED CHILDREN

This protocol is based on the protocol for Management of the child with a serious infection or severe malnutrition (IMCI), Unicef WHO 2000.

Figure 1. Algorithm for Re-Feeding Plan



### Starter feed with F75 based on IMCI protocol

- feeds at 75-100kcal/kg/day (< 100kcal/kg/day in the initial phase)
- protein at 1-1.5 g/kg/day
- total volume 130mls/kg/day (if severe oedema, reduce to 100mls/kg/day)

### How to increase feeds?

- increase F75 gradually in volume, e.g. 10 ml/kg/day in first 3-4 days
- gradual decrease in feeding frequency – 2, then 3 and 4 hourly when improves
- calculate calorie and protein content daily
- consider F100 catch up formula when
  - calories 130/kCal/kg/day-140kCal/kg/day
  - child can tolerate orally well and gaining weight, without signs of heart failure

#### Note:

1. In a severely oedematous child this process might take about a week.
2. If you do not increase calories and proteins the child is not going to gain weight and ward stay will be prolonged.

### Monitoring

- **Avoid causing heart failure**
  - suspect if: sustained increase (> 2 hrs) of respiratory rate increases by 5/min, and / or heart rate by 25/min from baseline
  - if present: reduce feed to 100ml/kg/day for 24 hr then slowly increase as follows:
    - 115ml/kg/day for next 24 hrs; then 130ml/kg/day for next 48 hrs
    - then increase each day by 10 mls
- **Ensure adequate weight gain**
  - weigh child every morning before feeds; ideal weight gain is > 10g/kg/day
    - if poor weight gain < 5g/kg/day do a full reassessment
    - if moderate weight gain (5-10g/kg/day) check intake or check for infection
- **Watch for secondary infection**

### Introducing Catch up Growth formula (F100)

- gradual transition from F75 to F100 (usually over 48-72 hrs)
- increase successive feed by 10mls till some feeds remains uneaten
- modified porridge or complementary food can be used, provided they have comparable energy and protein levels
- gradually wean to normal diet, unlimited frequent feeds, 150-220 kCal/kg/day
- offer protein at 4-6 g/kg/day
- continue breast feeding if child is breastfed

*Note: If child refuses F75/F100 and is too vigorous for forced RT feeding, then give normal diet. However must calculate calories and protein (as above).*

## Discharge criteria

- not oedematous
- afebrile
- aged  $\geq 12$  mths (caution  $< 12$  mths - specialist opinion required before discharge)
- gaining weight well
- has completed antibiotics

*In situation where patient need to be transferred to district facilities make sure:*

- provide a clear plan on how to feed and how to monitor progress
- provide a dietary plan with adequate calorie and protein requirements
- a follow up appointment with a Paediatrician

**Table 1. Recipes for starter and catch-up formulas**

	<b>F-75</b> (starter)	<b>F-100</b> (catch-up)	<b>F-135</b> (catch-up)
Dried skimmed milk (g)*	25	80	90
Sugar (g)	100	50	65
Vegetable oil (g)	30 (or 35 ml)	60 (or 70 ml)	85 (or 95 ml)
Electrolyte/mineral solution (ml)	20	20	20
Water: make up to	1000 ml	1000 ml	1000 ml

## Contents per 100 ml

Energy (kcal)	75	100	135
Protein (g)	0.9	2.9	3.3
Lactose (g)	1.3	4.2	4.8
Potassium (mmol)	4.0	6.3	7.7
Sodium (mmol)	0.6	1.9	2.2
Magnesium (mmol)	0.43	0.73	0.8
Zinc (mg)	2.0	2.3	3.0
Copper (mg)	0.25	0.25	0.34
% energy from protein	5	12	10
% energy from fat	36	53	57
Osmolarity (mOsmol/L)	413	419	508

## Preparation

- using an electric blender: place some of the warm boiled water in the blender, add the milk powder, sugar, oil and electrolyte/mineral solution. Make up to 1000 ml, and blend at high speed
- if no blender is available, mix milk, sugar, oil and electrolyte/mineral solution to a paste, and then slowly add the rest of the warm boiled water and whisk vigorously with a manual whisk
- store made-up formula in refrigerator

*\*Alternative recipes: (other milk sources)*

### F-75 starter formulas (make up to 100 ml)

- full-cream dried milk 35 g, 100 g sugar, 20 g (or ml) oil, 20 ml electrolyte/mineral solution
- full-cream milk (fresh/long life) 300 ml, 100 g sugar, 20 g (or ml) oil, 20 ml electrolyte/mineral solution

### F-100 catch-up formulas (make up to 100 ml)

- full-cream dried milk 110 g, 50 g sugar, 30 g (or ml) oil, 20 ml electrolyte/mineral solution
- full-cream milk (fresh / long life) 880 ml, 75 g sugar, 20 g (or ml) oil, 20 ml electrolyte/mineral solution

**Table 2. WHO electrolyte/mineral solution recipe**

item	quantity (gm)	molar content (in 20 ml)	Note: if available:
potassium chloride: KCl	224	20 mmol	add <b>selenium</b>
tripotassium citrate: $C_6H_5K_3O_7 \cdot H_2O$	81	2 mmol	(sodium selenate
magnesium chloride: $MgCl_2 \cdot 6H_2O$	76	3 mmol	0.028 g),
zinc acetate: $Zn(CH_3COO)_2 \cdot 2H_2O$	8.2	300 $\mu$ mol	and <b>iodine</b>
copper sulphate: $CuSO_4 \cdot 5H_2O$	1.4	45 $\mu$ mol	(potassium iodide
water	to make up 25000 ml		0.012g) per 2500ml

## APPROACH TO A CHILD WITH GASTROINTESTINAL BLEEDING

### Definitions

- *haemetemesis* - vomiting out blood whether fresh or stale
- *malaena* - passing out tarry black stools per rectum

Both are medical emergencies that carry significant mortality

### Salient features

- duration and severity of haemetemesis and/or malaena
- evidence of hypovolaemic shock
- rule out bleeding diathesis

Figure 1. Acute resuscitation in a child with gastrointestinal bleeding

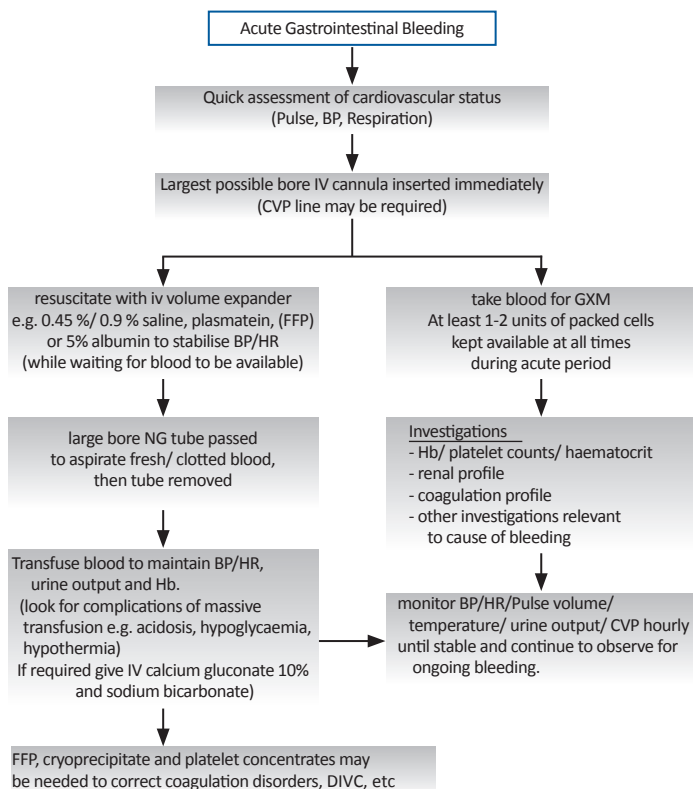


Table 1. Decision making after acute resuscitation

Reassessment of patients	Diagnostic measures to localise source of bleeding
<ul style="list-style-type: none"> <li>When patient's condition is stable and resuscitative measures have been instituted, <b>assess patient for</b> <ul style="list-style-type: none"> <li>cause of bleeding</li> <li>need for surgery</li> </ul> </li> <li><b>History is reviewed.</b> Ask for history of chronic liver disease, dyspepsia, chronic or intermittent gastrointestinal bleeding (e.g. polyps), drug ingestion (anticoagulants, aspirin), or acute fever (dengue haemorrhagic fever), easy bleeding tendencies, etc.</li> <li><b>Physical exam</b> should be directed towards looking for signs of chronic liver disease (spider angiomas, palmar erythema, portal hypertension or splenomegaly) or telangiectasia / angiomas in mouth, trunk, etc.)</li> </ul>	<ul style="list-style-type: none"> <li><b>Oesophagogaastro-duodenoscopy (OGDS) or colonoscopy</b> can be performed when patient's condition is stable.</li> <li><b>Double contrast barium study</b> less useful than endoscopy but may be indicated in patients when endoscopy cannot precisely locate the source of bleeding (e.g. in intussusception)</li> <li><b>Visceral angiography</b> can precisely locate the source of bleeding. But is only reserved for patients with a difficult bleeding problem.</li> </ul>

Table 2. Definitive measures to management of gastrointestinal bleeding

Medical Cause	Surgical Cause
<b>Bleeding peptic ulcer</b> <ul style="list-style-type: none"> <li>start H2 receptor antagonist (e.g. cimetidine or ranitidine)</li> <li>if biopsy shows presence of <i>Helicobacter pylori</i> infection, treat accordingly.</li> <li>stop all incriminating drugs e.g. aspirin, steroids and anticoagulant drugs, if possible</li> </ul> <b>Bleeding oesophageal varices ulcer</b> <ul style="list-style-type: none"> <li>do not transfuse blood too rapidly as this will lead to increase in CVP and a rapid increase in portal pressure will precipitate further bleeding.</li> <li>refer paediatric surgeon and paediatric gastroenterologist to consider use of octreotide.</li> </ul> <b>Pseudomembranous colitis</b> <ul style="list-style-type: none"> <li>stop all antibiotics</li> <li>start oral metronidazole or</li> <li>oral vancomycin immediately.</li> </ul>	<p>When surgical cause is suspected, early referral to the surgeon is important so that a team approach to the problem can be adopted.</p> <ul style="list-style-type: none"> <li>intussusception requires immediate surgical referral and intervention.</li> <li>Meckel's diverticulum</li> <li>malrotation</li> </ul>

## ACUTE HEPATIC FAILURE IN CHILDREN

### Definitions

- **Fulminant hepatic failure (HF)** - hepatic dysfunction (hepatic encephalopathy and coagulopathy) within 8 weeks of evidence of symptoms of liver disease and absence of pre-existing liver disease in any form.
- **Hyperacute/ Fulminant HF** - encephalopathy within 2 weeks of onset of jaundice
- **Subfulminant HF** - encephalopathy within 2-12 weeks of onset of jaundice
- **Subacute/ Late-onset HF** - encephalopathy later than 8 weeks to 6 months of onset of symptoms.

### Salient features

- jaundice with impalpable liver or a liver of reducing size
- encephalopathy - may worsen rapidly (needs frequent review)
- bruising, petechiae or bleeding from deranged clotting unresponsive to vitamin K.
- failure to maintain normoglycaemia (which aggravates encephalopathy) or presence of hyperammonaemia
- increased intracranial pressure (fixed dilated pupils, bradycardia, hypertension and papilloedema)

Table 1. Grading of hepatic encephalopathy

Grading of Coma level	
<b>Grade 1</b>	irritable, lethargic
<b>Grade 2</b>	mood swings, aggressive, photophobia, not recognising parents, flap
<b>Grade 3</b>	sleepy but rousable, incoherent, sluggish pupils, hypertonia ± clonus, extensor spasm
<b>Grade 4</b>	comatose; decerebrate, decorticate or no response to pain

### Principles of management

#### Supportive Treatment

- nurse in quiet darkened room with head-end elevated at 20° with
- no neck flexion (to decrease ICP and minimise cerebral irritability).
- DO NOT SEDATE unless already ventilated
  - this may precipitate respiratory failure and death.
- maintain blood glucose between 6-9 mmol/l using *minimal fluid volume* (40-60 ml/kg/day crystalloid) with high dextrose concentrations e.g. 10-20%. Add Potassium as necessary.
- check dextrostix 2 - 4 hourly.
- strict monitoring of urine output and fluid balance. Catheterise if necessary.
- check urinary electrolytes, serum urea, creatinine, electrolytes and osmolarity.
- frequent neurological observations (1-4 hourly).
- maintain oxygenation with facial oxygen.
- give vitamin K to attempt to correct prolonged PT. If frank bleeding (GIT/oral) occurs, consider prudent use of FFP or IV cryoprecipitate at 10 ml/kg.
- prophylactic ranitidine plus oral antacid to prevent gastric, duodenal ulceration.
- full septic screen (excluding LP) on admission, CXR. Treat sepsis aggressively, monitoring levels of aminoglycosides frequently.
- stop oral protein initially. Gradually reintroduce 0.5-1g/kg/day.
- lactulose to produce 3-4 loose stools per day.
- **\*strict fluid balance is essential** - aim for urine output < than 0.5 ml/kg/hour.
- consider N-acetylcysteine.

**Clinical Pearls In a comatose patient:**

- in the presence of *sudden coma*, consider intracranial bleed  
- request a CT Brain.
- patients in Grade 3 or 4 coma require mechanical ventilation to maintain normal cerebral perfusion pressure.

**Table 2. Causes of hepatic failure****Infection**

hepatitis A, B, non A- non B, CMV,  
leptospirosis, Dengue

**Drugs**

carbamazepine, valproate,  
paracetamol, halothane

**Ingested toxins**

mushrooms, *Amanita phalloides*

**Metabolic**

fructosaemia, galactosaemia, tyrosaemia,  
Wilson's disease

**Ischaemic shock**

gram negative septicaemia,  
Budd Chiari syndrome

**Tumour**

histiocytosis, lymphoproliferative disorder

**Table 3. Fluid management in liver failure**

	Normal Liver Function	Liver failure
Volume given if no dehydration and losses are not abnormal		
Body Weight		
< 10 kg	120-150 ml/kg/day	60-80 ml/kg/day
10-20 kg	90-120 ml/kg/day	40-60 ml/kg/day
> 20 kg	50-90 ml/kg/day	30-50 ml/kg/day
Fluid type	Dextrose 4 – 5 %	Dextrose ≥ 10% (adjust according to Dextrostix readings)
Potassium	1 - 3.5 mmol/kg/day	NIL WHILE ANURIC
Sodium	1.5 - 3.5 mmol/kg/day	NIL ADDED
Other Fluids	Albumin 20% 5 ml/kg	Albumin 20% 5 ml/kg
For transfusion	FFP 10-20 ml/kg	FFP 10-20 ml/kg
Blood volume (ml) = No. of grams to raise Hb by x body weight in kg x F Where F = 6 for whole blood, F = 4 for packed cells		





# INFECTIOUS DISEASE

**74** Sepsis / Septic Shock

**75** Paediatric HIV

**76** Malaria

**77** Tuberculosis

**78** BCG Lymphadenitis

**79** Dengue Fever



# SEPSIS, SEPTIC SHOCK

## Definitions

Table 1. Definitions of sepsis and shock

<b>SIRS</b> (Systemic Inflammatory Response Syndrome)	non-specific systemic inflammatory response to infection, trauma, burns, surgery etc. Characterized by abnormalities in 2 or more of the following [one of which must be abnormal temperature or leukocyte count]: <ul style="list-style-type: none"> <li>• body temperature</li> <li>• heart rate</li> <li>• respiratory function</li> <li>• peripheral leucocyte count</li> </ul>
<b>Sepsis</b>	SIRS in the presence of or as a result of suspected or proven infection.
<b>Severe sepsis</b>	Sepsis plus one of the following <ul style="list-style-type: none"> <li>• cardiovascular organ dysfunction</li> <li>• acute respiratory distress syndrome</li> <li>• two or more other organ dysfunction</li> </ul>
<b>Septic shock</b>	Severe sepsis with cardiovascular organ dysfunction i.e. hypotension (systolic blood pressure [SBP] < 5th centile for age).
<b>Early septic shock</b> (WARM shock)	Compensated warm phase of shock. Prompt response to fluids and pharmacologic treatment.
<b>Refractory septic shock</b> (COLD shock)	Late decompensated phase. Shock lasting more than 1 hour despite vigorous therapy necessitating vasopressor support.

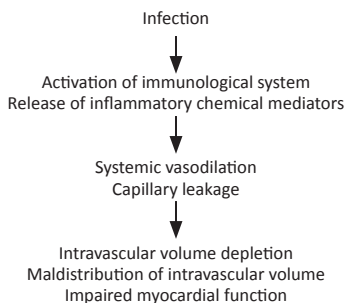
(based on the International Pediatric Sepsis Consensus Conference)

## Incidence

Non hospitalized immunocompetent children may develop community acquired sepsis. More commonly, hospitalized immunocompromised patients are at higher risk of developing serious nosocomial sepsis.

## Pathophysiology

Figure 1. Pathophysiology



## Clinical features

Sepsis, severe sepsis and septic shock are a clinical continuum.

- SEPSIS is present when 2 or more of the following features are present
    - fever ( $> 38.5^{\circ}\text{C}$ ) or hypothermia, often in neonate ( $< 36^{\circ}\text{C}$ )
    - hyperventilation
    - tachycardia
    - white blood count abnormalities: leukocytosis or leucopenia
- AND there is clinical evidence of infection.

Other constitutional symptoms such as poor feeding, diarrhea, vomiting, lethargy may be present.

- with progression to SEVERE SEPSIS, there are features of compromised end organ perfusion such as

Table 2. Features of compromised end organ perfusion

Neurology	altered sensorium, irritability, agitation, confusion, unresponsiveness or coma
Respiratory	tachypnoea, increase breathing effort, apnoea / respiratory arrest, cyanosis (late sign)
Renal	oliguria less than 0.5ml/kg per hour

- when SEPTIC SHOCK sets in, look for features of *warm* or *cold* shock (Table 3)

Table 3. Features of warm and cold shock

	WARM shock	COLD shock
Peripheries	warm, flushed	cold, clammy, cyanotic
Capillary refill	$< 2$ sec	$> 2$ sec
Pulse	bounding	weak, feeble
Heart rate	tachycardia	tachycardia or bradycardia
Blood pressure	relatively maintained	hypotension
Pulse pressure	widened	narrowed

Look out for localizing signs - most useful but not always present (Table 4)

Table 4. Localising signs

<b>Central nervous system</b> meningism, encephalopathy	<b>Bone and soft tissue</b> focal erythema, tenderness and oedema
<b>Respiratory</b> localized crepitations, evidence of consolidation	<b>Head and neck</b> cervical lymphadenopathy, sinus tenderness, inflamed tympanic membrane, stridor, exudative pharyngotonsillitis
<b>Cardiovascular</b> changing murmurs	<b>Skin</b> pustular lesions
<b>Gastrointestinal</b> focal or rebound tenderness, guarding	

## Complications

Multiorgan Failure:

- acute respiratory distress syndrome
- acute renal failure
- disseminated intravascular coagulopathy
- central nervous system dysfunction
- hepatic failure

## Investigations

As in Table 5.

Table 5. Investigations

Septic work - up	Monitoring severity and progress
blood C&S	full blood count
urine C&S	renal profile
Where appropriate	electrolytes, calcium, magnesium
CSF C&S	blood sugar
tracheal aspirate C&S	blood gases
pus / exudate C&S	+/- lactate levels
fungal cultures	coagulation profile
serology, viral studies	liver function test
imaging studies	
e.g. Chest X-ray	
ultrasound, CT scan	

### Supporting evidence of infection:

#### Full blood count

leukocytosis or leukopenia

#### Peripheral blood film

increase in immature neutrophil count

#### C-reactive protein

elevated c-reactive protein levels

Abbreviation. C&S, culture and sensitivity

## Management

### • Initial resuscitation - ABC

- Secure airway, Support breathing, Restore circulation

*Caution: the use of sedation in septic or hypotensive children may result in crash of blood pressure. If sedation is required, use low dose IV Midazolam or Ketamine, volume infusion should be continued and inotropes should be initiated, if time permits.*

### • Fluid therapy

- aggressive fluid resuscitation with crystalloids or colloids at 20 mls/kg as rapid IV push over 5-10 mins. Can be repeated up to 60 mls/kg or more.
- correct hypoglycaemia and hypocalcaemia

### • Inotropic Support

- if fluid refractory shock\*, establish central venous access  
Start inotropes — IV Dopamine 5 - 15 µg/kg/min *or*  
IV Dobutamine 5 - 15 µg/kg/min
- for fluid refractory and dopamine/dobutamine refractory shock with
  - warm shock : titrate IV Noradrenaline 0.05 – 2.0 µg/kg /min
  - cold shock : titrate IV Adrenaline 0.05 – 2.0 µg/kg /min
- the aim of titration of inotropes include normal clinical endpoints and where available,  $S_{cVO_2} > 70\%$ .
- inotropes should be infused via a central line (whenever possible) or a large bore peripheral canula.
- use dedicated line or lumen. Avoid concurrent use for other IV fluids, medication.
- fluids and inotropes to be titrated to optimal vital signs, urine output and conscious level.

\*hypotension, abnormal capillary refill or extremity coolness

- **Antimicrobial therapy**
  - IV antibiotics should be administered immediately after appropriate cultures are taken. Start empirical, broad spectrum to cover all likely pathogens, considering
    - risk factors of patient and underlying illness
    - local organism prevalence and sensitivity patterns
    - protocols of the institution
  - antibiotic regime to be modified accordingly once C&S results are back.
  - source control:
    - evaluate patient to identify focus of infection
    - drainage, debridement or removal of infected devices to help control infection

- **Respiratory Support**

- use PEEP and FIO<sub>2</sub> to keep SaO<sub>2</sub> > 90%, PaO<sub>2</sub> > 80 mmHg

Caution: use sufficient PEEP to ensure alveolar recruitment in cases of sepsis with acute lung injury. Too high PEEP can result in raised intrathoracic pressure which can compromise venous return and worsen hypotension.

- **Supportive Therapy**

- packed cells transfusion if Hb < 10g%
- platelet concentrate transfusion if platelet count < 20 000
- if overt clinical bleeding, correct coagulopathy or DIVC
- bicarbonate therapy: give bicarbonate only in refractory metabolic acidosis, if pH < 7.1 (ensure adequate tissue perfusion and ventilation to clear by-product CO<sub>2</sub>)
- aim to maintain normal electrolytes and blood sugar

- **Monitoring**

- frequent serial reevaluation is essential to guide therapy and gauge response, as in Table 6.

Table 6. Monitoring in children with sepsis

Clinical	Laboratory
<i>Vital signs</i>	<i>As outlined in Table 5</i>
heart rate via cardiac monitor	
capillary return	
skin temperature	
pulse volume	
blood pressure	
- non invasive	
- invasive – ideal if available	
SpO <sub>2</sub> via pulse oximeter	
central venous pressure (CVP)	
Urine output via continuous bladder drainage	
Head chart (GCS)	

## Screening of children for HIV status

In newborns and in children, the following groups need to be tested:

- babies of HIV positive mothers
- abandoned babies / street children
- babies of mothers with high risk behaviour (e.g. drug addicts / prostitutes / multiple sex partners / single-teenage or underage)
- sexually abused children and children with sexually transmitted disease
- children receiving regular blood transfusions or blood products e.g. Thalasseemics

## Deliveries and infant nursing

- standard precautions must be observed at all times. It is vital to use protective barriers such as arm length gloves, mask, goggles and gown with waterproof sleeves. Boots are to be used for institutional deliveries:
  - during deliveries.
  - during handling of placenta tissue
  - during handling of babies such as wiping liquor off babies
  - all equipment, including resuscitation equipment should be cleaned and sterilised
- for home deliveries, battery operated suction device should be used
- standard precautions are to be observed in caring for the babies
- for parents or relatives, gloves are given for use when handling the placenta after discharge, or during burial of stillbirth or dead babies at home. The placenta from HIV positive mothers should be soaked in formalin solution before disposal. Alternatively, the placenta can be sealed in a plastic bag or other leakproof container with clear instructions to parents not to remove it from the container.

## Immunisation

- vaccines protect HIV-infected children from getting severe vaccine-preventable diseases, and generally well tolerated.
- all routine vaccinations can be given according to schedule, with special precautions for live vaccines i.e. BCG, OPV and MMR:
  - BCG: safe in child is asymptomatic and not immunosuppressed (e.g. at birth); omit if symptomatic or immunosuppressed
  - OPV: safe; small theoretical risk of transmission to other immunocompromised family members. Preferably give IPV (killed polio vaccine) if available.
  - MMR: safe; omit in children with severe immunosuppression ( $CD4 < 15\%$ )
- other recommended vaccines:
  - *pneumococcal polysaccharide vaccine* when  $> 2$  years of age; booster 3-5 years later. Where available, use Pneumococcal conjugate vaccine (more immunogenic)
  - *varicella-zoster vaccine*, where available. 2 doses with 2 months interval. omit in those with severe immunosuppression ( $CD4 < 15\%$ )

*Despite vaccination, remember that long term protection may not be achieved in severe immune suppression i.e. they may still be at risk of acquiring the infections!*



## Interventions to limit perinatal transmission

Vertical transmission of HIV may occur while in utero, during the birth process or through breast-feeding. The rates vary from 25 - 30%.

Breastfeeding confers an additional 14% risk of transmission, and is therefore contraindicated.

The risk of transmission of HIV infection from blood transfusion is very small, though not absent, and thus blood and blood products should be used judiciously.

Several interventions have proven effective in reducing vertical transmission:

- total substitution of breastfeeding with infant formula
- elective Caesarean section
- antiretroviral (ARV) prophylaxis

## Management of Babies Born to HIV Infected Mothers

Children born to HIV positive mothers are usually asymptomatic at birth. However, all will have acquired maternal antibodies. In uninfected children, antibody testing becomes negative by 10 - 18 months age.

### During pregnancy

- counsel mother regarding:
  - transmission rate (without intervention) –25 to 30%
  - ARV prophylaxis reduces transmission to 8%
  - elective LSCS + ARV prophylaxis reduces transmission to ~ 3%
- to feed with infant formula as breast feeding doubles the risk of transmission
- difficulty in making early diagnosis because of presence of maternal antibody in babies. Stress importance of regular blood tests and follow-up.

### Neonatal period

- admit to ward or early review by paediatric team (if not admitted).
- examine baby for
  - evidence of other congenital infections
  - symptoms of drug withdrawal (reviewing maternal history would be helpful)
- most babies are asymptomatic and only require routine perinatal care
- start on prophylaxis ARV as soon as possible (see Figure 1)
- sample blood for:
  - HIV DNA PCR (done in IMR, do not use cord blood; sensitivity 90% by 1 month age)
  - FBC
  - Other tests as indicated:
    - LFT, RFT, HbsAg, Hepatitis C, Toxoplasmosis, CMV, VDRL serology

Table 1. Factors associated with higher transmission rate

#### Maternal

low CD 4 counts  
high viral load  
advanced disease  
seroconversion during pregnancy

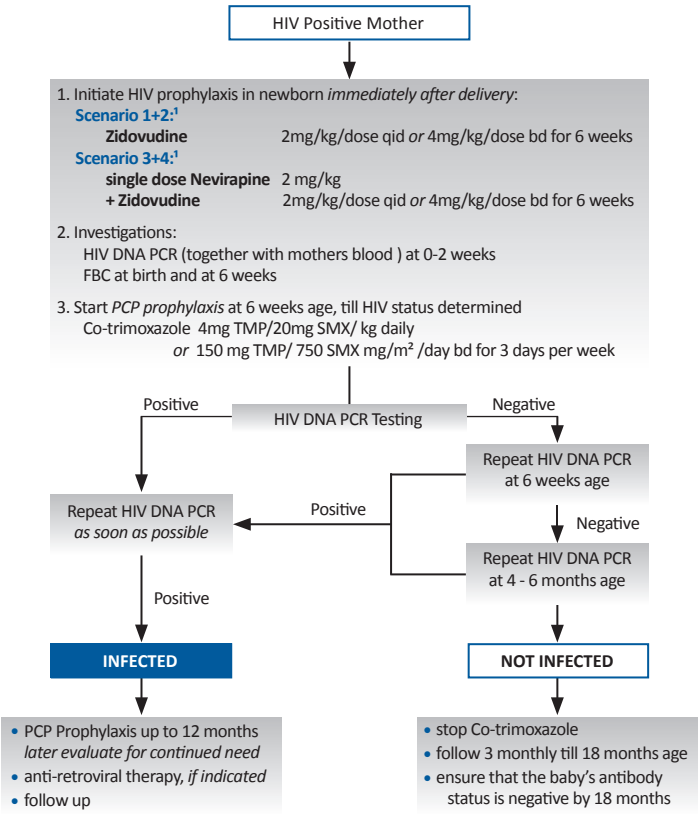
#### Foetal

premature delivery of the baby

#### Delivery and procedures

invasive procedures such as episiotomy  
foetal scalp electrodes  
foetal blood sampling and amniocentesis  
vaginal delivery  
rupture of membranes > 4 hours  
chorioamnionitis

Figure 1. Management of HIV exposed infants (from Malaysian CPG Guidelines 2008)



<sup>1</sup> foot note:

Scenario 1: HIV - infected mother who is already on HAART

Scenario 2: HIV - infected mother who has been started on Zidovudine at 14-28 weeks gestation

Scenario 3: HIV - infected mother at delivery who has received inadequate ARV (< 4 weeks)

Scenario 4: Infant born to HIV - infected mother who has not received any ARV

Abbreviations:

ARV, antiretroviral prophylaxis; HAART, highly active antiretroviral therapy;

PCP, pneumocystis carinii pneumonia.

Management of HIV in Children

Clinical Features

Common presenting features are:

- persistent lymphadenopathy
- failure to thrive
- recurrent infections (respiratory, skin, gastrointestinal)
- hepatosplenomegaly
- developmental delay, regression

Diagnosis of HIV infection

- in children > 18 months age: 2 consecutive positive HIV antibody tests.
- in children < 18 months age: 2 positive HIV DNA PCR tests.

Monitoring

- monitor disease progression through clinical, immunological (CD4+ count or %) and viral load status. Viral load assay is available in regional centres.
- CD4+ count and viral load assay are done at diagnosis, 2-3 months after initiation or change of ART and every 3-4 months thereafter (more frequently if change of therapy is made or progression of disease occurs).

Antiretroviral Therapy

Clinical outcome following the use of highly active antiretroviral therapy (HAART) in children is excellent, with reduced mortality (67 - 80%) reported from various cohorts. However, this needs to be balanced with: failure of current drugs to eradicate infection, medication side effects and compliance-adherence issues.

When to start?

- before starting ART, intensive education to parents, care-givers and older children-patients need to be stressed. Do not start in haste as we may repent at leisure! Assess family's capacity to comply with often difficult and rigid regimens. Stress that non-adherence to medications allows continuous viral replication and encourages the emergence of drug resistance and subsequent treatment failure.
- young infants have a much higher risk of disease progression to clinical AIDS or death when compared to older children or adults and hence the treatment recommendations are more aggressive. Recommendation for when to start ARV is shown in Table 6.
- please consult a specialist/consultant before starting treatment.

Table 2. Goals of therapy

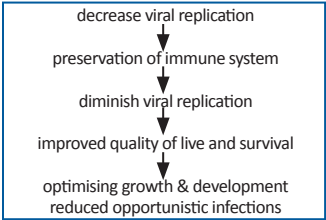


Table 3. WHO classification of HIV-associated immunodeficiency using CD4 count

Classification of HIV-associated Immunodeficiency	Age-related CD4 values			
	<11 months (CD4 %)	12–35 months (CD4 %)	36–59 months (CD4 %)	≥5 years (cells/mm <sup>3</sup> or CD4 %)
Not significant	>35	>30	>25	>500
Mild	30–35	25–30	20–25	350–499
Advanced	25–29	20–24	15–19	200–349
Severe	<25	<20	<15	<200 or <15%

## Clinical categories

There are 2 widely used clinical classification systems: CDC's 1994 Revised Paediatric Classification and the WHO Clinical Classification system. Both classification systems are similar with only minor differences

**Table 4. WHO Clinical Staging Of HIV for Infants and Children With Established HIV infection (Adapted from WHO 2006)**

<b>Clinical Stage 1 (Asymptomatic)</b> asymptomatic persistent generalized lymphadenopathy	<b>Clinical stage 4 (Severe) *</b> unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy pneumocystis pneumonia recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) chronic herpes simplex infection (orolabial or cutaneous of > 1 month's duration, or visceral at any site) extra pulmonary TB Kaposi sarcoma oesophageal candidiasis (or Candida of trachea, bronchi or lungs) central nervous system toxoplasmosis (after the neonatal period) HIV encephalopathy cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, onset age > 1 month extra pulmonary cryptococcosis (including meningitis) disseminated endemic mycosis (extra pulmonary histoplasmosis, coccidiomycosis) chronic cryptosporidiosis (with diarrhoea) chronic isosporiasis disseminated non-tuberculous mycobacteria infection cerebral or B cell non-Hodgkin lymphoma progressive multifocal leukoencephalopathy HIV-associated cardiomyopathy or nephropathy
<b>Clinical stage 2 (Mild) *</b> unexplained persistent hepatosplenomegaly papular pruritic eruptions extensive wart virus infection extensive molluscum contagiosum recurrent oral ulcerations unexplained persistent parotid enlargement lineal gingival erythema herpes zoster recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) fungal nail infections	
<b>Clinical stage 3 (Advanced) *</b> unexplained moderate malnutrition not adequately responding to standard therapy unexplained persistent diarrhoea (> 14 days) unexplained persistent fever (above 37.5 °C, intermittent or constant, > 1 month) persistent oral candidiasis (> 6 weeks of life) oral hairy leukoplakia acute necrotizing ulcerative gingivitis, periodontitis lymph node TB pulmonary TB severe recurrent bacterial pneumonia symptomatic lymphoid interstitial pneumonitis chronic HIV-associated lung disease including bronchiectasis unexplained anaemia (<8.0 g/dl), neutropenia (<0.5 x 10 <sup>9</sup> /L) or chronic thrombocytopenia (<50 x 10 <sup>9</sup> /L)	footnote: (*) <i>Unexplained refers to where the condition is not explained by other causes.</i>

**Table 5. Main categories of antiretroviral drugs available in Malaysia**

Nucleoside reverse transcriptase inhibitors (NRTI)	Non nucleoside reverse transcriptase inhibitor (NNRTI)	Protease inhibitors (PI)
Zidovudine (ZDV)	Nevirapine (NVP)	Ritonavir
Stavudine(d4T)	Efavirenz (EFZ)	Indinavir
Lamivudine (3TC)		Lopinavir/Ritonavir (Kaletra)
Didanosine (ddI)		Saquinavir
Abacavir (Abc)		
<b>Fixed-dose combination tablets (FDC)</b>		
ZDV + 3TC combined tablet (Combivir / Duovir)		
d4T+ 3TC + NVP combined tablet (SLN 30 / 40)		

## Which drugs to use?

Always use combination of at least 3 drugs (see Table 7):

- either
  - 2 NRTI\* + 1 NNRTI (Efavirenz (age > 3 years) or Nevirapine (age < 3 years)) or
  - 2 NRTI\* + 1 PI (Lopinavir/r)

\* Recommended 2 NRTI combinations: ZDV + 3TC; ZDV + ddI; ddI + 3TC

Alternative 2 NRTI combinations : d4T + 3TC ; d4T + ddI (use of d4T-based regimen is associated with higher incidence of lipodystrophy)

- Not Recommended
  - any monotherapy (except mother-to-child transmission prophylaxis during neonatal period)
  - d4T + ZDV: pharmacologic and antiviral antagonism

Table 6. When to start ARV? (adapted from Malaysian CPG 2008)

Age	Initiate Treatment	Consider	Defer
<12 months	symptomatic (WHO Stage 2,3,4) OR asymptomatic (WHO Stage 1) and CD4 < 25%	asymptomatic (WHO Stage 1) and CD4 ≥25%	-
1-<3 years	AIDS or significant HIV-related symptoms (WHO Stage 3* or 4) OR asymptomatic, mild symptoms (WHO Stage 1, 2) and CD4 < 20%	asymptomatic or mild symptoms and - CD4 20-24 % or - VL ≥ 100,000 copies /ml	asymptomatic and - CD4 ≥ 25 % and - VL <100,000 copies /ml
3-12 years	AIDS or significant HIV-related symptoms (WHO Stage 3* or 4) OR asymptomatic, mild symptoms (WHO Stage 1, 2) and CD4 < 15%	asymptomatic or mild symptoms and - CD4 15-24 % or - VL ≥100,000 copies /ml	asymptomatic and - CD4 ≥ 25 % and - VL <100,000 copies /ml
>12 years	AIDS or significant HIV-related symptoms (WHO Stage 3* or 4) OR asymptomatic, mild symptoms (WHO Stage 1 & 2) and CD4 < 200 cells /mm <sup>3</sup> or <15%	asymptomatic or mild symptoms and - CD4 201-350 cells/mm <sup>3</sup> or - VL ≥100,000 copies /ml	asymptomatic and - CD4 >350 cells/mm <sup>3</sup> and - VL <100,000 copies /ml

\* Except with Tuberculosis, lymphoid interstitial pneumonitis (LIP), Oral hairy leukoplakia (OHL) or thrombocytopenia (Starting antiretroviral in children with these conditions will depend on their CD4 count / %) VL, Viral Load

## When to change?

- treatment failure based on clinical, virologic and immunological parameters e.g. deterioration of condition or dropping of CD4 count/%.
- toxicity or intolerance of the current regimen

If due to toxicity or intolerance:

- choose drugs with toxicity profiles different from the current regimen
- changing a single drug is permissible
- avoid reducing dose below lower end of therapeutic range for that drug

*If due to treatment failure:*

- assess and review adherence
- preferable to change all ARV (or at least 2) to drugs that the patient has not been exposed to before.

Choices are very limited! Do not add a drug to a failing regime.

- consider potential drug interactions with other medications
- when changing therapy because of disease progression in a patient with advanced disease, the patient's quality of life must be considered.
- doing genotypic resistant testing will help to choose the appropriate ARV, however, the test is not widely available in Malaysia
- consult infectious diseases specialist before switching.

Table 7. Antiretroviral drugs dosages and common side effects

Drug	Dosage	Side effects	Comments
<b>Zidovudine (AZT)</b>	180-240mg/m <sup>2</sup> /dose bd Neonate: 2mg/kg qid or 4mg/kg bd (max. dose 300mg bd)	anaemia, neutropenia, headache	large volume of syrup not well tolerated in older children
<b>Didanosine (ddI)</b>	90-120mg/m <sup>2</sup> /dose bd (max. dose 200mg bd)	diarrhoea, abdo pain, peripheral neuropathy	taken on empty stomach (1hr before or 2h after food)
<b>Lamivudine (3TC)</b>	4mg/kg/dose bd (max. dose 150mg bd)	diarrhoea, abdo pain; pancreatitis (rare)	well tolerated; use solution within 1 month of opening
<b>Stavudine (d4T)</b>	1mg/kg/dose bd (max. dose 40mg bd)	headache, peripheral neuropathy, pancreatitis	capsule may be opened and sprinkle on food or drinks
<b>Abacavir (Abc)</b>	8 mg/kg/dose bd (max. dose 300 mg bd)	diarrhoea, nausea, rash, headache; hypersensitivity, Steven-Johnson (rare)	NEVER restart Abc after hypersensitivity reaction (may cause death)
<b>Efavirenz (EFZ)</b>	350mg/m <sup>2</sup> od 13-15kg 200mg 15-20kg 250mg 20-25kg 300mg 25-32kg 350mg 33-40kg 400mg > 40kg 600mg od	rash, headache, insomnia	Inducer of CYP3A4 hepatic enzyme; so has many drug interactions Capsules may be opened and added to food
<b>Nevirapine (NVP)</b>	150-200mg/m <sup>2</sup> /day od for 14 days, then increase to 300-400mg/m <sup>2</sup> /day bd (max. dose 200mg bd)	severe skin rash, headache, diarrhea, nausea	little data on use with PI. Practice is to increase PI dose by about 30%
<b>Ritonavir (RTV)</b>	350-450mg/m <sup>2</sup> /dose bd (max. dose 600mg bd)	vomiting, nausea, headache, diarrhoea, hepatitis (rare)	take with food to increase absorption and reduce GI side effects; Solution bitter as contains 43% alcohol
<b>Kaletra (Lopinavir/ Ritonavir)</b>	230/57.5mg/m <sup>2</sup> /dose bd 7-14kg 12/3 mg/kg bd 15-40kg 10/2.5mg/kg bd > 40kg 400/100mg bd	diarrhea, asthenia	low volume, but a bitter taste. Higher dose used with NNRTI
<b>Indinavir (IDV)</b>	500mg/m <sup>2</sup> /dose, tds (max. dose 800mg tds)	headache, nausea, abdominal pain, hyperbilirubinemia, renal stones	use in older children that can swallow tablets; Take on an empty stomach. Advise to drink more fluids

## Follow up

- usually every 3 - 4 months, if just commencing/switching HAART, then every 2 weeks
- ask about medication:
  - adherence (who, what, how and when of taking medications)
  - side effects e.g. vomiting, abdominal pain, jaundice
- examine: growth, head circumference, pallor, jaundice, oral thrush, lipodystrophy syndrome (if on Stavudine &/or PI)
- FBC, CD4 count, viral load 3-4 monthly, RFT, LFT, Ca/Po<sub>4</sub> (amylase if on ddl) 6 monthly;
- if on PI also do fasting lipid profiles and blood sugar yearly
- explore social, psychological, financial issues e.g. school, home environment. Many children are orphans, live with relatives, adopted or under NGO's care. Referral to social welfare often required. Compliance - adherence to therapy strongly linked to these issues.

## Other issues

- HIV / AIDS is a notifiable disease. Notify health office within 1 week of diagnosis.
  - screen other family members for HIV.
  - refer parents to Physician Clinic if they are HIV infected and not on follow up.
  - disclosure of diagnosis to the child (would-be teenager, issues on sexual rights)
  - be aware of Immune Reconstitution Inflammatory Syndrome (IRIS)
    - in this condition there is a paradoxical worsening of a known condition (e.g. pulmonary TB or lymphadenitis) or the appearance of a new condition after initiating ARV.
- This is due to restored immunity to specific infectious or non-infectious antigens.

## Horizontal transmission within families

Despite sharing of household utensils, linen, clothes, personal hygiene products; and daily interactions e.g. biting, kissing and other close contact, repeated studies have failed to show transmission through contact with saliva, sweat, tears and urine (except with exposure to well defined body fluids i.e. blood, semen, vaginal fluids).

It is important to stress that the following has not transmitted infection:

- casual contact with an infected person
- swimming pools
- droplets coughed or sneezed into the air
- toilet seats
- sharing of utensils such as cups and plates
- insects

*Note: It is difficult to isolate the virus from urine and saliva of seropositive children. So day care settings are not a risk. However, due to a theoretical risk of direct inoculation by biting, aggressive children should not be sent to day care. Teachers should be taught to handle cuts/grazes with care.*

## Guidelines for post exposure prophylaxis

Goal is to prevent HIV infection among those sustaining exposure, and provide information and support during the follow up until infection is diagnosed or excluded with certainty

### *Risk for occupational transmission of HIV to Health Care Workers (HCW)*

- risk for HIV transmission after a percutaneous exposure to HIV infected blood is 0.3%; risk after mucous membrane exposure is 0.1%.
- risk is dependent on :
  - type, volume of body fluid involved
  - type of exposure that has occurred
  - viral load of the source patient
  - disease stage

## Treatment of an Exposure Site

- wash wounds, skin exposure sites with soap, water; flush mucous membranes with water
- notify supervisor; refer HCW to designated doctor as in hospital needlestick injury protocol

# MALARIA

## Uncomplicated malaria

Symptomatic infection without signs of severity or evidence of vital organ dysfunction

## Complicated (severe) malaria

- almost always due to *P. falciparum*
- suspect mixed infections if vivax / malariae malaria appear unusually severe

### Danger signs of severe malaria

- changes in behaviour
- impaired consciousness
- jaundice
- parasitaemia > 2%
- continued vomiting
- hyperpyrexia
- oliguria
- severe metabolic acidosis

### Complications of falciparum malaria

- cerebral malaria
- pulmonary edema / ARDS
- renal failure
- haemoglobinuria
- haemorrhage due to DIC
- shock
- hypoglycaemia
- severe anemia (Hb < 5 g%)

### Uncomplicated Plasmodium falciparum infection

First line therapy		
<b>Preferred treatment</b> <b>Artesunate / mefloquine</b> <b>(Artequine)</b>	<10kg : Artesunate 25mg ODX 3d Mefloquine 125mg single dose	20-40kg: Artesunate: 100mg ODX 3d Mefloquine 250mg OD X 3d
D1-3: Artesunate 4mg/kg OD D1-3: Mefloquine 25mg/kg over 2 days or 8.3mg/kg daily	10-20kg: Artesunate 50mg ODX 3d Mefloquine 125mg ODX 3d	>40kg Artesunate 200mg OD X 3d Mefloquine 500mg OD X 3d
<b>Alternative treatment</b> <b>Artemether / lumefantrine</b> <b>(Riamet)</b>	5 -14 kg: D1: 1 tablet stat , 1 tablet 8 hours later D2-3 1 tablet BD  15 – 24kg: D1: 2 tablets stat, 2 tablets 8 hours later D2-3: 2 tablets BD	25 – 35kg: D1: 3 tablets stat, 3 tablets 8 hours later D2-3: 3 tablets BD  >35kg: D1: 4 tablets stat, 4 tablets 8 hours later D2-3: 4 tablets BD
Second line therapy		
<b>Children &lt; 8 years</b> Oral Quinine 10 mg salt/kg 8 hourly Oral Clindamycin 10 mg/kg BD	<b>Children &gt; 8 years</b> Oral Quinine 10 mg salt/kg 8 hourly Oral Doxycycline: 3.5 mg/ kg OD	Total duration 7 days
Add primaquine 0.75mg/kg single dose OD if gametocytes present at any time during treatment. Check G6PD before giving primaquine.		

### Complicated Plasmodium falciparum infection

First line therapy		
D1: IV artesunate 2.4 mg/kg on admission, then repeat again at 12h D2-7: IV artesunate 1.2mg/kg OD		
Second line therapy		
D1: IV Quinine loading 7mg/kg over 1 hour then infusion 10mg/kg over 4 hours then 10mg/kg q8hourly (Dilute quinine in 250ml D5%, run over 4 hours)  or Loading 20mg/kg over 4 hours then IV 10mg/kg q8 hourly D2-7: IV Quinine 10mg/kg q8h AND Doxycycline (>8yrs) (3.5 mg/kg OD) or Clindamycin (<8yrs) (10 mg/kg/dose bd) given for 7 days		
Change to oral Quinine if able to tolerate orally. Maximum Quinine per dose = 600mg.		



Plasmodium vivax infection

**First line therapy**

Total chloroquine 25mg base/kg divided over 3 days

D1: 10 mg base/kg stat then 5 mg base/kg 6 hours later

D2: 5 mg base/kg OD

D3: 5 mg base/kg OD

*PLUS*

Primaquine\* 0.25 mg base/kg daily for 14 days

**Relapse**

Repeat Choroquine and primaquine

\*Check G 6 PD status before giving primaquine.

In G6PD deficiency, primaquine 0.75 mg base/kg once a week for 8 weeks.

Plasmodium knowlesi or malariae infection

**First line therapy**

Total chloroquine 25mg base/kg divided over 3 days

D1: 10 mg base/kg stat then 5 mg base/kg 6 hours later

D2: 5 mg base/kg OD

D3: 5 mg base/kg OD

**Second line therapy**

Treat as complicated Plasmodium falciparum

Treatment for *Mixed* infections

Treat as for Plasmodium falciparum

**Malaria chemoprophylaxis**

**Preferred prophylaxis**

Mefloquine 5mg/kg once a week

To start one week before travel and continued till 4 weeks after leaving endemic area

**Alternative prophylaxis**

Doxycycline 2mg/kg OD(max 100mg/day) in children >8 years old.

To start one week before travel and continued till 4 weeks after leaving

**Notes:**

• *Artequine/mefloquine*

- Artesunate + mefloquine is available in 3 formulations:
- Artequine Paediatric in pellets form for small children < 20kg
- Artequine 300/750 for those between 20-40kg
- Artequine 600/1500 for > 40kg

**Caution:**

- AS/MQ may cause seizure in children with epilepsy
- AS/MQ interact with quinine, choroquine and halofantrine may cause arrhythmia
- GIT symptoms such as abdominal pain, nausea, vomiting and diarrhea are the most common side effects. Others symptoms include headache, dizziness and insomnia, convulsions and other CNS symptoms.

• *Riamet*

Artemether-lumefantrine is available as co-formulated tablets containing 20mg of artemether and 120 mg of lumefantrine. Lumefantrine absorption is enhanced by co-administration with fat containing food or milk.

## TUBERCULOSIS

### Definition

The presence of symptoms, signs and /or radiographic findings caused by MTB complex (*M. tuberculosis* or *M. bovis*).

Disease may be pulmonary or extrapulmonary, (i.e. central nervous system (CNS), disseminated (miliary), lymph node, bone & joint) or both.

### Clinical features

- pulmonary disease is commonest. Symptoms include fever, cough, weight loss, night sweats, respiratory distress.
- extrapulmonary disease may manifest as prolonged fever, apathy, weight loss, enlarged lymph nodes (cervical, supraclavicular, axillary), headache, vomiting, increasing drowsiness, infants may stop vocalising. Swellings and loss of function may suggest bone, joint or spinal TB.
- phlyctenular conjunctivitis, erythema nodosum and pleural effusions are considered hypersensitivity reactions of TB disease.

### Diagnosis of TB disease

Diagnosis in children is usually difficult. Features suggestive of tuberculosis are:

- *recent contact* with a person (usually adult) with active tuberculosis. This constitutes one of the strongest evidence of TB in a child who has symptoms and x ray abnormalities suggestive of TB.
- *symptoms and signs suggestive of TB* are as listed above. Infants are more likely to have non specific symptoms like low-grade fever, cough, weight loss, failure to thrive, and signs like wheezing, reduced breath sounds, tachypnoea and occasionally frank respiratory distress.
- *positive Mantoux test* (>10 mm induration at 72 hours; tuberculin strength of 10 IU PPD).
- *suggestive chest X-ray*:
  - enlarged hilar lymph nodes +/- localised obstructive emphysema
  - persistent segmental collapse consolidation not responding to conventional antibiotics.
  - pleural effusion.
  - calcification in lymph nodes, this usually develops > 6 months after infection.
- *laboratory tests*  
Presence of AFB on smears of clinical specimens and positive histopathology or cytopathology on tissue specimens are highly suggestive of TB. Isolation of *M. tuberculosis* by culture from appropriate specimens is confirmatory.

### Diagnostic Work-up

- efforts should be made to collect clinical specimens for AFB smear, cytopathology or histopathology, special stains and AFB culture to assure confirmation of diagnosis and drug susceptibility.
- if the source case is known, it is important to utilize information from the source such as culture and susceptibility results to help guide therapy. the diagnostic work-up for TB disease is tailored to the organ system most likely affected (see Table 1).

**Table 1. Diagnostic workup according to organ system involved**

<b>Pulmonary TB</b>	<b>Abdominal TB</b>
- chest radiograph	- CT abdomen with contrast
- early morning gastric aspirates <sup>1</sup>	- biopsy of mass / mesenteric lymph node <sup>1</sup>
- sputum (if >12 years, able to expectorate sputum) <sup>1</sup>	
- pleural fluid <sup>1</sup> or biopsy <sup>1</sup>	<b>TB osteomyelitis</b>
	- CT/MRI of affected limb
	- biopsy of affected site <sup>1</sup>
<b>Central Nervous System (CNS) TB</b>	<b>Miliary / Disseminated TB</b>
- CSF for FEME , AFB smear and TB culture <sup>1</sup>	- as for pulmonary TB
- CT head with contrast	- early morning urine <sup>1</sup>
<b>TB adenitis</b>	- CSF <sup>1</sup>
- excisional biopsy or fine needle aspirate <sup>1</sup>	

<sup>1</sup>Note: These specimens should be sent for AFB smear and TB culture and susceptibility testing. Cytopathology or histopathology should be carried out on appropriate specimens.

In addition, all children evaluated for TB disease require a chest x-ray to rule out pulmonary

Abbreviations: AFB, acid fast bacilli; CT, computed tomography scan; CSF, cerebrospinal fluid

### Treatment of TB disease

- antimicrobial therapy for TB disease requires a multidrug treatment regimen
- drug selection is dependent on drug susceptibility seen in the area the TB is acquired, disease burden and exposure to previous TB medications.
- therapeutic choices are best made according to drug susceptibility of the organism cultured from the patient.
- for any one patient, the treatment regimen would depend on the diagnosis (pulmonary or extrapulmonary), severity and history of previous treatment. directly observed therapy is recommended for treatment of active disease.

**Table 2. Tuberculosis chemotherapy in children**

Drug		Daily dose		Intermittent dose (biweekly)		Intermittent dose (thrice weekly)	
		mg/kg/day	max dose (mg)	mg/kg/day	max (mg)	mg/kg/day	max (mg)
Streptomycin	S	15-30	1000	15	1000	15	1000
Isoniazid	H	5-10	300	15	1200	10	900
Rifampicin	R	10	600	10	600	10	600
Pyrazinamide	Z	20-40	2000	not used	not used	-	-
Ethambutol	E	15-25	2500	not used	not used	30-50	-

### Short course therapy

This consists of a 6 month regimen, and is suitable for pulmonary tuberculosis and non-severe extrapulmonary tuberculosis. It is not recommended for drug resistant TB. The short course consists of:

- **Intensive Phase (2 months)**
    - daily Isoniazid, Rifampicin and Pyrazinamide
    - a 4th drug (either Ethambutol or Streptomycin) is added if initial drug resistance is present or the burden of organisms is high.
  - **Maintenance Phase (4 months)**
    - Isoniazid and rifampicin for the remaining 4 months.
    - given daily (preferred) or biweekly or thrice weekly.
- Note: WHO does not recommend a twice weekly regimen but advocates a thrice weekly regimen for intermittent dosing.
- all intermittent dose regimens must be directly supervised.

### Pulmonary TB and less severe extrapulmonary TB

- recommended regimen is short course therapy as above
- less severe extrapulmonary TB include lymph node disease, unilateral pleural effusion, skin, and bone / joint (single site) excluding spine

### Extrapulmonary TB (severe forms)

- these include meningeal, CNS and spinal TB, abdominal TB, bilateral pleural or pericardial effusion, bone and joint TB (> 1 site) and disseminated disease
- treat with intensive phase as above, but continuation phase for 7 - 10 months

### Corticosteroids

- indicated for children with TB meningitis
- may be used in children with pleural and pericardial effusion (hastens reabsorption of fluid), severe miliary disease (if hypoxic) and endobronchial disease
- give steroids only when accompanied by appropriate antituberculous therapy  
dose: prednisolone 1-2mg/kg/day for 3-4 weeks, then taper over 3-4 weeks.

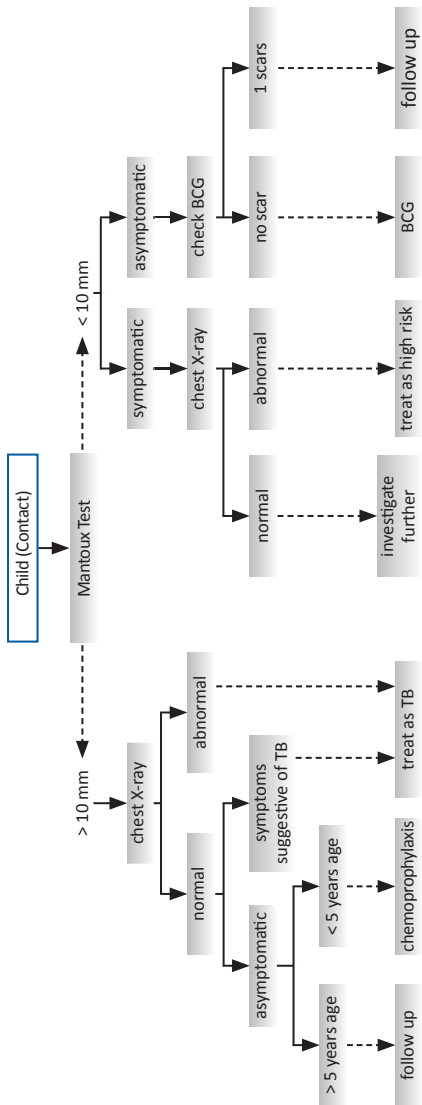
### Monitoring of drug toxicity

- baseline and routine monitoring of serum transaminases and bilirubin are recommended *only if these risk factors are present*:
  - severe TB disease
  - clinical symptoms of hepatotoxicity
  - underlying hepatic disease
  - HIV infection
  - use of other hepatotoxic drugs (especially anticonvulsants)
- monitor for visual acuity and colour discrimination if Ethambutol is used

### Breast-feeding and the mother with pulmonary tuberculosis

- tuberculosis treatment in lactating mothers is safe as the amount of drug ingested by the baby is minimal. Hence if the mother is already on treatment and is non-infective, the baby can be breastfed.
- women who are receiving isoniazid and are breastfeeding should receive pyridoxine.
- if the mother is diagnosed to have active pulmonary TB and is still infective:
  - the newborn should be separated from the mother for at least two weeks while the mother is being treated
  - breast feeding is best avoided during this period, however, expressed breast milk can be given
  - the infant should be evaluated for congenital TB. If this is excluded, BCG is deferred and the baby should receive isoniazid for 3 months and then tuberculin tested.
    - if tuberculin negative and mother has been adherent to treatment and non-infectious, isoniazid can be discontinued and BCG given.
    - if tuberculin positive, the infant should be reassessed for TB disease and if disease is not present, isoniazid is continued for total of 9 months and BCG given at the end of treatment.
  - other close household contacts should be evaluated for TB.
- congenital TB is rare but should be suspected if the infant born to a tuberculous mother fails to thrive or is symptomatic.

Figure 1. Management of children with a positive history of contact with tuberculosis



## BCG LYMPHADENITIS

- BCG lymphadenitis refers to cases where the lymph nodes have become large enough to be easily palpable and a cause of concern for the parents
- most of the cases appear within 6 months of the BCG
- ipsilateral axillary glands are involved in > 95% of cases, though the cervical or supraclavicular glands may be enlarged in isolation or in association
- 2 forms are recognized: non-suppurative (simple) which resolves spontaneously in a few weeks, or suppurative, with fluctuation, erythema and oedema of the overlying skin.
- once suppuration has occurred, the subsequent course is one of spontaneous perforation, discharge and sinus formation. Healing eventually occurs through cicatrization and closure of the sinus, the process taking several months.

### Management

- BCG lymphadenitis without suppuration (no fluctuation)
  - drugs are not required
  - reassurance and follow-up is advised.
  - several controlled trials and a recent metaanalysis (Cochrane database) have suggested that drugs such as antibiotics (e.g. erythromycin) or antituberculous drugs neither hasten resolution nor prevent its progression into suppuration.
- BCG lymphadenitis with suppuration (fluctuation)
  - needle aspiration is recommended. Usually one aspiration is effective, but repeated aspirations may be needed for some patients.
  - surgical excision is needed when needle aspiration has failed (in multiloculated and matted nodes) or when suppurative nodes have drained with sinus formation.
  - surgical incision is not recommended

#### Needle aspiration:

- prevents spontaneous perforation and associated complications
- safe, shortens the duration of healing

- persistent lymphadenitis
  - in patients with large and persistent or recurrent lymphadenopathy, possibility of underlying immunodeficiency should be investigated. Thus all infants presenting with BCG lymphadenitis should be followed up till resolution.

### BCG Vaccination

Development of the normal BCG papule and scar

- small papule with induration should appear in most infants within 3-4 weeks
- the papule increases in size for a few weeks (up to 10mm in diameter)
- this subsides gradually, followed by a local lesion that may ulcerate 6-8 weeks later
- lesion will heal spontaneously and leave a small flat scar 3-6 months later

#### Correct technique to give BCG:

- needle:** short (10mm) 26-27 gauge, with a short bevel using a BCG or insulin syringe
- site:** left arm at deltoid insertion
- dose:** 0.05 mls for infants (< 1 year of age)  
0.1 ml for children > 1 year.
- route:** intradermal

*Note: Do not give BCG at other sites where lymphatic drainage makes subsequent lymphadenitis difficult to diagnose and dangerous (esp. on buttocks where lymphatic drains to inguinal and deep aortic nodes)*

# DENGUE HAEMORRHAGIC FEVER & DENGUE SHOCK SYNDROME

Figure 1. Clinical spectrum of Dengue infection

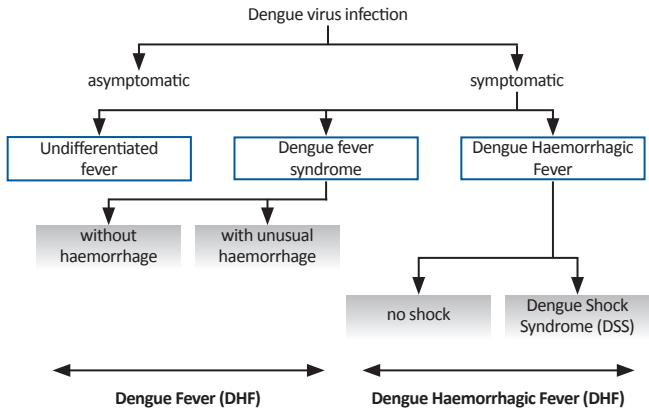


Table 1. Clinical Pointers to diagnosis

Pointers to clinical diagnosis of Dengue infection
<ul style="list-style-type: none"><li>• high fever of 3 or more days duration</li><li>• petechial haemorrhage, positive tourniquet test or other bleeding tendencies</li><li>• hepatomegaly</li><li>• pleural effusion or ascites</li><li>• shock</li><li>• fall in platelet count that precedes or occurs with a rise in haematocrit</li><li>• normal or low WBC with relative lymphocytosis</li><li>• maculopapular rash or generalised flushing</li></ul> <p><i>Note: all criteria need not be present at the same time</i></p>

Note:

- Grade 3 and 4 = Dengue Shock Syndrome
- thrombocytopenia and haemoconcentration (rise in PCV by 5 g%) differentiates Grade 1 and 2 DHF from DF
- clinical differentiation of grade 1 and 2 DHF from DF is not always clear cut due to variation in baseline haematocrit
- all patients ill enough to need IV drip should be notified as DHF if baseline haematocrit unknown

## WHO case definition of DHF

ALL of the following criteria must be present:

- fever, of high grade and continuous for 2-7 days duration.
- haemorrhagic diathesis or positive tourniquet test except in shock.
- thrombocytopenia (less than 100,000/mm<sup>3</sup>)
- haemoconcentration (HCT  $\geq$  20% relative to baseline) or evidence of plasma leakage

Table 2. WHO grading of DHF /DSS

<b>Grade 1</b> Fever with constitutional symptoms. A positive Hess test.
<b>Grade 2</b> Spontaneous bleeding (skin $\pm$ other bleeds) in addition to manifestations of grade 1
<b>Grade 3</b> Circulatory failure (rapid weak pulse, pulse pressure < 20mmHg) but systolic BP still normal
<b>Grade 4</b> Profound shock (hypotension, undetectable blood pressure and heart rate)

*Other clinical manifestations suggestive of DHF:*

- hepatomegaly
- circulatory disturbances (cool extremities, capillary refill > 2sec, tachycardia.)
- a fall in haematocrit following volume replacement.

**Atypical Presentations**

- acute abdominal pain, diarrhoea, severe gastro-intestinal haemorrhage
- severe headache, convulsions, altered consciousness
- encephalitis
- hepatic failure, obstructive jaundice,
- raised liver enzymes, Reye's syndrome
- acute renal failure,
- haemolytic uraemic syndrome
- disseminated intravascular coagulation
- vertical transmission in newborns

*Table 3. How to do a Hess test*

BP cuff pressure maintained between systolic and diastolic BP for 5 minutes. Positive if > 20 petechiae / 2.5 cm<sup>2</sup> area.

*Table 4. Laboratory investigations*

FBC, platelet, haematocrit  
urea & electrolytes, creatinine,  
liver function tests  
PT/PTT  
GXM - FFP, Platelet concentrates, whole blood  
Blood culture  
Dengue Blot Test  
Hess Test (see Table 3)

In clinical practice, the following classification of dengue infection is proposed:

- *Dengue Fever*
  - Without increased vascular permeability
- *Dengue Haemorrhagic fever*
  - increased vascular permeability and fragility
  - evidence of pleural effusion, ascites or haemoconcentration > 20%

DHF can be further graded as follows:

- *DHF with no shock*
- *DHF with shock (DSS)* which can be further graded into:
  - DHF with compensated shock
    - signs of shock – tachycardia out of proportion to temperature, decreased tissue perfusion as (cool extremities, late capillary refill time, narrow pulse pressure, weak pulses, oliguria, encephalopathy)
    - systolic pressure within the normal range
  - DHF with decompensated shock
    - signs of shock – tachycardia, cool extremities, late capillary refill time, weak or absent pulses, oliguria and altered conscious level
    - systolic hypotension

**Assessment of circulation**

- fluid intake for previous 1-2 days, vomiting losses
- urine output for past 24 hours and time of last micturation
- bleeding and amount
- degree of dehydration
- peripheral circulation
  - temperature and colour of extremities, capillary refill
  - distal pulses, pulse volume



- mental status: headache, irritability, combativeness, drowsiness, coma, seizures  
(may indicate reduce cerebral perfusion, cerebral oedema or intracranial bleed)
- pleural effusion and ascites (third space loss)
- abdominal pain  
(may indicate GI bleed, acute liver enlargement, hypovolaemia with intestinal ischaemia (shock))
- hypotension is a late sign.

## Management

### Grade 1 and 2 DHF

- admission, place IV cannulae.
- encourage oral fluids. IV fluids using 1/2 NS + D5% if unable to take orally and patients with evidence of plasma leakage.
- paracetamol for fever. Avoid NSAIDs.
- monitoring
  - clinical: pulses, temperature, heart rate, respiratory rate, and blood pressure
  - input/output chart, urine specific gravity
  - packed cell volume (PCV), platelets, Hb 8-12 hourly

Observations are continued until temperature returns to normal, in 1-2 days, and throughout the critical period, during the transition from febrile to afebrile phase (after 3rd day). Haemoconcentration usually precedes changes in pulse pressure and rate.

## Dengue Shock Syndrome

- admit to ICU.
- obtain IV access.
- resuscitation: *refer Fluid Therapy flow chart for DSS*
- monitor:
  - vital signs, peripheral perfusion
  - PCV or haematocrit
  - urea & electrolytes, serum creatinine
  - ABG
  - blood pressure hourly till stable
  - platelet count 6 hrly
  - urine output
- fluid maintenance:
  - following fluid resuscitation, continue with 0.45% saline 5% dextrose at 1-2 times maintenance, guided by haematocrit, urine output and vital signs.
  - in general, the duration of vascular permeability lasts 1-2 days following onset of shock, after which further infusion of large volume of fluids may result in pulmonary oedema and pleural effusion.
- electrolyte and metabolic disturbances:
  - hyponatremia and metabolic acidosis occur in DSS. Isotonic fluids and restoration of tissue perfusion correct both problems.
  - correct hypoglycaemia that may occur in liver failure
- transfusion of blood and blood products.
- *Blood transfusion. Indications:*
  - significant haemorrhage
  - persistent shock despite crystalloids and low or declining haematocrit
 Fresh whole blood is preferable.
- *Platelet concentrate :Indications*
  - platelet count < 50,000/mm<sup>3</sup> with bleeding
  - platelet count < 10,000 - 20,000/mm<sup>3</sup>
 Dose 10-20 ml/kg or 4 units/m<sup>2</sup> BSA over 1 hour.

- in the presence of Disseminated Intravascular coagulation (DIC)
  - cryoprecipitate (1 unit per 5 kg body weight ) followed by
  - platelet concentrate (10-20 ml/kg or 4 units/m<sup>2</sup> BSA over 1 hour)
  - fresh frozen plasma (10-20 ml/kg)
- monitor coagulation profile regularly. i.e. PT, PTT, fibrinogen, D-dimer, or FPD and platelet counts.
- oxygen supplement via nasal cannula or mask.
- consider mechanical ventilation in
  - respiratory distress from massive pleural effusion
  - ascites or pulmonary oedema
  - severe shock with multi-organ failure
  - encephalopathy for cerebral resuscitation
- H<sub>2</sub> antagonists and Vitamin K

### Complications of Dengue Shock Syndrome

- shock either persistent or recurrent
- pleural effusion and ascites
- bleeding - usually gastrointestinal
- hepatic dysfunction may result from dengue viral hepatitis or shock
- encephalopathy, usually occurs early before onset of plasma leakage
- beware of fluid overload and cardiac failure during the reabsorption phase

### Special Notes

- insertion of nasogastric tube carries risk of trauma and bleeding.  
If required, use an oral route.
- blood product transfusion carry risk of disease transmission.  
Avoid if vital signs stable
- insertion of chest tubes carries risk of haemorrhage. Careful titration of iv fluids with doses of frusemide 0.25-0.5 mg/kg for 1-2 doses should make it possible to avoid chest tube insertion.
- central line insertion carries risk of bleeding. Intraosseous route is acceptable.
- use of steroids and immunoglobulin in DSS has no beneficial effect

### Laboratory Diagnosis

#### Serology

- Dengue IgM Dot Enzyme Immunoassay
- interpret results in a clinical context. Serology may be negative if done early.  
A repeat study in 10 days will help confirm the diagnosis.

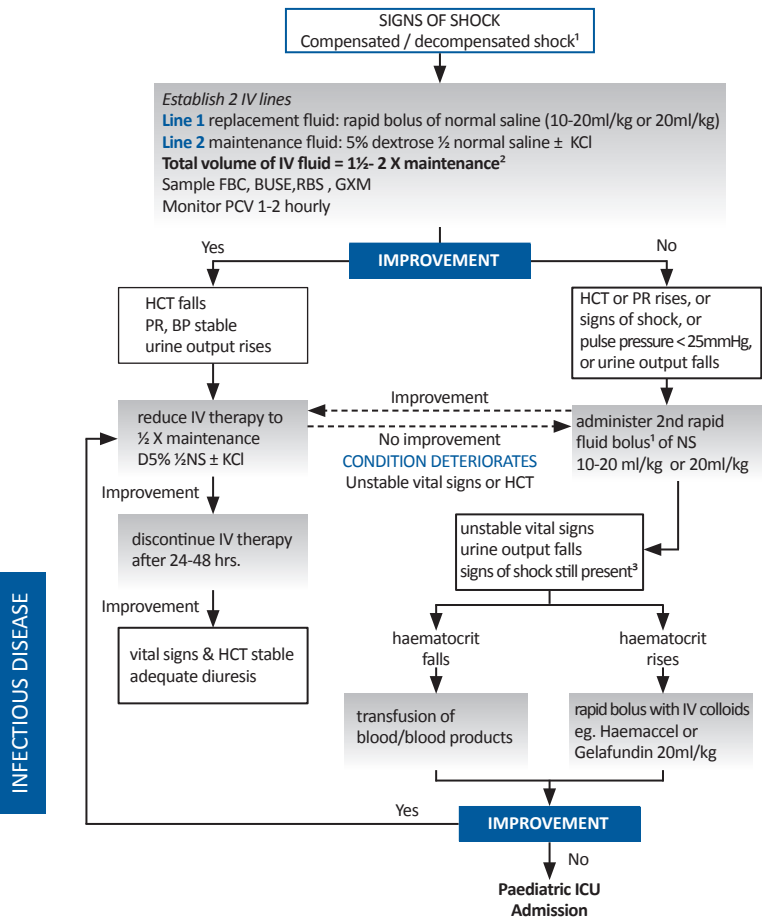
#### Virus isolation

- the most definitive diagnostic test. Availability limited.
- if patient dies soon after admission, a liver biopsy specimen sent in viral transport media may be useful in confirming the diagnosis.

#### Dengue RNA PCR

- may be indicated to confirm diagnosis

Figure 2. Fluid therapy for patients with DHF and DSS



footnote:

<sup>1</sup>rapid fluid bolus

-in decompensated shock, give 20ml/kg fast

- in compensated shock give 10-20ml/kg over 30-60 minutes if patients is warming up

<sup>2</sup> use weight adjusted to height centile for age to calculate the volume of maintenance fluids

<sup>3</sup> ensure good IV, check urinary catheter

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# DERMATOLOGY

**80** Atopic Dermatitis

**81** Impetigo

**82** Scabies

**83** Steven-Johnson Syndrome



# ATOPIC DERMATITIS

## Definition

A common chronic relapsing inflammatory skin disease, characterized by intense itching, dry skin, inflammation and exudation.

- first symptoms commonly develop in infancy; 50% are diagnosed by 1 year age
- often familial and frequently associated with asthma, food allergy, allergic rhinitis and recurrent secondary skin infections.
- prevalence of atopic dermatitis is 10-15% of children under 5 years of age.
- typically a long term condition:  $\frac{1}{3}$  of patients have persisting disease in adulthood

**Table 1. Diagnostic criteria**

**Major features** (must have 3) *Hanifin and Rajka criteria*

- pruritus
- typical morphology and distribution
  - facial and extensor involvement in infancy, early childhood
  - flexural lichenification and linearity by adolescence
- chronic or chronically relapsing dermatitis
- personal or family history of atopy (asthma, allergic rhinoconjunctivitis, atopic dermatitis)

**Minor / less specific features**

- xerosis
- preauricular fissures
- ichthyosis / palmar hyperlinearity / keratosis pilaris
- Ig E reactivity
- hand/foot dermatitis
- cheilitis
- scalp dermatitis (cradle cap)
- susceptibility to cutaneous infection (e.g. Staph. aureus and Herpes simplex)
- perifollicular accentuation (especially in pigmented races)

**Table 2. Triggering factors**

- infection:
  - bacterial, viral or fungal
- emotional stress
- sweating & itching
- irritants:
  - hand washing soap, detergents
- extremes of weathers
- allergen
  - food : egg, peanuts, milk, fish, soy, wheat
  - aeroallergens : house dust mite, pollen, animal dander and molds

## Management

- goal of therapy is control of skin inflammation, pruritus, and secondary infection.
- at present there is no 100% life-long cure for atopic eczema.
- management comprise combining adjuvant basic therapy, anti-inflammatory measurements and identification and avoidance of triggering factors.
- major factor in successful management is *compliance* and proper *communication* between doctor and patient.

## Treatment measures

### Bath & Emollients

- baths are helpful in soothing itching and removing crusting. They should be lukewarm and limited to 10 minutes duration. Avoid soaps. Use soap substitute e.g. aqueous cream or emulsifying ointment instead of soap.
- moisturizers work to reduce dryness in the skin by trapping moisture. They should be applied to normal and abnormal skin. They should be applied at least twice a day and more frequently in severe cases. Emollients are best applied after bath. e.g. aqueous cream, ung. emulsificans, and urea cream



*N.B. Different classes of moisturiser are based on their mechanism of action, including occlusives, humectants, emollients and protein rejuvenators. In acute exudative form KMnO<sub>4</sub> 1:10,000 solution or normal saline daps or soaks are useful - as mild disinfectant and desiccant.*

### Topical Corticosteroids

Topical corticosteroid is an anti-inflammatory agent and the mainstay of treatment for atopic eczema. Topical steroid are often prescribed intermittently for short term reactive treatment of acute flares and supplemented by emollients.

- choice depends on a balance between efficacy and side-effects
- the more potent the steroid, the more the side-effect
- apply steroid cream twice daily
- potent steroid can be used initially but only on a short term or intermittent basis
- avoid sudden discontinuation to prevent rebound phenomenon
- use milder steroids for face, flexures and scalp

Amount of topical steroid to be used – *the finger tip* (FTU) is convenient way of indicating to patients how much of a topical steroid should be applied to skin at any one site. 1 FTU is the amount of steroid expressed from the tube to cover the length of the flexor aspect of the terminal phalanx of the patient's index finger.

Number of FTU required for the different body areas.

1 hand / foot / face	1 FTU
1 arm	3 FTU
1 leg	6 FTU
Front and back of trunk	14 FTU

Adverse effect results from prolonged use of potent topical steroids. Local effects include skin atrophy, telangiectasia, purpura, striae, acne, hirsutism and secondary infections. Systemic effects are adrenal axis suppression, Cushing syndrome.

### Systemic Therapy

Consists of :

- relief of pruritus,
- treatment of secondary infection, and
- treatment of refractory cases

#### Relief of Pruritis (Antihistamines)

- for sedation and as anti-pruritus.
- helpful to reduce scratching.

#### Treatment of Secondary Infection

Secondary bacterial skin infection is common and may cause acute exacerbation of eczema. Systemic antibiotics are necessary when there is evidence of extensive infection.

- predominant pathogen is *Staphylococcus aureus*.
- useful in exudative form where superinfection occurs.
- choice:
  - oral Erythromycin 125mg tds 6 hourly for 5 days.
  - if suspected resistance - use cloxacillin / cephalosporin.
  - consider prolonged antibiotics (1 month) if pustular infection over the extremities
- secondary infection can arise from Herpes simplex virus causing *Eczema Herpeticum*. Treatment using antiviral e.g. Acyclovir may be necessary.

## Refractory cases

Refractory cases do not respond to conventional topical therapy and have extensive eczema. Refer such cases to the Dermatologist for treatment and monitoring:

- systemic steroid
- cyclosporin A
- interferon
- azathioprine
- phototherapy

## Other Measures

- avoid woollen toys, clothes, bedding.
- keep nails short.
- reduce use of detergent (esp. biological).
- double rinse clothes of patient.
- BCG contraindicated till skin improves
- tar/UV light might be useful.
- swimming useful (MUST apply moisturiser immediately upon exiting pool)

## Avoid Aggravating Factors

### For Relapse

- check compliance.
- suspect secondary infection – send for skin swab; start antibiotics.
- exclude scabies.
- for severe eczema, emollient and topical steroid can be applied under occlusion with ‘wet wrap’. This involves the use of a layer of wet, followed by a layer of dry Tubifast to the affected areas i.e. limbs and trunk. The benefits are probably due to cooling by evaporation, relieving pruritus, enhanced absorption of the topical steroid and physical protection of the skin from excoriation.

## Prognosis

- tendency towards improvement throughout childhood
- two third will clear by adolescence

# IMPETIGO

## Definition

Superficial, contagious skin infection occurring in the epidermis and / or dermis, associated with formation of blisters. It is the most common skin infection in children.

There are two types of impetigo:

- a bullous form caused by infection with *Staphylococcus aureus*
- a non-bullous form caused by infection with group A *Streptococci* and may have secondary infection with *Staphylococcus aureus*.

The causative organism should be identified by taking skin swabs from affected sites.

## Clinical features

- crusted lesions, usually yellow in colour, most commonly on the face.
- typically there may be scattered surrounding lesions, known as ‘satellite lesions’.
- usually patients are asymptomatic.
- commonly spread to other areas of the body if not treated.
- it is contagious and can be passed to other family members.

## Treatment

- localised infection: may be treated with topical mupirocin ointment which is active against infection due to both *Staphylococcus* and *Streptococcus*.
- more severe, generalised infection: should be treated with systemic antibiotics according to the sensitivities to the causal organism but Erythromycin or Cloxacillin are generally suitable.

### Definition

Infestation caused by the mite *Sarcoptes scabiei*. Any part of the body may be affected, and transmission is by skin to skin contact.

### Clinical features

#### Symptoms

- mites burrow into the skin where they lay eggs. The resulting offspring crawl out onto the skin and makes new burrows.
- absorption of mite excrement into skin capillaries generates a hypersensitivity reaction. The main symptom, which takes 4-6 wks to develop, is generalised itch – especially at night

#### Signs

- characteristic silvery lines may be seen in the skin where mites have burrowed.
- classic sites: interdigital folds, wrists, elbows, umbilical area, genital area and feet
- *Nodular Scabies*- papules or nodules seen at the site of mite infestation often affect the scrotum, axillae, back, or feet of children.
- *Crusted or Norwegian Scabies*- seen in young infants or immunosuppressed patients. Widespread mite infestation causing a hyperkeratotic and/or crusted generalized rash.

### Diagnosis

- the clinical appearance is usually typical, but there is often diagnostic confusion with other itching conditions such as eczema
- scrapings taken from burrows examined under light microscopy may reveal mites

### Management

#### General advice

- parents are given a detailed explanation of condition, and clear, accurate written information on applying the treatment
- treat everyone in the household or close contacts. Ignore pleas that someone does not itch; infected people can be asymptomatic and reinfect household members.
- change bedding, nightclothes & towels on night of treatment and clean them in a hot wash & hot iron after.

### Treatment

#### Infants: 2 months onwards

- Prementrin 5% lotion
  - one application and repeat another application after 2 weeks
  - to be applied to the whole body (may include the face if lesions are found on the face), overnight (8-12 hours) and washed off the following morning
- Crotamiton cream
  - applied to all lesions 3 times a day for 2 weeks (anti-pruritic, symptomatic relief)

#### Children: 6 years above

- Benzyl Benzoate Lotion (EBB) 12.5% (6-9 years); 25% (> 10 years)
  - applied to whole body from neck down; washed after 8-12 hrs; 3 consecutive nights
- Prementrin 5% lotion
  - one application and repeat another application after 2 weeks
  - applied to whole body overnight (8-12 hours); washed off the following morning.
- Sulpha (3-6%) with calamine
  - applied to all lesions 3 times a day for 5 days (anti-pruritic, symptomatic relief).
- antihistamine may also be helpful in relieving the itch.

# STEVEN-JOHNSON SYNDROME (SJS) AND TOXIC EPIDERMAL NECROLYSIS (TEN)

## Definitions

### Steven Johnson Syndrome (SJS):

- severe erosions of at least two mucosal surfaces with extensive necrosis of lips and mouth, and a purulent conjunctivitis.
- epidermal detachment may occur in SJS, but less than 10% of the body surface area is involved.
- morbidity with this disease is high, and can include photophobia, burning eyes, visual impairment and blindness.

### Toxic Epidermal Necrolysis (TEN):

- severe exfoliative disease associated with systemic reaction characterized by rapid onset of widespread erythema and epidermal necrolysis.
- involves more than 30% loss of epidermis.

### Aim of treatment:

To remove the cause and prevent complications

### Salient features

- acute prodromal flu-like symptoms, fever, conjunctivitis and malaise.
- skin tenderness, morbilliform to diffuse or macular erythema target lesions, vesicles progressing to bullae. Blisters on the face, and upper trunk, then exfoliation with wrinkled skin which peels off by light stroking (Nikolsky' sign).
- buccal mucosa involvement may precede skin lesion by up to 3 days in 30% of cases. Less commonly the genital areas, perianal area, nasal and conjunctival mucosa
- in the gastrointestinal tract, esophageal sloughing is very common, and can cause bleeding and diarrhoea
- in the respiratory tract, tracheobronchial erosions can lead to hyperventilation, interstitial oedema, and acute respiratory disease syndrome
- skin biopsy of TEN - Extensive eosinophilic necrosis of epidermis with subbasal cleavage plane
- renal profile – raised blood urea, hyperkalaemia and creatinine
- glucose - hypoglycaemia

**Table 1. Aetiology**

#### Drugs

##### Antibiotics

sulphonamides, amoxycillin  
ampicillin, ethambutol, isoniazid

##### Anticonvulsants

phenobarbitone, carbamazepine,  
phenytoin

##### Non-Steroidal Anti-Inflammatory Drugs

phenylbutazone, salicylates

#### Infection

##### Virus

herpes simplex, enteroviruses,  
adenoviruses, measles, mumps

##### Bacteria

*Streptococcus*, *Salmonella typhi*  
*Mycoplasma pneumoniae*

## Management

### *Supportive Care*

- admit to isolation room where possible
- may need IV fluid resuscitation for shock
- good nursing care (Barrier Nursing and hand washing)
- use of air fluidized bed, avoid bed sores
- adequate nutrition – nasogastric tubes, IV lines, parenteral nutrition if severe mucosal involvement

### *Specific treatment*

- eliminate suspected offending drugs
- IV Immunoglobulins at a dose of 0.4mg/kg/per day for 5 days. IVIG is a safe and effective in treatment for SJS/TEN in children. It arrests the progression of the disease and helps complete re-epithelialization of lesions.

### *Monitoring*

- maintenance of body temperature. Avoid excessive cooling or overheating
- careful monitoring of fluids and electrolytes – BP/PR
- intake / output charts, daily weighing & renal profile

## Prevent Complications

### *Skin care*

- cultures of skin, mucocutaneous erosions, tips of Foley's catheter.
- treat infections with appropriate antibiotics.
- topical antiseptic preparations: saline wash followed by topical bacitracin or 10% Chlorhexidine wash
- dressing of denuded areas with paraffin gauze / soffra-tulle
- surgery may be needed to remove necrotic epidermis

### *Eye care*

- frequent eye assessment
- antibiotic or antiseptic eye drops 2 hourly
- synechia should be disrupted

### *Oral care*

- good oral hygiene aimed at early restoration of normal feeds.

## METABOLIC AND GENETIC DISORDERS

- 84** Inborn Errors Of Metabolism: Approach to Investigations and Management in a Sick Child
- 85** Investigating Inborn Errors Of Metabolism in a Child with Chronic Symptoms
- 86** Approach to Recurrent Hypoglycaemia
- 87** Down Syndrome



# INBORN ERRORS OF METABOLISM (IEM): APPROACH TO DIAGNOSIS AND EARLY MANAGEMENT IN A SICK CHILD

## Introduction

Over 300 human diseases due to IEM are now recognized and a significant number of them are amenable to treatment.

IEMs may present as

- an acute metabolic emergency in a sick child
- chronic problems involving either single or multiple organs, either recurrent or progressive, or permanent

It will become ever more important to initiate a simple method of clinical screening by first-line paediatric doctors with the goal 'Do not miss a treatable disorder'.

## Classification

From a therapeutic perspective, IEMs can be classified into five useful groups:

Table 1. Classifying IEM disorders from a therapeutic perspective

### Group 1. Disorders that give rise to acute intoxication

*aminoacidopathies*

maple syrup urine disease, tyrosinaemia, PKU\*, homocystinuria\*

*most organic acidurias*

methylmalonic, propionic, isovaleric, etc.

urea cycle defects

*sugar intolerances*

galactosaemia, hereditary fructose intolerance

*defects in long-chain fatty acid oxidation*

(\* chronic intoxication)

Specific emergency and long term treatment available for most diseases

### Group 2. Disorders with reduced fasting tolerance due to cytoplasmic energy defects

*disorders of glucose homeostasis*

glycogen storage diseases, disorders of gluconeogenesis

*fatty acid oxidation defects*

*disorders of ketogenesis/ketolysis*

Specific emergency and long term treatment available for most diseases

### Group 3. Disorders of neurotransmission

*non ketotic hyperglycinemia*

*disorders of biogenic amine metabolism*

*disorders of GABA metabolism*

*pyridoxine- /pyridoxal phosphate-/folinic acid-responsive seizures*

*glucose transporter (GLUT1) deficiency*

Some are treatable

### Group 4. Disorders involving complex molecules

*lysosomal storage disorders*

*peroxisomal disorders*

*congenital disorders of glycosylation*

*creatine biosynthesis disorders*

*sterol biosynthesis disorders*

*purine metabolism disorders*

Very few are treatable

### Group 5. Disorders of mitochondrial energy defects

*respiratory chain enzymes deficiencies*

*PDHc deficiency*

*pyruvate carboxylase deficiency*

Mostly supportive care



Screening for treatable IEM in a sick child

- IEM should be considered as a differential diagnosis in acutely ill children:
  - neonates with unexplained, overwhelming, or progressive disease particularly after a normal pregnancy or birth, but deteriorates after feeding
  - children with acute encephalopathy, particularly preceded by vomiting, fever or fasting
  - in children with unexplained symptoms and signs of metabolic acidosis, hypoglycaemia, acute liver failure or Reye-like syndrome
- targeted to pick up treatable diseases in Groups 1 and 2 as early as possible.
- many clues may be gained from a detailed history and physical examination
  - unexplained death among sibling(s) due to sepsis or “SIDS”
  - unexplained disorders in other family members (HELLP (Haemolytic anaemia, Elevated Liver enzymes, Low Platelet) syndrome, progressive neurological disease)
  - consanguinity
  - deterioration after a symptom-free interval in a newborn
  - unusual smell - burnt sugar (MSUD), sweaty feet (isovaleric acidemia)
- actively investigate for IEM in any acutely ill child of unknown aetiology, as early as possible during the course of illness. According to the clinical situation, basic and special metabolic investigations must be initiated in parallel.

Table 2. Investigations in children with suspected IEM

Basic metabolic investigations <sup>1</sup>		Special metabolic investigations <sup>1</sup>
ammonia* glucose lactate* blood gases Ketostix (urine)	must be included in work-up of an acutely ill child of unknown aetiology <sup>2</sup>	acylcarnitines (dried blood spot on Guthrie card ) amino acids (plasma or serum) <sup>3</sup> organic acids (urine) orotate (urine) - if suspected urea cycle defect
blood count, electrolytes, ALT, AST, creatine kinase, creatinine, urea, uric acid, coagulation		[send to the metabolic lab immediately ( e.g. by courier) especially when the basic metabolic investigations are abnormal, particularly if there is hyperammonaemia or persistent ketoacidosis]
* must send immediately (within 15 minutes) to lab with ice		

Footnote: 1. will pick up most diseases from Group 1 and 2, and some diseases in other groups (which often require more specialized tests)  
2. Routine analysis of pyruvate is not indicated  
3. Urinary amino acids are the least useful as they reflect urinary threshold. Their true value is only in the diagnosis of specific renal tubular transport disorders (e.g. cystinuria).

Table 3. Useful normal / abnormal values

Basic metabolic tests	Values	Notes
Serum ammonia	Neonates healthy : <110µmol/L sick : up to 180µmol/L suspect IEM : >200µmol/L After the neonatal period normal : 50-80 µmol/L suspect IEM : >100µmol/L	1. False elevations are common if blood sample is <i>not analyzed immediately</i> 2. Secondary elevation may occur in severe liver failure
Anion gap	Calculation [Na <sup>+</sup> ] + [K <sup>+</sup> ] – [Cl <sup>-</sup> ] – [HCO <sub>3</sub> <sup>-</sup> ] normal : 15-20mmol/L	Normal: renal or intestinal loss of HCO <sub>3</sub> Increased: organic acids, lactate, ketones
Plasma lactate	blood : < 2.4mmol/L CSF : < 2.0mmol/L	False elevations are common due to poor collection or handling techniques

Table 4. "Typical" basic laboratory constellations

Disorders	Ammonia	Glucose	Lactate	pH	Ketonuria	Others
Urea cycle defects	↑↑↑	Normal	Normal	↑	Normal	
Organic acidemias	↑↑	↓, Normal	↑↑	↓ ↓ ↓	↑↑↑	↑ anion gap, neutropenia, thrombocytopenia
MSUD	Normal	Normal	Normal	Normal	↓, Normal	
GSD	Normal	↓ ↓ ↓	↑↑	↓	Normal	↑ triglyceride, ↑ uric acid, ↑ ALT
FAOD	↑	↓ ↓ ↓	↑	↓	↓ ↓ ↓	↑ creatine kinase
Mitochondrial disorders	Normal	Normal	↑↑↑	↓ ↓	Normal	↑ alanine
Tyrosinemia I	Normal	Normal to ↓	Normal	Normal to ↓	Normal	liver failure, ↑ α-fetoprotein, renal Fanconi syndrome

- early contact with the metabolic laboratory will help target investigations, avoid unnecessary tests, and speed up processing of samples and reporting of results

### Emergency management of a sick child suspected IEM

In the critically ill and highly suspicious patient, treatment must be started immediately, in parallel with laboratory investigations

This is especially important for Group 1 diseases

#### Step 1

If the basic metabolic test results and the clinical findings indicate a disorder causing acute endogenous intoxication due to disorder of protein metabolism (Group 1 diseases – UCD, organic acidemias or MSUD), therapy must be intensified even without knowledge of the definitive diagnosis.

Anabolism must be promoted and detoxification measures must be initiated.

- immediately stops protein intake
- reduce catabolism by providing adequate calories
  - 10% glucose infusion, 150ml/kg/day (~60kcal/kg/day), with appropriate electrolytes
  - use commercially available protein-free formula for oral feeding [e.g. Pro-phree® (Ross), Calo-Lipid (ComidaMed®), basic-p (milupa) ] if basic metabolic tests are suggestive of disorders of protein metabolism (urea cycle defects, organic acidemias or MSUD)
- add insulin 0.1-1U/kg/hr if blood glucose > 15mmol/L to promote anabolism
- correct hypoglycaemia and metabolic acidosis
- carry out detoxifying measures depending on the laboratory findings
- consult clinical geneticist/metabolic clinician
- supportive/intensive care
  - respiratory insufficiency: provide artificial ventilation
  - septicemia: administer antibiotics
  - seizures: prescribe anticonvulsants
  - cerebral oedema: therapeutic hyperventilation; use mannitol, frusemide; avoid hypotonic fluid overload

**Table 4. Specific detoxification measures for hyperammonemia [urea cycle defects]**

Therapy	Specifics	Indications
Anti-hyperammonemic drug cocktail	<p><i>Loading dose</i></p> <ul style="list-style-type: none"> <li>- IV sodium benzoate 250mg/kg</li> <li>- IV sodium phenylbutyrate 250mg/kg</li> <li>- IV L-arginine 250mg/kg (mix together in D10% to a total volume of 50mls, infuse over 90 min)</li> </ul> <p><i>Maintenance dose</i></p> <p>same dilution as above but infuse over 24 hours</p>	<ul style="list-style-type: none"> <li>• ammonia &gt; 200μmol/L</li> <li>• symptomatic (encephalopathic)</li> </ul>
Dialysis	<p>Haemodialysis or haemofiltration, if available</p> <p>If not, peritoneal dialysis is the alternative</p> <p>Exchange transfusion is <i>not effective</i></p> <p><i>(The method of choice depends on local availability and the experience of the medical personnel)</i></p>	<ul style="list-style-type: none"> <li>• ammonia &gt; 400μmol/L</li> <li>• symptomatic (encephalopathic)</li> <li>• inadequate reduction or rising ammonia despite drug cocktail</li> </ul>

**Table 5. Specific detoxification measures for other IEMs presented as acute intoxication**

Disorder	Pharmacological	Non-Pharmacological
Maple syrup urine disease	nil	<p><i>Dialysis</i></p> <p>Indication:</p> <ul style="list-style-type: none"> <li>• plasma leucine &gt;1500 μmol/L</li> <li>• symptomatic (encephalopathic)</li> </ul>
Organic acidemias	carnitine 100mg/kg/day	<p><i>Dialysis</i></p> <p>Indication:</p> <ul style="list-style-type: none"> <li>• intractable metabolic acidosis</li> <li>• symptomatic</li> </ul>
Tyrosinemia type 1	NTBC 1-2mg/kg/day	none

Abbreviation: NTBC, 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3- cyclohexanedione

## Step 2

Adaptation and specification of therapy according to the results of the special metabolic investigations/definitive diagnosis.

- specific precursor free amino acids
- natural protein (breast milk or infant formula) is gradually added when child is improving to meet the daily requirement for optimal growth
- oral anti-hyperammonemia drugs cocktail (for urea cycle defects)
- carnitine (for organic acidemias)
- vitamin therapy in vitamin-dependent disorders (e.g. Vit B12-responsive methylmalonic acidemia)
- transfer the child to a metabolic centre for optimisation of therapy
  - plan nutritional management according to child's protein tolerance

## Step 3

- be prepared for future decompensation
  - instruction to parents
  - gastrostomy/tube-feeding
  - an emergency letter for the patient detailing the management protocol (usually prepared by metabolic clinician, kept by parents) to use in the event of illness

Table 6. Management considerations in selected disorders

### Acute intoxication due to classical galactosaemia

- use a lactose-free infant formula
- send dry blood spots (Guthrie card) for galactose and galactose-1-P uridyltransferase (GALT) measurement

### Disorders with reduced fasting tolerance due to cytoplasmic energy defects (Group 2)

- *acute phase*: 10% glucose infusion, 120- 150ml/kg/day
- *long term*: avoid fasting; take frequent meals, nocturnal continuous feeding, uncooked cornstarch (older children)  
(see also approach to hypoglycaemia)

### Disorders of mitochondrial energy defects (Group 5)

- *clinical*: suspect in unexplained multi-systemic disorders, especially if involves neuromuscular system
- *laboratory markers*: persistently elevated blood/CSF lactate, plasma alanine
- *diagnosis*: respiratory enzyme assay in muscle biopsy/skin fibroblast, targeted mtDNA mutation study and others  
(discuss with metabolic clinician)
- *treatment*: ensure adequate nutrition; treat fever/seizure/epilepsy efficiently, avoid drugs that may inhibit the respiratory chain (e.g. valproate, tetracycline, chloramphenicol and barbiturates)  
- use of vitamins and cofactors is controversial (insufficient evidence)  
- useful website: <http://www.mitosoc.org/>, [www.umdj.org/](http://www.umdj.org/)

### Management of a asymptomatic newborn but at risk of having IEM

- ideally the diagnosis of treatable IEM should be made *before* a child becomes symptomatic. This may be possible through screening for high risk newborns:
  - a previous child in the family has had an IEM
  - multiple unexplained early neonatal deaths
  - mother has HELLP\* syndrome or fatty liver disease in pregnancy

\* Haemolysis, Elevated Liver enzymes, Low Platelet syndrome

#### Role of first-line paediatric doctors

- assist in early diagnosis
- assist initial management, stabilization of patients
- participate in long term care (shared-care with metabolic clinician)
  - rapid action when child is in catabolic stress (febrile illness, surgery etc)
  - adequate hydration and temporary adjustments in nutrition management and pharmacotherapy according to emergency protocol will prevent catastrophic metabolic decompensation

- affected babies may need to be transferred in utero or soon after delivery to a centre with facilities to diagnose and manage IEM
- admit to nursery for observation.
- if potential diagnosis is known: screen for the specific condition  
e.g. urea cycle disorders – monitor ammonia, plasma amino acid, maple syrup urine disease – monitor plasma leucine (amino acids)
- if potential diagnosis is unknown: Guthrie cards, collect on second day after feeding, mail it immediately and get the result as soon as possible.  
Other essential laboratory monitoring: ammonia, VBG, blood glucose.  
*Please discuss with the metabolic clinician.*

- to prevent decompensation before baby's status is known:
  - provide enough calories (oral/intravenous);
  - may need to restrict protein especially if index case presented very early (during first week of life).
  - protein-free formula should be given initially; small amount of protein (e.g. breast milk) is gradually introduced after 48 hours depending on baby's clinical status.
- if the index patient presented after the first week of life, the new baby should be given the minimum safe level of protein intake from birth (approximately 1.5 g/kg/day). Breast feeding should be allowed under these circumstances with top-up feeds of a low protein formula to minimise catabolism.
- get the metabolic test results as soon as possible to decide whether the baby is affected or not

## INVESTIGATING INBORN ERRORS OF METABOLISM (IEM) IN A CHILD WITH CHRONIC SYMPTOMS

### Introduction

IEMs may cause variable and chronic disease or organ dysfunction in a child resulting in global developmental delay, epileptic encephalopathy, movement disorders, (cardio)-myopathy or liver disease. Thus it should be considered as an important differential diagnosis in these disorders.

The first priority is to diagnose treatable conditions. However, making diagnosis of non-treatable conditions is also important for prognostication, to help the child find support and services, genetic counselling and prevention, and to provide an end to the diagnostic quest.

#### *Problem 1: Global developmental delay (GDD)*

- defined as significant delay in 2 or more developmental domains
- investigation done only after a thorough history and physical examination
- if diagnosis is not apparent after the above, then investigations as in Table 1 may be considered. Even in the absence of abnormalities on history or physical examination, basic screening investigations may identify aetiology in 10-20%.
- in the absence of any other clinical findings or abnormalities in the baseline investigations then further investigations are not indicated.

*Table 1. Suggested investigations in children with global developmental delay*

Basic screening investigations	
Karyotyping	Metabolic screening using Guthrie card <sup>1</sup>
Serum creatine kinase	Plasma Amino acids <sup>2</sup>
Thyroid function test	Urine organic acid <sup>2</sup>
Serum uric acid	Neuroimaging <sup>3</sup>
Blood Lactate	Fragile X screening (in boys)
Blood ammonia	

*Footnote: 1. This minimal metabolic screen should be done in all even in the absence of risk factors*

*2. This is particularly important if there is one or more of following risk factors: consanguinity, family history of developmental delay, unexplained sibling death, unexplained episodic illness.*

*3. MRI is more sensitive than CT, with increased yield. It is not a mandatory study and has a higher diagnostic yield when indications exist (e.g. macro/microcephaly; seizure; focal motor findings on neurologic examination such as hemiplegia, nystagmus, optic atrophy; and unusual facial features e.g. hypo/hypertelorism)*

- if history and physical examination reveal specific clinical signs and symptoms, a number of potential further investigations for possible IEM may be available. Many of these highly specialised investigations are expensive – it is not suggested that they are all undertaken but considered. Referral to a clinical geneticist, paediatric metabolic physicians or paediatric neurologist is useful at this stage to help with test selection based on “pattern recognition”.

**Table 2. Interpretation of basic screening investigations**

Test Abnormality	Possible causes of abnormal results
Creatine kinase ↑	muscle injury muscular dystrophy fatty acid oxidation disorders
Lactate ↑	excessive screaming, tourniquet pressure glycogen storage disorders; gluconeogenesis disorders disorders of pyruvate metabolism mitochondrial disorders is plasma alanine also increased? <i>If yes, then it is suggestive of true elevation of lactate</i>
Ammonia ↑	sample contamination sample delayed in transport/processing specimen haemolysed urea cycle disorders liver dysfunction
Uric acids	any abnormality - high or low result is significant glycogen storage disorders (↑ uric acid) purine disorders (↑ uric acid) molybdenum cofactor deficiency (↓ uric acid)

**Table 3. Metabolic/Genetic tests for specific clinical features**

Developmental delay and .....	Disorders	Investigations
severe hypotonia	peroxisomal disorders purine/pyrimidine disorders neurotransmitters deficiencies neuropathic organic academia Pompe disease Prader Willi syndrome	very long chain fatty acids (B) purine/pyrimidine analysis (U) neurotransmitters analysis (C) organic acid analysis (U) lysosomal enzyme (G) methylation PCR (B)
neurological regression + organomegaly + skeletal abnormalities	mucopolysaccharidoses oligosaccharidoses	urine MPS (U) oligosaccharides (U)
neurological regression ± abnormal neuroimaging e.g. leukodystrophy	other lysosomal disorders mitochondrial disorders biotinidase deficiency peroxisomal disorders Rett syndrome (girl)	lysosomal enzyme (B) respiratory chain enzymes (M/S) biotinidase assay (G) very long chain fatty acids (B) MECP2 mutation study
progressive myopia ± lens subluxation	homocystinuria	total homocysteine (B)
abnormal hair	Menkes disease argininosuccinic aciduria trichothiodystrophy	copper (B), ceruloplasmin (B) amino acid (U/B) hair microscopy

*Legend: B=blood, C=cerebrospinal fluid, U=urine, G=Guthrie card, CGH=comparative genomic hybridization*

**Table 3. Metabolic/Genetic tests for specific clinical features (continued)**

Developmental delay and .....	Disorders	Investigations
macrocephaly	glutaric aciduria type I Canavan disease vanishing white matter disease megalecephalic leukodystrophy with subcortical cysts (MLC)	organic acid (U) organic acid (U) DNA test DNA test
dysmorphism	microdeletion syndromes peroxisomal disorders Smith Lemli Opitz syndrome congenital disorders of glycosylation	FISH, CGH very long chain fatty acids (B) sterol analysis (B) transferrin isoforms (B)
dystonia	Wilson disease neurotransmitters deficiencies  neuroacanthocytosis	copper (B), ceruloplasmin (B) phenylalanine loading test, neurotransmitters analysis (C)  peripheral blood film, DNA test
epileptic encephalopathy	nonketotic hyperglycinemia molybdenum cofactor deficiency glucose transporter defect pyridoxine dependency PNPO deficiency congenital serine deficiency cerebral folate deficiency ring chromosome syndromes neuronal ceroid lipofuscinosis  creatine biosynthesis disorders adenylosuccinate lyase deficiency cerebral dysgenesis e.g. lissencephaly Angelman syndrome	glycine measurement (B and C) sulphite (fresh urine) glucose (blood and CSF) pyridoxine challenge amino acid (C), organic acid (U) amino acid (B and C) CSF folate karyotype peripheral blood film, lysosomal enzymes (B)  MR spectroscopy purine analysis (U) MRI brain  methylation PCR
spastic paraparesis	arginase deficiency neuropathic organic academia Sjogren Larsson syndrome	amino acid (B) organic acid (U) detailed eye examination

*Legend: B=blood, C=cerebrospinal fluid, U=urine, G=Guthrie card, CGH=comparative genomic hybridization*

### **Problem 2: Liver disease**

- a considerable number of IEM cause liver injury in infants and children, either as isolated liver disease or part of a multisystem disease
- the hepatic clinical response to IEM is often indistinguishable from acquired causes, such as infections
- while IEM should be considered in any child with liver disease, it is essential to understand many pitfalls in interpreting the results
- liver failure can produce a variety of non-specific results: hypoglycaemia, ↑ NH<sub>3</sub>, ↑ lactate, ↑ plasma amino acids (tyrosine, phenylalanine, methionine), positive urine reducing substances (including galactose), an abnormal urine organic acid/blood acylcarnitine profiles.
- primary paediatric doctors must communicate closely with the metabolic clinician, hepatologist and laboratory

**Table 4. Approach to metabolic liver disease according to clinical manifestation**

**A. Acute/subacute hepatocellular necrosis**

(↑AST, ↑ALT jaundice, hypoglycaemia, ↑NH<sub>3</sub>, bleeding tendency, ↓albumin, ascites)

Metabolic / genetic causes	Clues	Diagnostic tests
<i>Neonatal/ early infantile</i>		
• Neonatal haemochromatosis	↑↑↑ ferritin	liver biopsy
• Galactosaemia	+ve urine reducing sugar, cataract	GALT assay
• Long-chain fatty acid oxidation disorders	associated (cardio)myopathy	blood acylcarnitine
• mtDNA depletion syndrome	muscular hypotonia, multi-system disease, encephalopathy, nystagmus, ↑↑ lactate (blood and CSF)	liver biopsy for respiratory enzyme assay
• tyrosinaemia type I	severe coagulopathy, mild ↑AST, ↑ ALT, renal tubulopathy, ↓ phosphate, ↑↑↑AFP	urine organic acids including succinylacetone
• congenital disorders of glycosylation	multi-system disease, protein-losing enteropathy	transferrin isoform analysis
<b>Must rule out infections:</b> TORCHES, echovirus, parvovirus B19, enteroviruses, HIV, EBV, Hep B, Hep C		serology, urine/stool viral culture

*Late infancy to childhood*

• above causes		
• α-1-antitrypsin deficiency	see below	α-1-antitrypsin level
• fructosaemia	symptoms after fructose intake, renal tubulopathy	
• Wilson disease	KF rings, neurological symptoms, haemolysis	serum/urine copper, caeruloplasmin

**Must rule out chronic viral hepatitis & autoimmune diseases**

**B. Cholestatic liver disease**

(conjugated bilirubin >15%, acholic stool, yellow brown urine, pruritus, ↑↑ ALP )  
GGT (gamma-glutamyltranspeptidase) may be low, normal or high - useful to differentiate various causes.

Metabolic / genetic causes	Clues	Diagnostic tests
<i>Neonatal/ early infantile</i>		
• Alagille syndrome	eye, cardiac, vertebral anomalies	DNA study
• inborn error of bile acid synthesis	↓ or normal GGT	liver biopsy, DNA study
• Progressive familial intrahepatic cholestasis (PFIC)	↓ or normal GGT except PFIC type III	liver biopsy, DNA study
• citrin deficiency	↑ plasma citrulline, ↑ galactose, +ve urine reducing sugar	plasma amino acids, DNA study
• Niemann Pick C	hypotonia, ophthalmoplegia, hepatosplenomegaly	bone marrow examination
• peroxisomal disorders	severe hypotonia, cataract, dysmorphism, knee calcification	very long chain fatty acids
• α-1-antitrypsin deficiency	commonly presents as cholestatic jaundice, gradually subsides by 6 months age. Some develop cirrhosis	α-1-antitrypsin levels



## B. Cholestatic liver disease (continued)

Metabolic / genetic cause	Clues	Diagnostic tests
<i>Late infancy to childhood</i>		
• above causes		
• Rotor syndrome	normal liver function	} diagnosis by
• Dublin-Johnson	normal liver function	} exclusion

## C. Cirrhosis

(end stage of chronic hepato-cellular disease)

chronic jaundice, clubbing, spider angiomas, ascites, portal hypertension

Metabolic / genetic cause	Clues	Diagnostic tests
• Wilson disease	KF ring, neurological symptoms, haemolysis	serum/urine copper, ceruloplasmin
• haemochromatosis	↑↑ ferritin, cardiomyopathy, hyperpigmentation	liver biopsy, DNA study
• GSD IV	cirrhosis around 1 year, splenomegaly, muscular hypotonia/atrophy, cardiomyopathy, fatal < 4year	liver biopsy
• α-1-antitrypsin	see above	α-1-antitrypsin levels

**Must rule out: chronic viral hepatitis, autoimmune diseases, vascular diseases, biliary malformation etc**

### Problem 3: Cardiomyopathy

- cardiomyopathy can be part of multi-systemic manifestation of many IEMs
- in isolated cardiomyopathy: actively screen for subtle extra-cardiac involvement, i.e. renal, liver function; ophthalmological and neurological examinations
- cardiomyopathy may be part of clinical features of genetic syndromes e.g. Noonan syndrome, Costello syndrome, Cardiofaciocutaneous syndrome.
- sarcomeric protein mutations may cause familial cardiomyopathy

Table 5. IEM that may present predominantly as cardiomyopathy

Disorder	Cardiac Finding	Clues
Primary carnitine deficiency	dilated cardiomyopathy	↓ serum free carnitine
Long chain fatty acid oxidation disorders	hypertrophic or dilated cardiomyopathy	myopathy, retinopathy, hypoketotic hypoglycaemia, abnormal acylcarnitine profile
Mitochondrial disorders	hypertrophic or dilated cardiomyopathy	associated with multi-system abnormalities, ↑↑ lactate Kearns– Sayre syndrome: Chronic progressive external ophthalmoplegia, complete heart block
Barth syndrome	dilated cardiomyopathy	neutropenia, myopathy, abnormal urine organic acid (↑3-methylglutaconic aciduria)
Infantile pompe disease	hypertrophic cardiomyopathy	ECG - Short PR, very large QRS; ↑ Creatine kinase, ↑ AST, ↑ ALT
Glycogen storage disease type III	hypertrophic cardiomyopathy	hepatomegaly, ↑ creatine kinase, ↑ AST, ↑ ALT, ↑ triglycerides ,

# Problem 4: Haematological disorders

Table 6. Inborn errors of metabolism presenting as haematological disorders

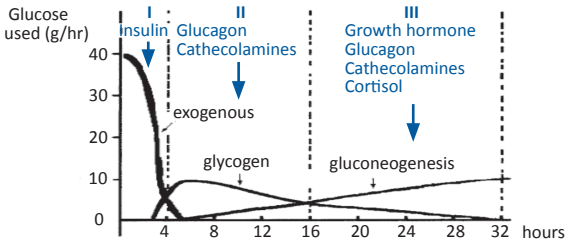
Clinical problem	Metabolic /Genetic causes	Clues / tests
megaloblastic anaemia	<ul style="list-style-type: none"> <li>defective transportation or metabolism of B<sub>12</sub></li> <li>orotic aciduria</li> <li>disorders of folate metabolism</li> </ul>	methylmalonic aciduria, ↑ homocysteine, ↓/normal serum B <sub>12</sub> ↑↑ urinary orotate ↓serum folate
global marrow failure	<ul style="list-style-type: none"> <li>Pearson syndrome</li> <li>Fanconi anaemia</li> <li>dyskeratosis congenita</li> </ul>	exocrine pancreatic dysfunction, lactate, renal tubulopathy cafe au lait spots, hypoplastic thumbs, neurological abnormalities, increased chromosomal breakage abnormal skin pigmentation, leucoplakia and nail dystrophy, premature hair loss and/or greying

# APPROACH TO RECURRENT HYPOGLYCAEMIA

## Introduction

Definition of hypoglycemia: blood glucose <2.6 mmol/L for all ages

Figure 1. Glucose homeostasis time course



Origin of blood glucose	diet	glycogen gluconeogenesis	hepatic glycogen gluconeogenesis
Tissues using glucose	all	all except liver, muscle	brain, blood cells, renal medulla
Major fuel of brain	glucose	glucose	glucose

## Clinical approach

- rule out: liver failure, septicemia, severe systemic illness, small for gestational age, maternal diabetes and drugs
- determine the fasting tolerance: when does hypoglycemia occur in relation to last meal?
- is it *ketotic or hypoketotic* hypoglycemia?
- any hepatomegaly?
- any clues and clinical signs to suggest an endocrine cause?
  - small genitalia, hyperpigmentation, short stature.
  - abnormal neonatal hypothyroidism screening result
  - glucose requirement > 10 mg/kg/min indicates hyperinsulinism unless there is marked loss in urine

## Laboratory tests during symptomatic hypoglycemia

Adequate laboratory tests will help identify the cause, or else the diagnosis may be missed. Ensure samples are taken *before* correcting the hypoglycemia.

Table 2. List of investigations

Essential Tests	Other Tests
<ul style="list-style-type: none"><li>• ketones (serum or urine)</li><li>• acylcarnitine (dried blood spots on Guthrie card)</li><li>• blood lactate</li><li>• venous blood gas</li><li>• blood ammonia</li><li>• urine organic acids</li><li>• free fatty acids (if available)</li><li>• serum insulin</li><li>• serum cortisol</li><li>• serum growth hormone</li></ul>	<ul style="list-style-type: none"><li>• serum cholesterol/triglyceride</li><li>• serum uric acid</li><li>• liver function test</li><li>• creatine kinase</li><li>• urine reducing sugar</li><li>• urine tetraglucoside</li><li>• plasma amino acids</li><li>• consider toxicology tests C-peptide</li><li>• fasting tolerance test/glucagon test (only by metabolic clinician/ endocrinologist)</li><li>• other special tests e.g. fatty oxidation study in cultured fibroblasts</li></ul>

Table 3. Determining the cause of hypoglycemia

Ketone level	Timing of hypoglycemia	Other clues	Diagnosis
hypoketotic	no specific timing	↑insulin <sup>1</sup> when glucose <2.6mmol/L, ↑ ammonia in HIHA	Hyperinsulinism
ketotic	no specific timing	↓GH, ↓ cortisol, ↓ TSH, midline defect, micropenis	Hypopituitarism
hypoketotic	infant: < 3 hr	permanent hepatomegaly, ↑↑ lactate, ↑ uric acid, ↑ TG, ↑ cholesterol, ↑ ALT, ↑ AST	GSD type I
ketotic	3-8 hr	hepatomegaly, ↑lactate, ↑uric acid, ↑ TG, ↑ cholesterol, ↑ ALT, ↑ AST, ↑ CK (some GSD III), ↑ urine tetraglucoside (hypoglycaemia usually mild compared to GSD I)	GSD III/VI/IX
ketotic	>8 hr	hepatomegaly in acute phase, ↑ lactate, ↑ urine glycerol/2-ketoglutaric	Gluconeogenesis defects
hypoketotic	infant: >8 hr older children: >16 hr	hepatomegaly during acute phase, absent ketones, mild ↑ NH <sub>3</sub> , mild ↑ lactate, mild ↑ AST/ALT, abnormal acyl-carnitine profile, ↓ free fatty acid, urine organic acid - dicarboxyluria	Fatty acid oxidation disorders
ketotic	1-2 hr	jaundice, liver dysfunction, GI symptoms, positive urine reducing sugar, galactosaemia: ↑Gal-1-P uridyltransferase (GALT), ↓Gal-1-P	Sugar intolerance (galactosaemia, fructosaemia)
ketotic	3-8 hr	no hepatomegaly; fasting: ↓glucose, ↓lactate, ↓alanine, ↑ketone postprandial: hyperglycemia, glucosuria, ↓ ketone, ↑ lactate; mild ↑ ALT/AST; liver biopsy: absent glycogen	GSD 0
ketotic	during acute crisis	metabolic acidosis, ↑ acetate, abnormal acylcarnitine and urine organic acids. Ketolytic defect: urine ketone persistently positive even when patient well	Organic acidurias/ketolytic defects

Abbreviations: HIHA, Hyperinsulinism-hyperammonaemia syndrome; GSD, Glycogen storage disease

GH, growth hormone; TSH, thyroid stimulating hormone; TG, triglyceride; CK, creatine kinase; NH<sub>3</sub>, ammonia

Footnote: 1. normal range for insulin level: 2-5mU/L.

### Differential diagnosis of congenital hyperinsulinism

- **transient hyperinsulinism in the neonate**  
diabetic fetopathy, asphyxia, sepsis, rhesus incompatibility, etc.
- **overgrowth syndromes with diazoxide sensitive hypoglycaemia**  
Beckwith-Wiedemann syndrome (macrosomia, macroglossia, omphalocele, lateral ear lobe crease), Simpson-Golabi-Behmel syndrome, Sotos syndrome, Perlman syndrome.
- **hyperinsulinism-hyperammonaemia (HIHA) syndrome**  
mild to moderate hyperammonaemia 100-200µmol/L (unaffected by feeding or fasting), usually hyperammonaemia is asymptomatic, may be prominent early but may disappear later in childhood, often leucine-sensitive, respond well to medical therapy with diazoxide.

- *monogenic forms of hyperinsulinism*

mutations in sulfonylurea receptor gene (SUR1, autosomal recessive), inward-rectifying potassium channel gene (Kir 6.2, autosomal recessive), glucokinase (autosomal dominant). Hypoglycemia is more severe and refractory to medical treatment with diazoxide and octreotide, and affected infants may require near-total pancreatectomy to control the hypoglycaemia.

- *mitochondrial short-chain 3-hydroxyacyl-CoA dehydrogenase deficiency*

- *congenital disorders of glycosylation (CDGs)*

- *Leprechaunism and Rabson-Mendenhall's syndrome*

autosomal recessive, mutations in insulin receptor gene; clinical features: severe IUGR, lipodystrophy, facial dysmorphism, paradoxical fasting hypoglycemia and postprandial hyperglycemia during infancy

## Treatment

- ensure good IV line
- IV Glucose 7 - 10 mg/kg/min or glucose 10% 110 - 150 ml/kg/day
- aim to keep blood sugar > 5.5 mmol/L
- hourly blood sugar until the level is normalized
- if bolus glucose needed, do not give > 200 mg/kg or glucose 10% 2 ml/kg
- await results of special investigations mentioned above
- consult metabolic clinician or endocrinologist if necessary

### Note:

- hypoglycemia due to metabolic disorders is easily corrected with IV glucose but may recur if the underlying metabolic defect is not treated.
- in contrast, hypoglycemia due to endocrine disorders especially hyperinsulinism is persistent and difficult to control requiring agents such as
  - IV glucagon (1 mg/day or 5 - 10 mcg/kg/hour, continuously over 2 - 3 days),
  - diazoxide (15mg/kg/day in 3 doses, takes up to 5 days to work, may cause cardiac failure which may require hydrochlorothiazide 2mg/kg/day in 2 doses)
  - IV somatostatin (1 - 5 mcg/kg/hour IV),
  - octreotide (3 to 20 mcg/kg/day in 3 to 4 doses) for long term treatment,
  - oral nifedipine (0.5 - 2 mg/kg/day) may be justified in selective cases.
- glycogen storage diseases/Gluconeogenesis disorders
  - frequent meals
  - nocturnal continuous feeding during infancy till preschool
  - uncooked cornstarch in older children
  - prevent prolonged fasting and catabolic states

# DOWN SYNDROME

## A. Medical problems

### Newborn

- cardiac defects (50%): AVSD [most common], VSD, ASD, TOF or PDA
- gastrointestinal (12%): duodenal atresia [commonest], tracheo-oesophageal fistula, anorectal malformation, pyloric stenosis and Hirshsprung disease.
- vision: congenital cataracts (3%), glaucoma.
- hypotonia & joint laxity
- feeding problems. Usually resolve after a few weeks.
- congenital hypothyroidism (1%)
- congenital dislocation of the hips

### Infancy and Childhood

- delayed developmental milestones
- mild to moderate intellectual impairment (IQ 25 to 50)
- seizure disorder (6%)
- recurrent respiratory infections
- hearing loss (>60%) due to secretory otitis media, sensorineural deafness, or both
- visual impairment – squint (50%), cataract (3%), nystagmus (35%), glaucoma, refractive errors (70%)
- sleep related upper airway obstruction. Often multifactorial.
- leukaemia (relative risk:15 to 20 times). Incidence 1%
- atlantoaxial instability. Symptoms of spinal cord compression include neck pain, change in gait, unusual posturing of the head and neck (torticollis), loss of upper body strength, abnormal neurological reflexes, and change in bowel/bladder functioning. (see below)
- hypothyroidism (10%). Prevalence increases with age
- short stature – congenital heart disease, sleep related upper airway obstruction, coeliac disease, nutritional inadequacy due to feeding problems and thyroid hormone deficiency may contribute to this
- over/underweight

### Adolescence and Adulthood

- puberty – in *Girls* menarche is only slightly delayed. Fertility presumed
- in *Boys* are usually infertile due to low testosterone levels
- increased risk of dementia /Alzheimer disease in adult life
- shorter life expectancy

## Management

- communicating the diagnosis is preferably handled in private by a senior medical officer or specialist who is familiar with the natural history, genetic aspect and management of Down syndrome.
- careful examination to look for associated complications.
- investigations: 1. echocardiogram by 2 weeks (if clinical examination or ECG were abnormal) or 6 weeks. 2. Chromosomal analysis. 3. T4 /TSH at birth or by 1-2 weeks of life.

Table 1. Incidence of Down syndrome

Overall Incidence: 1 in 800-1000 newborns	
Maternal Age-Specific Risk for Trisomy 21 at livebirth	
Age (years)	Incidence
20	1 in 1500
30	1 in 900
35	1 in 350
40	1 in 100
41	1 in 70
42	1 in 55
43	1 in 40
44	1 in 30
45	1 in 25

Source Hecht and Hook '94

- early intervention programme should begin at diagnosis if health conditions permit
- assess strength & needs of family. Contact with local parent support group should be provided (Refer list of websites below)
- health surveillance & monitoring: see Table 5

#### *Atlantoaxial instability*

- seen in X rays in 14% of patients; symptomatic in 1-2%.
- small risk for major neurological damage but cervical spine X rays in children have no predictive validity for subsequent acute dislocation/ subluxation at the atlantoaxial joint
- children with Down's syndrome should not be barred from taking part in sporting activities
- appropriate care of the neck while under general anaesthesia or after road traffic accident is advisable

*Table 2. Karyotyping in Down syndrome*

Non-disjunction trisomy 21	95%
Robertsonian Translocation	3%
Mosaicism	2%
<b>Recurrence Risk by Karyotype</b>	
<b>Nondisjunction Trisomy</b>	
47(XX or XY) + 21	1%
<b>Translocation</b>	
both parents normal	low; <1%
other carrier	10%
father carrier	2.5%
either parent t(21q;21q)	100%
Mosaics	< 1%

#### **Useful websites**

- The Down Syndrome Medical Interest Group (UK): [www.dsmig.org.uk](http://www.dsmig.org.uk)
- Down Syndrome: Health Issues: [www.ds-health.com](http://www.ds-health.com)
- Growth charts for children with Down Syndrome: [www.growthcharts.com](http://www.growthcharts.com)
- Educational issues: [www.downsed.org](http://www.downsed.org)
- Kiwanis Down Syndrome Foundation: [www.kdsf.netmyne.com](http://www.kdsf.netmyne.com)
- Educational & support centre. <http://www.disabilitymalaysia.com/>
- Parents support group. <http://groups.yahoo.com/group/DownSyndromeMalaysia>
- Jabatan Pendidikan Khas. <http://www.moe.gov.my/jpkhas/>.
- Jabatan Kebajikan Malaysia. <http://www.jkm.gov.my/>

Table 5. Recommendations for Medical Surveillance for children with Down Syndrome

	Birth - 6 weeks	6 - 10 months	12 months	18 mths - 2½ yrs	3 - 3½ years	4 - 4½ years
Thyroid blood tests <sup>1</sup>	T4 & TSH		T4 & TSH including antibodies		T4 & TSH including antibodies	
Growth monitoring <sup>2</sup>	Length, weight and head circumference checked regularly and plotted on Down's syndrome growth charts.					
Eye check	Visual behaviour: Check for congenital cataract	Visual behaviour: Check for congenital cataract	Visual behaviour: Check for congenital cataract	Orthoptic examination, refraction and ophthalmic examination <sup>3</sup>		Visual acuity, refraction and ophthalmic examination <sup>3</sup>
Hearing check	Neonatal screening, if locally available	Full audiological review (hearing, impedance, otoscopy) by 6-10 months and then annually				
Heart check and other advice	Echocardiogram 0-6 weeks	dental advice				
<b>Age 5 to 19 years</b>						
Paediatric review	Annually					
Hearing	2 yearly audiological review (as above)					
Vision / Orthoptic check	2 yearly					
Thyroid blood tests	At age 5 years, then 2 yearly					
School performance	Check performance and placement					
Sexuality & employment	To discuss when appropriate during adolescence					
<i>Note: The above table are suggested ages. Check at any other time if there are parental or other concerns. Perform developmental assessment during each visit.</i>						
<i>(adapted from Down Syndrome Medical Interest Group (DSMIG) guidelines)</i>						



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## PAEDIATRIC SURGERY

- 88 Appendicitis
- 89 Persistent Vomiting in the Neonate and Child
- 90 Intussusception
- 91 Inguinal Hernias, Hydroceles
- 92 Undescended Testis
- 93 The Acute Scrotum
- 94 Penile Conditions



## APPENDICITIS

Appendicitis is the most common surgical condition of the abdomen in children over the age of 4 years and yet can be a challenge to diagnose and manage. Although diagnosis and treatment have improved over the years, it continues to cause considerable morbidity and even mortality in Malaysia. The deaths appear to be due to delay and difficulty in diagnosis, inadequate perioperative fluid replacement and sepsis.

### Clinical Features

- *Abdominal pain* – Lower abdominal pain is an early and almost invariable feature. Usually the pain starts in the epigastrium or periumbilical region before localising to the lower abdomen or the right iliac fossa. However the younger child may not be able to localise the pain. If there is free pus, the pain is generalised.
- *Nausea and vomiting* occurs in about 90% of children and is an early symptom. Most children have a loss of appetite. A hungry child rarely has appendicitis.
- *Diarrhoea* is more common in the younger age group causing confusion with gastroenteritis. It can be due to pelvic appendicitis or collection of pus within the pelvis.
- *Dysuria and frequency* are also commonly present in the child with pelvic appendicitis or perforated appendicitis

### Physical Findings

- *General* – the child is usually *quiet* and may be dehydrated.
- *Dehydration* must be actively sought for especially in the obese child and the child with perforated appendicitis. A history of vomiting, tachycardia, poor urine output and poor perfusion are indicators of dehydration.
- *Tenderness* on palpation or percussion is essential for the diagnosis. However it may be localised to the right iliac fossa or be generalised. The tenderness may also be mild initially and difficult to elicit in the obese child or if the appendix is retrocaecal. Rebound tenderness is usually not required to make the diagnosis and can cause unnecessary discomfort.
- *Guarding* signifies peritonitis but may be subtle especially if the child is toxic and very dehydrated.
- Rectal examination is only required if other diagnosis are suspected e.g. ovarian or adnexal pathology.

### Investigations

- *Full blood count* – The total white blood cell count may be elevated but a normal count does not exclude appendicitis
- *Blood Urea and Serum Electrolytes* – The sodium level may be apparently normal if the child is dehydrated
- *Serum Amylase* – If pancreatitis cannot be ruled out
- *Ultrasound and CT scan* have been suggested to improve the diagnostic accuracy in doubtful cases. So in our setting the recommendation is that the children need to be assessed by a specialist preoperatively.

## Complications

- *Perforation* can occur within 36 hours of the onset of symptoms. Perforation rate increases with the duration of symptoms and delayed presentation is an important factor in determining perforation rate.

Perforation rate: Adolescent age group - 30-40%

Younger child - up to about 70%.

However, "active observation" with adequate fluid resuscitation and preoperative antibiotics before embarking upon surgery has not shown an increase in morbidity or mortality. Delaying surgery for both perforated and non perforated appendicitis till the daytime did not significantly affect the perforation rate, complications or operating time.

- *Appendicular abscess*, mass and perforation may be treated with intravenous antibiotics to settle the inflammatory and infectious process. If the child settles, this can then be followed by an interval appendicectomy which needs to be done within 14 weeks of the original disease process as recurrent appendicitis has been reported between 10-46 %.

## Management

- children with appendicitis (suspected or confirmed) should be reviewed by a specialist.
- dehydration should be actively looked for in a child with appendicitis especially if it is advanced and if they have a history of vomiting and diarrhoea. The heart rate, perfusion and the urine output should be closely monitored. The blood pressure is usually maintained in the children until they have decompensated.
- rehydration must be aggressive using 20 mls/kg boluses of normal saline or Hartmann's solution given fast up to over 2 hours. The child should be reviewed after each bolus and the rehydration continued until the child's heart rate, perfusion and urine output and electrolytes are within normal limits. Maintenance fluid –  $\frac{1}{2}$  saline + 5% D/W
- antibiotics must be started soon after the diagnosis is made.
- inotropes may need to be started early if the child is in severe sepsis
- there is no rush to go to take the child to the operating theatre and it is recommended that appendicectomies not be performed after 11 pm especially in the sick child. However, the time should be utilised to continue the resuscitation and antibiotics with close monitoring of the child.
- at surgery, a thorough peritoneal washout with copious amount of normal saline is done after the appendicectomy. No drains are required and the skin can be closed with a subcuticular suture.

# PERSISTENT VOMITING IN THE NEONATE AND CHILD

- vomiting in the child is **NOT** normal
- bilious vomiting is **ALWAYS** significant until otherwise proven

## GASTRO-OESOPHAGEAL REFLUX

- more common in infancy than generally recognized
- majority (>90%) resolve spontaneously within the first year of life
- small percentage develop complications

Figure 1. Pathophysiology of Reflux

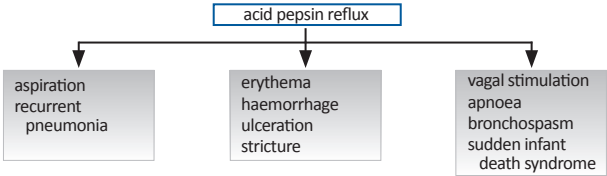


Table 1. Mechanisms of Reflux

### Mechanisms preventing Reflux

#### Anatomical

- length and pressure of the lower and intra-abdominal oesophagus
- angle of His
- hiatal pinch of cock effect

#### Physiological

- coordinate effective peristaltic clearance
- normal gastric emptying

### Factors causing Reflux

- immature lower oesophageal sphincter
- increased intra-gastric pressure, e.g.: pyloric stenosis
- associated anomalies, e.g.: hiatal hernia
- neurologically impaired children

Table 2. Clinical features

#### Infants

- vomiting
- failure to thrive
- repeated otitis media
- oesophagitis- crying, irritability, anemia
- stricture - dysphagia
- aspiration - recurrent infections, asthma
- apnoeic spells, sudden infant death syndrome (SIDS)

#### Children

- vomiting
- heartburn
- regurgitation
- haematemesis
- dysphagia
- aspiration
- Sandifer's Syndrome

## Investigations

- high index of suspicion
- barium swallow and meal
- 24-hour pH monitoring
- endoscopy and biopsy

## Treatment

### Medical

- small frequent feeds
- thickened feeds: cornstarch, cereal, carobel
- position > 30° prop-up for 24 hours a day
- H<sub>2</sub> antagonists/ proton pump blockers

### *Surgical*

- fundoplication
- correction of associated anomalies

### **Complications of fundoplication**

- recurrence
- gas bloat
- inability to vomit
- dysphagia

### **PYLORIC STENOSIS**

- cause- unknown
- usually first born baby boy usually presenting at the 2nd to 8th week of life
- strong familial pattern

### **Clinical Features**

- vomiting - frequent, forceful, non-bilious with/without haematemesis. The child is keen to feed but unable to keep the feed down
- failure to thrive
- dehydration
- constipation
- seizures

### **Physical Examination**

- dehydrated
- a test feed can be given with the child in the mother's left arm and visible gastric peristalsis (left to right) observed for. The doctor's left hand then palpates beneath the liver feeling for a palpable olive sized pyloric tumour against the vertebra.

### **Investigation**

- investigation to confirm diagnosis usually unnecessary
  - abdominal ultrasound
  - barium meal
- pre-operative assessment is very important
  - metabolic alkalosis is the first abnormality
  - hypochloraemia  $< 100$  mmol/l
  - hyponatraemia  $< 130$  mmol/l
  - hypokalaemia  $< 3.5$  mmol/l
  - hypocalcaemia  $< 2.0$  mmol/l
  - jaundice
  - hypoglycemia
  - paradoxical aciduria - a late sign

### **Therapy**

- rehydration
  - low (rapid will cause cerebral oedema) except if perfusion is poor

- fluid
  - ½ saline + 10%D/W (+ 5-10 mmol KCL/kg/day) at 150 ml/kg/day + % dehydration
  - replace nasogastric losses with normal saline
  - *Do Not* give Hartmann's solution (the lactate will be converted to bicarbonate)
- insert a nasogastric tube – 4 hourly aspiration with free flow
- pyloromyotomy after the electrolytes have been corrected

## MALROTATION

A term which embraces a number of different types of abnormal rotation. Important because of the propensity for volvulus of the midgut around the superior mesenteric artery causing vascular compromise of most of the small bowel and colon.

### Types of Clinical Presentation

- *Acute Volvulus*
  - sudden onset of bilious/ non-bilious vomiting
  - abdominal distention with/without a mass
  - bleeding per rectum is a late sign
  - ill baby with distended tender abdomen
- *Chronic Volvulus*
  - caused by intermittent or partial volvulus and results in lymphatic and venous obstruction and enlargement of mesenteric lymph nodes
  - recurrent abdominal pain and vomiting that is usually bilious
  - malabsorption
- Internal Herniation
  - due to lack of fixation of the colon.
  - cause entrapment of bowel by the mesentery of caecum and colon
  - recurrent intermittent intestinal obstruction

## Investigations

- plain Abdominal X-ray
  - all the small bowel is to the right side
  - dilated stomach +/- duodenum with rest of abdomen being gasless
- Barium meal and follow through
  - duodeno-jejunal junction to the right of the spine
  - duodenal obstruction, often with spiral or corkscrew appearance of barium flow
  - presence of small bowel mainly on the right side

## Treatment

### Pre-operative Management

- rapid rehydration with correction of electrolytes
- orogastric or nasogastric tube with 4 hourly aspiration and free flow
- antibiotics (+ inotropes) if septic

### Operative

- reduction of volvulus +/- resection (aim to preserve maximum bowel) (consider 2nd look operation) with division of Ladd's bands



## BILIOUS VOMITING IN A BABY OR CHILD – PLEASE REFER EARLY

Causes of persistent vomiting: numerous: see Table 3

Table 3. Causes of persistent vomiting in children	
<b>Neonates</b>	<b>Infants</b>
<i>General</i>	<i>General</i>
<ul style="list-style-type: none"> <li>• sepsis</li> <li>- meningitis</li> <li>- hydrocephalus/ neurological disorder</li> <li>- urinary tract infection</li> <li>• motility disorder</li> <li>• poor feeding techniques</li> </ul>	<ul style="list-style-type: none"> <li>• sepsis</li> <li>- meningitis</li> <li>- hydrocephalus/ neurological disorder</li> <li>- urinary tract infection</li> <li>• tumours</li> <li>• metabolic disease</li> </ul>
<i>Swallowing disorder</i> - incoordinate	<i>Oesophageal stricture</i>
<i>Oesophageal</i>	<i>Stomach</i>
<ul style="list-style-type: none"> <li>• atresia</li> <li>• webs</li> </ul>	<ul style="list-style-type: none"> <li>• gastro-oesophageal reflux</li> <li>• pyloric stenosis</li> </ul>
<i>Stomach</i>	<i>Small intestines</i>
<ul style="list-style-type: none"> <li>• gastro-oesophageal reflux</li> <li>• duodenal atresia/ stenosis</li> </ul>	<ul style="list-style-type: none"> <li>• malrotation/ volvulus</li> <li>• adhesions</li> <li>• Meckel's diverticulum</li> </ul>
<i>Small intestines</i>	<i>Appendix- rare</i>
<ul style="list-style-type: none"> <li>• malrotation</li> <li>• stenosis/ atresia</li> <li>• adhesions</li> <li>• meconium peritonitis/ ileus</li> <li>• enterocolitis</li> </ul>	<i>Large intestines</i>
<i>Large intestine and rectum</i>	<ul style="list-style-type: none"> <li>• intussusception</li> <li>• Hirschprung's disease</li> <li>• enterocolitis/gastroenteritis</li> </ul>
<ul style="list-style-type: none"> <li>• stenosis/ atresia</li> <li>• Hirschprung's disease</li> <li>• anorectal malformation</li> </ul>	
<b>Older children</b>	
<i>General</i>	<i>Small intestines</i>
<ul style="list-style-type: none"> <li>• sepsis</li> <li>• neurological disorder</li> <li>• tumours</li> <li>• metabolic disease</li> </ul>	<ul style="list-style-type: none"> <li>• malrotation/ volvulus</li> <li>• adhesions</li> <li>• Meckel's diverticulum</li> <li>• foreign body</li> </ul>
<i>Oesophageal stricture</i>	<i>Appendicitis/ peritonitis</i>
<i>Stomach</i>	<i>Large intestines</i>
<ul style="list-style-type: none"> <li>• gastro-oesophageal stricture/ reflux</li> <li>• peptic ulcer disease</li> <li>• pyloric stenosis</li> <li>• gastric volvulus</li> </ul>	<ul style="list-style-type: none"> <li>• intussusception</li> <li>• worm infestation</li> <li>• constipation: habitual</li> </ul>

## INTUSSUSCEPTION

Intussusception is the invagination of one portion of intestine into another with 80% involving the ileocaecal junction. The mortality and morbidity from intussusception in Malaysia is still high due to delay in diagnosis, inadequate intravenous fluid therapy and surgical complications.

It is the most common form of intestinal obstruction in infancy and early childhood with the **peak age group being 2 months to 2 years**. Majority of the children in this age group have **no pathological lead point**. Lymphoid hyperplasia has been implicated. The children may also have a preceding viral illness.

**Common lead points** (usually in the age group outside the above)

- structural – Meckel's diverticulum, duplication cysts,
- neoplastic – lymphoma, polyps, vascular malformations,
- vascular – Henoch-Schonlein purpura, leukaemia
- miscellaneous – foreign body

### Clinical Features

- previously healthy or preceding viral illness
- pain - sudden onset, severe intermittent cramping pain lasting seconds to minutes
- during the time in between attacks lasting between 5 to 30 minutes, the child may be well or quiet
- vomiting – early reflex vomiting consists of undigested food but if the child presents late; the vomiting is bilious due to obstruction.
- stools- Initially normal, then become dark red and mucoid (redcurrant jelly)
- note that small bowel intussusception may have an atypical presentation

### Physical Findings

- well- looking / drowsy / dehydrated / seizures (due to hyponatremia) depending on the stage of presentation
- abdominal mass may be difficult to palpate in a distended abdomen
- abdominal distension is a late sign

### Investigations

- *plain abdominal X-ray* – target sign, absence of caecal gas, loss of visualization of the tip of the liver, paucity of bowel gas in the right lower quadrant, small bowel obstruction (late sign)
- *ultrasound* – useful diagnostic tool. Characteristic signs - target sign on transverse section (figure 2) and pseudo-kidney sign on longitudinal section. May also help to identify lead points if present.
- *barium enema* – for diagnosis and reduction if present (Figure 3)



Figure 1. Plain abdominal X-ray showing dilated loops of small bowel

## Management

### Resuscitation

- aggressive rapid rehydration with boluses of 20 mls/kg of Normal saline/ Hartmann's solution till parameters are normal
- Do NOT proceed to enema reduction or surgery till fully resuscitated
- close monitoring of vital signs and urine output
- antibiotics and inotropes as required

### Non operative reduction

- should be attempted in most patients, if there are trained radiologists and surgeons available, as successful reduction rate is about 80-90%.
- methods
  - barium enema reduction
  - air or oxygen reduction
  - ultrasound guided saline reduction
- the younger child who has been sick for a longer duration of more than 36 hours and has complete bowel obstruction is **at risk of colonic perforation** during attempted enema reduction
- delayed repeat enemas done after 30 minutes or more after the initial unsuccessful reduction enema may improve the outcome of a select group of patients. These patients are clinically stable and the initial attempt had managed to move the intussusceptum.

**Table 1. Contraindications to enema reduction**

- peritonitis
- bowel perforation
- severe shock
- neonates or children > 3 years old
- history > 48 hours

**Table 2. Indications for surgery**

- failed non-operative reduction
- bowel perforation
- suspected lead point
- small bowel intussusception

### Recurrence of intussusception

- rate – 5-10% with lower rates after surgery
- success rate for non operative reduction in recurrent intussusception is 30-60%

*Successful management of intussusception depends on high index of suspicion, early diagnosis, adequate resuscitation and prompt reduction.*

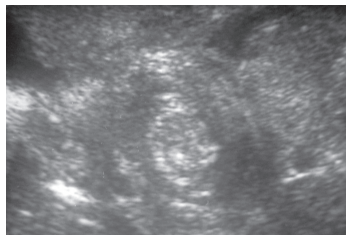


Figure 2. Ultrasound showing target sign



Figure 3. Barium enema reduction showing intussusceptum ("claw sign")

## INGUINAL HERNIAS, HYDROCOELE

Both are due to a patent processus vaginalis peritonei. The patent communication in the hydrocoele is smaller and so sac contains only fluid. The hernial sac can contain bowel, omentum or ovaries.

### INGUINAL HERNIA

- Incidence – 0.8%-4.4% in children, but 16-25% in premature babies  
Boys:girls = 6 : 1
- Site: 60% right side but 10% may be bilateral

**Table 1. Presentation**

- bulge in groin – extends into scrotum when crying/straining. Reducible.
- with complications
- lump in groin (girls) – sliding hernia containing ovary (rule out testicular feminization syndrome if bilateral)

**Table 2. Complications**

- incarceration/ irreducibility
  - highest incidence (2/3) < age 1 year
- testicular atrophy
- torsion of ovary

### Management

- hernia: operate as soon as possible
  - premature: before discharge (corrected age-44 to 60 week)
  - infant: as soon as possible
  - older child: on waiting list
- operation: herniotomy

#### *Incarcerated hernia*

- attempt manual reduction as soon as possible to relieve compression on the testicular vessels. The child is rehydrated and then given intravenous analgesic with sedation. Constant gentle manual pressure is applied in the direction of the inguinal canal to reduce the hernia. The sedated child can also be placed in a Trendelenburg position for an hour to see if the hernia will reduce spontaneously.
- herniotomy is performed 24 to 48 hours later

### HYDROCOELE

- usually present since birth. May be communicating or encysted
- is typically a soft bluish swelling which is not reducible but may fluctuate in size

### Management

- the patent processus closes spontaneously within the first year of life, in most children
- if the hydrocoele does not resolve after the age of 2 years, herniotomy with drain age of hydrocoele is done

## UNDESCENDED TESTIS

An empty scrotum may be due to the testis being undescended, ectopic, retractile or absent. Familial predisposition present in 15%. 10 - 25% are bilateral.

### Incidence

- at birth: Full term infant 3.4%  
Premature infant 30.3%
- at 1 year: Full term infant 0.8 %  
Premature 0.8%
- adult 0.7-1%

*Spontaneous descent may occur within the 1st year of life. after which descent is rare.*

### Complications

- trauma (especially if in inguinal canal).
- torsion extravaginal type
- decreased spermatogenesis. Damage occurs in the first 6-12 months of life. 90% of patients with orchidopexy before 2 years have satisfactory spermatogenesis. If done after >15 years old, fertility is 15%.
- testicular tumour: Risk is 22 times higher than the normal population (Intra-abdominal 6 times more than inguinal). It makes the testis more accessible to palpation and thus early diagnosis.
- associated with hernias (up to 65%), urinary tract anomaly (3%, e.g. duplex and horseshoe), anomalies of epididymis or vas deferens and problems of intersex.
- psychological problems

### Management

1. Ask mother whether she has ever felt the testis in the scrotum, more easily felt during a warm bath.
2. Examine patient (older children can be asked to squat). A normal sized scrotum suggests retractile testis. The scrotum tends to be hypoplastic in undescended testis.
3. If bilateral need to rule out dysmorphic syndromes, hypopituitarism, and chromosomal abnormalities (e.g. Klinefelter). Exclude virilized female (Congenital Adrenal Hyperplasia).
4. Observe the child for the 1st year of life. If the testis remains undescended after 1 year of life surgery is indicated. Surgery should be done between 6-18 months of age.
5. For bilateral impalpable testis: Management of choice is Laparoscopy ± open surgery. Ultrasound, CT scan or MRI to locate the testes have not been shown to be useful. Check chromosomes and 17 OH progesterone levels if genitalia are ambiguous.

# THE ACUTE SCROTUM

## Torsion of the Testis

***Torsion of the testis is an emergency as failure to detort testis within 6 hours will lead to testicular necrosis***

There are 2 types of torsion:

- **Extravaginal**

The torsion usually occurs in the perinatal period or during infancy and is thought to be probably due to an undescended testis

- **Intravaginal**

This is due to a high investment of tunica vaginalis causing a “bell-clapper” deformity. It usually occurs in boys between 10-14 years old.

**Table 1. Causes of the acute scrotum**

- acute testicular torsion
- torsion of epididymal and testicular appendages
- epididymo-orchitis
- incarcerated inguinal hernia
- idiopathic scrotal oedema
- acute hydrocoele
- Henoch-Schonlein purpura
- tumours
- trauma
- scrotal (Fournier’s) gangrene
- symptomatic varicocele

**Table 2. Symptoms**

- sudden severe pain (scrotum and referred to lower abdomen)
- nausea and vomiting
- no fever or urinary tract infection symptoms until later

**Table 3. Physical findings**

**Early**

- involved testis - high, tender, swollen
- spermatic cord - swollen, shortened, tender
- contralateral testis - abnormal lie, usually transverse

**Late**

- reactive hydrocele
- scrotal oedema

## Investigation

- doppler /radioisotope scan. It may be normal initially

## Management

- exploration: salvage rate: 83% if explored within 5 hours  
20% if explored after 10 hours
- if viable testis, fix bilaterally
- if non-viable, orchidectomy to prevent infection and sympathetic orchitis (due to antibodies to sperm) and fix the opposite testis

## TORSION OF APPENDAGES OF TESTIS AND EPIDIDYMIS

Appendages are Mullerian and mesonephric duct remnants

Importance - in a late presentation there may be confusion with torsion of testis

**Table 4. Symptoms**

- age 8 - 10 years old
- sudden onset of pain, mild initially but gradually increases in intensity

**Table 5. Physical findings**

**Early**

- minimal redness of scrotum with a normal non-tender testis
- tender nodule “blue spot” (usually at upper pole of testis) is pathognomonic

**Late**

- reactive hydrocele with scrotal oedema making palpation of testis difficult

### Treatment:

- if sure of diagnosis of torsion appendages of testis, the child can be given the option of non-operative management with analgesia and bed rest
- if unsure of diagnosis, explore and remove the twisted appendage (this ensures a faster recovery of pain too!)

### EPIDIDYMO-ORCHITIS

Can occur at any age.

#### Route of infection

- reflux of infected urine
- blood borne secondary to other sites
- mumps
- sexual abuse

**Table 6. Symptoms**

- gradual onset of pain with fever
- may have a history of mumps
- +/- dysuria or frequency

**Table 7. Physical findings**

- testis may be normal with a reactive hydrocoele
- epididymal structures are tender and swollen

#### Treatment

- if unsure of diagnosis, explore
- investigate underlying abnormality (renal ultra sound, MCU and IVU if a urinary tract infection is also present)
- treat infection with antibiotics

### IDIOPATHIC SCROTAL OEDEMA

The cause is unknown but has been postulated to be due to an allergy.

#### Symptoms

- sudden acute oedema and redness of scrotum
- painless
- starts as erythema of perineum and extending to lower abdomen
- well child, no fever
- testes: normal

#### Treatment

This condition is self-limiting but the child may benefit from antibiotics and antihistamines.

## PENILE CONDITIONS

### PHIMOSIS

**Definition :** True preputial stenosis

(In a normal child the foreskin is non-retractile till age of 5 years)

**Table 1. Causes**

- congenital - rare
- infection- balanoposthitis
- recurrent forceful retraction of foreskin
- Balanoxerotica obliterans (BXO)<sup>1</sup>

**Table 2. Symptoms**

- ballooning of foreskin on micturition
- recurrent balanoposthitis
- urinary retention
- urinary tract infection

<sup>1</sup>**BXO:**

- chronic inflammation with fibrosis of foreskin and glans causing a whitish appearance with narrowing of prepuce and meatus
- treatment: careful circumcision +/- meatotomy
- will require long term follow-up to observe for meatal stenosis

### Management

- treat infection if present
- elective circumcision

### BALANOPOSTHITIS

#### Definition

*Balanitis* - inflamed glans, *Posthitis* - inflamed foreskin

Cause effect: phimosis with or without a urinary tract infection

#### Treatment

- check urine cultures
- Sitz bath
- analgesia
- antibiotics
- circumcision later if there is associated phimosis or recurrent infection

### PARAPHIMOSIS

Cause: forceful retraction of foreskin (usually associated with phimosis)

#### Treatment

- immediate reduction of the foreskin under sedation/analgesia (Use an anaesthetic gel or a penile block, apply a warm compress to reduce oedema and then gentle constant traction on foreskin distally)
- if reduction is still unsuccessful under a general anaesthetic then a dorsal slit is performed
- the child will usually need a circumcision later



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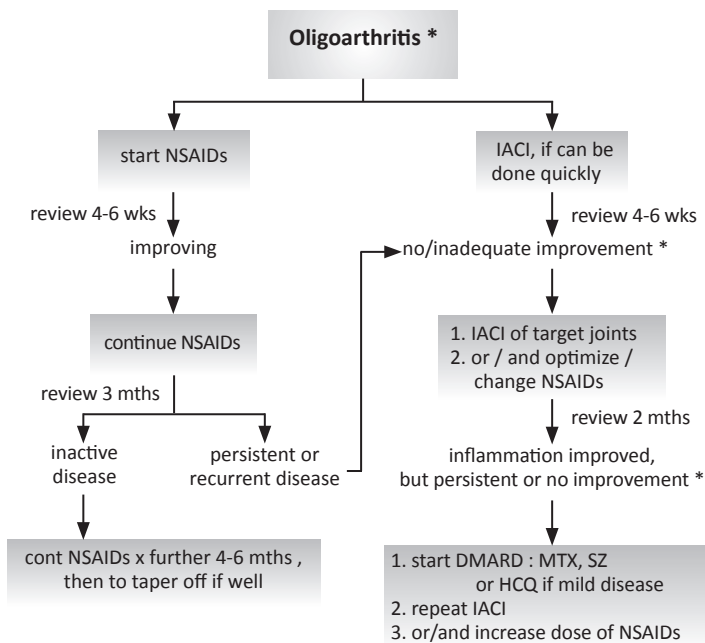
# RHEUMATOLOGY

95 Juvenile Idiopathic Arthritis



## TREATMENT FOR CHILDREN WITH CHRONIC ARTHRITIS

### Oligoarthritis (1-4 joints)



### Remember to screen for uveitis

#### Note:

All patients with persistent inflammation should be on DMARDs within 6 months of diagnosis even if only having oligoarthritis.

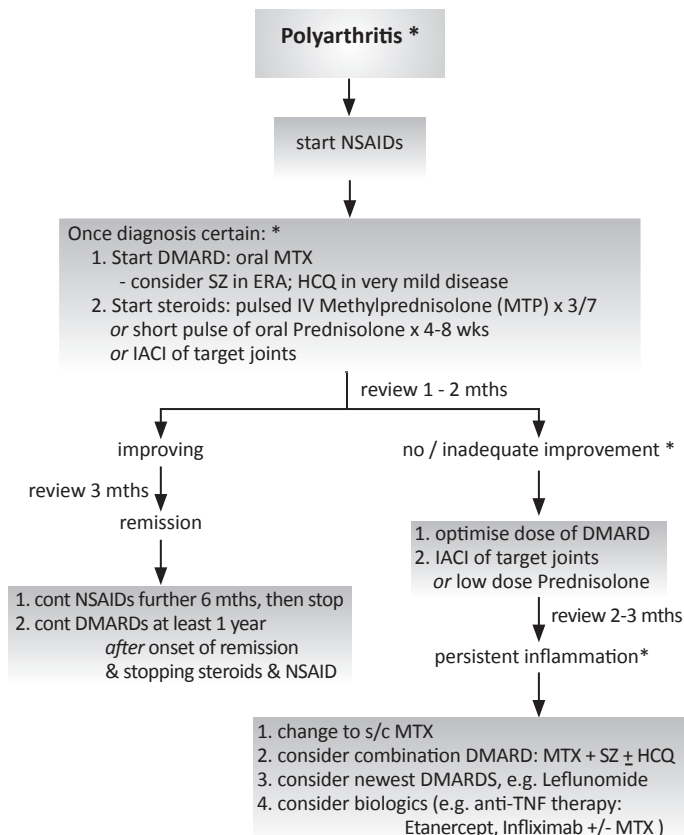
**Abbreviations** \*: consider referral to Paeds Rheumatologist / reconsider diagnosis;

IACI : Intra-articular corticosteroid injection; MTX : methotrexate; SZ : sulphasalazine;

HCQ: hydroxychloroquine; DMARD, disease modifying anti-rheumatic drugs.

## TREATMENT FOR CHILDREN WITH CHRONIC ARTHRITIS

### Polyarthritis ( $\geq 5$ joints)



### Remember to screen for uveitis

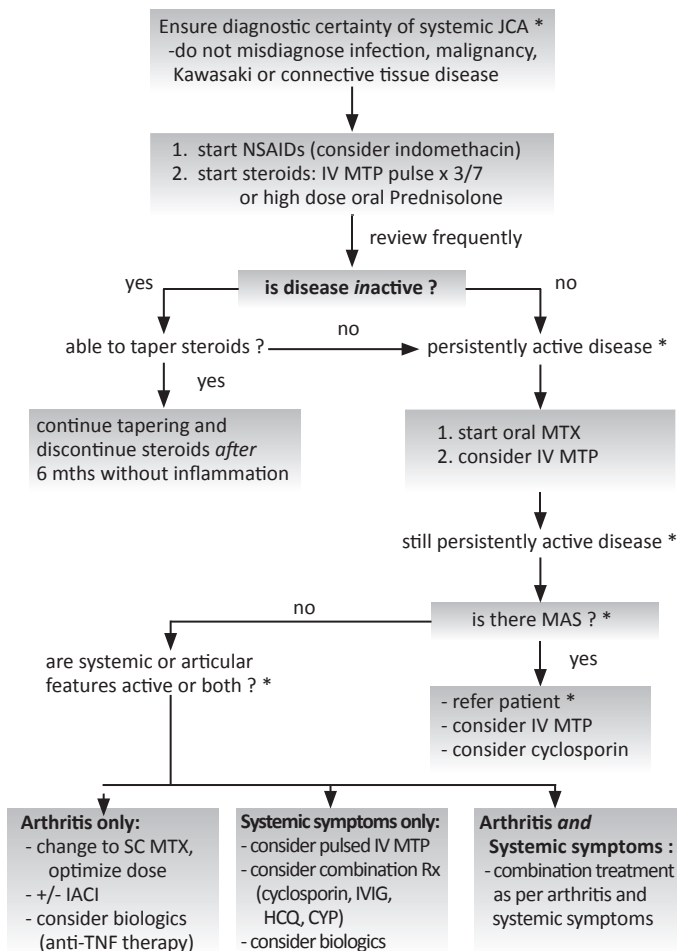
Best opportunity to achieve remission in first two years of disease

Avoid accepting low grade inflammation until all avenues explored

**Abbreviations \***: consider referral to Paeds Rheumatologist / reconsider diagnosis; IACI : Intra-articular corticosteroid injection; MTX : methotrexate; SZ : sulphasalazine; HCQ: hydroxychloroquine; ERA: enthesitis related arthritis; DMARD, disease modifying anti-rheumatic drugs.

## TREATMENT FOR CHILDREN WITH CHRONIC ARTHRITIS

### Systemic onset JIA



**Remember to screen for uveitis**

Avoid gold, penicillamine, SZ and caution with new drugs as risk of developing Macrophage Activation Syndrome (MAS)

**Abbreviations** - \*: consider referral to Paeds Rheumatologist / reconsider diagnosis; IACI : Intra-articular corticosteroid injection; MTX : methotrexate; SZ : sulphasalazine; HCQ: hydroxychloroquine; CYP: cyclophosphamide; IVIG: intravenous immunoglobulins

# JUVENILE IDIOPATHIC ARTHRITIS (JIA)

## 1. Definition

Definite arthritis of unknown aetiology, onset before the age 16 yrs; persists for 6 wks.

Table 1: Symptoms & Signs

articular	extra-articular
joint swelling joint pain joint stiffness / gelling after periods of inactivity joint warmth restricted joint movements limping gait	<b>general</b> fever, pallor, anorexia, loss of weight <b>growth disturbance</b> <ul style="list-style-type: none"> <li>• general – growth failure, delayed puberty</li> <li>• local - limb length / size discrepancy, micronagthia</li> </ul> <b>skin</b> <ul style="list-style-type: none"> <li>• subcutaneous nodules</li> <li>• rash – systemic, psoriasis, vasculitis</li> </ul> <b>others</b> hepatomegaly, splenomegaly, lymphadenopathy, serositis, muscle atrophy / weakness uveitis – chronic (silent), acute in Enthesitis related arthritis (ERA) <b>enthesitis*</b>

\* inflammation of the enthuses (the sites of insertion of tendon, ligament or joint capsule into bone)

## 2. Diagnosis and Differential diagnosis : JIA is a diagnosis of exclusion

Table 2. Helpful pointers in assessing articular symptoms:

	inflammatory	mechanical	psychosomatic
pain	+/-	+	+++
stiffness	++	-	+
swelling	+++	+/-	+/-
instability	+/-	++	+/-
sleep disturbance	+/-	-	++
physical signs	++	+	+/-

Table 3: Differential diagnosis of JIA

monoarthritis	polyarthritis
<b>Acute</b> acute rheumatic fever reactive arthritis – post viral/ post enteric / post streptococcal infection septic arthritis / osteomyelitis early JIA malignancy – leukaemia, neuroblastoma haemophilia trauma <b>Chronic</b> JIA – oligoarthritis, ERA, psoriatic chronic infections – TB, fungal, brucellosis pigmented villonodular synovitis sarcoidosis synovial haemangioma bone malignancy	JIA – polyarthritis (RF positive or negative), ERA, psoriatic arthritis reactive arthritis Lyme disease SLE other connective tissue diseases inflammatory bowel disease sarcoidosis familial hypertrophic synovitis syndromes immunodeficiency syndromes mucopolysaccharidoses

*Helpful pointers in diagnosis:*

- avoid diagnosing arthritis in peripheral joints if no observed joint swelling.
- consider other causes, particularly if only one joint involved.
- active arthritis can be present with the only signs are decreased range of movement and loss of function.
- in axial skeleton (including hips), swelling may not be seen. Diagnosis is dependent on inflammatory symptoms (morning stiffness, pain relieved by activity, pain on active and passive movement, limitation of movement). Investigations to exclude other diagnosis are important.
- in an ill child with fever, loss of weight or anorexia, consider infection, malignancy and other connective tissue diseases.

**3. Investigations**

The diagnosis is essentially clinical; laboratory investigations are only supportive. No laboratory test or combination of tests can confirm the diagnosis of JIA.

- FBC and Peripheral blood film – excludes leukaemia
- ESR or CRP – markers of inflammation
- X-ray/s of affected joint/s – esp. if single joint involved to look for malignancy
- Antinuclear antibody – identifies a risk factors for uveitis
- Rheumatoid factor – assess prognosis in polyarthritis and need for more aggressive therapy

*\*Antinuclear antibody and Rheumatoid factor are NOT required to make a diagnosis.*

*\* Other Ix done as necessary : complement levels, ASOT, Ferritin, immunoglobulins (IgG, IgA and IgM), HLA B27, synovial fluid aspiration for microscopy and culture, echocardiography, bone marrow aspiration.*

**4. Management**

(i) Medical treatment

- refer management algorithm (*see preceding pages*)

*Table 4. Dosages of drugs commonly used in JIA*

name	dose	frequency
Ibuprofen	5-10 mg/kg/dose	3-4/day
Naproxen	5-10 mg/kg/dose	2/day
Indomethacin	0.5 - 1 mg/kg/dose	2-3/day
Diclofenac	0.5 - 1 mg/kg/dose	3/day
Methotrexate	10 - 15 mg/m <sup>2</sup> /dose (max 25 mg/dose)	1/week
Folic acid	2.5 - 5 mg/kg/dose	1/week
Sulphasalazine	15 - 25 mg/kg/dose (start 2.5 mg/kg/dose & double weekly; max 2 Gm/day)	2/day
Hydroxychloroquine	5 mg/kg/dose	1/day
Methylprednisolone	30 mg/kg/dose (max 1 Gm / dose)	1/day x 3 days
Prednisolone	0.1 - 2 mg/kg/dose	1-3/day

*Note: Patients on DMARDs (e.g. Methotrexate, Sulphasalazine) and long term NSAIDs (e.g. Ibuprofen, Naproxen) require regular blood and urine monitoring for signs of toxicity*

(ii) Physiotherapy

- avoid prolonged immobilisation
- strengthens muscles, improves and maintains range of movement
- improves balance and cardiovascular fitness



(iii) Occupational Therapy

- splinting when necessary to reduce pain and preserve joint alignment
- to improve daily quality of life by adaptive aids and modifying the environment

(iv) Ophthalmologist

- all patients must be referred to the ophthalmologist for uveitis screening (as uveitis can be asymptomatic) and have regular follow-up even if initial screening normal

(v) Others

- ensure well balanced diet, high calcium intake
- encourage regular exercise and participation in sports and physical education
- family support and counselling when required
- referral to other disciplines as required: Orthopaedic surgeons, Dentist.

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# POISONS AND TOXINS

96 Snake Bites

97 Common Poisons

98 Anaphylactic Reactions



## SNAKE BITE

### Introduction

- in 1999-2001, there were a total of 19,335 admissions to hospitals throughout Malaysia due to venomous animal bites and stings. A significant numbers are due to snakebite and hymenoptera (bee) stings.
- not all snakes are venomous. In Malaysia there are approximately 40 species of venomous snakes (18 land snakes, all 22 of sea snakes) belonging to two families:
  - *Elapidae* – have short, fixed front fangs. The family includes cobras, kraits, coral snakes and sea snakes.
  - *Viperidae* – have a triangular shaped head and long, retractable fangs. The most important species in Malaysia are *Calloselasma rhodostoma* (Malayan pit viper) and *Trimeresurus genus* (green viper). The Malayan pit vipers are common in the northern part of Peninsular Malaysia but are not found in Sabah and Sarawak.
- cobra and Malayan pit vipers cause most of the cases of snakebites in Malaysia. Bites by sea snakes, coral snakes and kraits are uncommon.
- the snake venom is made up of procoagulant enzymes (activate coagulation cascade), phospholipase A2 (myotoxic, neurotoxic, cardiotoxic; causes haemolysis and increased vascular permeability), proteases (tissue necrosis), polypeptide toxins (disrupt neuromuscular transmissions) and other components.

Table 1. Venomous land snakes in Malaysia

Family	Scientific name	Common Malay name
<i>Viperidae</i>		
Malayan pit viper	<i>Calloselasma rhodostoma</i>	ular kapak bodoh
temple pit viper	<i>Trimeresurus wagleri</i>	ular kapak tokong
red-tailed pit viper	<i>Trimeresurus popeorum</i>	ular kapak ekor merah
mountain pit viper	<i>Trimeresurus monticola</i>	ular kapak gunung
Sumatran pit viper	<i>Trimeresurus sumatranus</i>	ular kapak sumatera
mangrove pit viper	<i>Trimeresurus purpureomaculatus</i>	ular kapak bakau
flat-nosed pit viper	<i>Trimeresurus puniceus</i>	ular kapak hidung pipeh
<i>Elapidae</i>		
common black cobra	<i>Naja naja</i>	ular senduk
king cobra	<i>Ophiophagus Hannah</i>	ular tedung selar
banded krait	<i>Bungarus fasciatus</i>	ular katang belang
Malayan krait	<i>Bungarus candidus</i>	ular katang tebu
red-headed krait	<i>Bungarus flaviceps</i>	ular katang kepala merah
spotted coral snake	<i>Callophis gracilis</i>	ular pantai bintik
small-spotted coral snake	<i>Callophis maculiceps</i>	ular pantai bintik kecil
blue Malayan coral snake	<i>Maticora bivirgata</i>	ular pantai biru biru
banded coral snake	<i>Maticora intestinalis</i>	ular pantai belang

### Clinical features

#### *Elapids*

- cobras usually cause pain and swelling at the bite site may progress to neurological dysfunction: ptosis, ophthalmoplegia, dysphagia, aphasia, respiratory paralysis
- Kraits cause minimal local effects but may cause central nervous system manifestations

- sea snakes cause minimal local effects and mainly musculoskeletal findings: myalgia, stiffness and paresis leading to myoglobinuria and renal failure. Paralysis can also occur.

### *Viperidae*

- pit vipers – cause extensive local effects: immediate pain, swelling, blisters and necrosis and systemic bleeding tendencies. The common sites of bleed are bite site, gingival sulci and venepuncture sites.

*Note: There may be overlap of clinical features caused by venoms of different species of snake. For example, some cobras can cause severe local envenoming (formerly thought to be due to only vipers).*

## **Management**

### *First aid*

The aims are to retard absorption of venom, provide basic life support and prevent further complications.

- reassure the victim – anxiety state increases venom absorption.
- immobilise the bitten limb with splint or sling (retard venom absorption)
- apply a firm bandage for some elapid bites (delay absorption of neurotoxic venom) but not for viper bites whose venom cause local necrosis
- leave the wound alone - DO NOT incise, apply ice or other remedies
- tight (arterial) tourniquets are not recommended
- do not attempt to kill the snake. However, if it is killed bring the snake to hospital for identification. Do not handle the snake with bare hands: even a severed head can bite!
- transfer the victim quickly to the nearest health facility

### *Treatment in the hospital*

- do rapid clinical assessment and resuscitation including Airway, Breathing, Circulation and level of consciousness. Monitor vital signs (blood pressure, respiratory rate, pulse rate).
- establish IV access; give oxygen and other resuscitations as indicated.
- history: inquire part of body bitten, timing, type of snake and history of atopy.
- examine
  - bitten part for fang marks (sometimes invisible), swelling, tenderness, necrosis
  - distal pulses (reduced or absent in compartment syndrome)
  - patient for bleeding tendencies – tooth sockets, conjunctiva, puncture sites
  - patient for neurotoxicity – ptosis, ophthalmoplegia, bulbar and respiratory paralysis
  - patient for muscle tenderness, rigidity (sea snakes)
  - urine for myoglobinuria
- send blood investigations (full blood count, renal function tests, prothrombin time/partial thromboplastin time, group and cross matching)
- perform a 20-min Whole Blood Clotting Test. Put a few mls of blood in a clean, dry glass test tube, leave for 20 min, and then tipped once to see if it has clotted. Unclotted blood suggests hypofibrinogenaemia due to pit viper bite and rules out an elapid bite.
- review immunisation history: give booster antitetanus toxoid injection if indicated.
- venom detection kit is used in some countries to identify species of snake. However, it is not available in Malaysia.
- admit to ward for at least 24 hours (unless snake is definitely non-venomous).

### Antivenom treatment

Antivenom is the only specific treatment for envenomation. Give as early as indicated for best result. However, it can be given as long as the signs of systemic envenomation are still present. For local effect, antivenom is probably not effective if given more than a few hours after envenomation.

Indications for antivenom:

- haemostatic abnormalities, e.g. spontaneous systemic bleeding, incoagulable blood or thrombocytopenia ( $<100 \times 10^9/\text{litre}$ ).
- neurotoxicity.
- cardiovascular dysfunction, e.g. hypotension or shock.
- generalised rhabdomyolysis (muscle aches and pains).
- acute renal failure.
- significant local effect, e.g. local swelling more than half the bitten limb, extensive blistering or bruising, bites on digit or rapid progression of swelling.
- helpful laboratory investigations suggesting envenomation include anaemia, thrombocytopenia, leucocytosis, raised serum enzymes (creatinase kinase, aspartate aminotransferase, alanine aminotransferase), hyperkalaemia, and myoglobinuria.

### Choice of antivenom

- if biting species is known, give monospecific (monovalent) antivenom (more effective and less adverse reactions).
- if it is not known, clinical manifestations may suggest the offending species:
  - local swelling with neurological signs = cobra bites
  - extensive local swelling + bleeding tendency = Malayan Pit vipers
- if still uncertain, give polyvalent antivenom.
- no antivenom is available for Malayan kraits, coral snakes and some species of green pit vipers. Fortunately, bites by these species are rare and usually cause only trivial envenoming.

### Dosage and route of administration

Amount given is usually empirical. Recommendations from manufacturers are usually very conservative as they are mainly based on animal studies (Table 2).

- repeat antivenom administration until signs of envenomation resolved.
- give through IV route only. Dilute antivenom in any isotonic solution (5-10ml/kg, bigger children dilute in 500mls of IV solution) and infuse the whole amount in one hour.
- infusion may be discontinued when satisfactory clinical improvement occurs even if recommended dose has not been completed
- do not perform sensitivity test as it poorly predicts anaphylactic reactions.
- do not inject locally at the bite site.

Table 2: Guide to initial dosages of some important antivenoms

Species	Antivenom manufacturer	Initial dose
Malayan pit viper	Thai Red Cross (Monovalent)	100 mls
Cobra	Twyford Pharmaceuticals (monovalent)	50 mls (local) 100 mls (systemic)
	Serum Institute of India;	50 mls (local)
	Biological E. Limited, India (Polyvalent)	100 - 150 mls (systemic)
King Cobra	Thai Red Cross (Monovalent)	50 - 100 mls
Common sea snake	CSL, Australia (polyvalent)	1 000 units (1 vial)

- prepare adrenaline, hydrocortisone, antihistamine and resuscitative equipment and be ready if allergic reactions occur.
- pretreatment with SC adrenaline remains controversial. Small controlled studies in adults have shown it to be effective in reducing risk of reactions. However, its effectiveness and appropriate dosing in children have not been evaluated. There is no strong evidence to support the use of hydrocortisone/antihistamine as premedications. Consider their use in the patient with history of atopy.

### *Antivenom reactions*

3 types of reactions may occur:

- early anaphylactic reactions
  - occur 10-180 minutes after starting antivenom
  - symptoms range from itching, urticaria, nausea, vomiting, and palpitation to severe systemic anaphylaxis: hypotension, bronchospasm and laryngeal oedema
  - stop antivenom infusion: give adrenaline IM (0.01ml/kg of 1 in 1000), antihistamine, e.g. chlorpheniramine 0.2mg/kg, hydrocortisone 4mg/kg/dose and IV fluid resuscitation (if hypotensive)
  - if only mild reactions, restart infusion at a slower rate
- pyrogenic reactions
  - occur 1-2 hours after treatment; are due to endotoxin compounds in antivenom
  - symptoms include fever, rigors, vomiting, tachycardia and hypotension
  - give treatment as above
  - treat fever with paracetamol and tepid sponging
- late reactions
  - occur about a week later
  - a serum sickness-like illness: fever, arthralgia, lymphadenopathy, etc.
  - treat with chlorpheniramine 0.2mg/kg/day in divided doses for 5 days
  - if severe, give oral prednisolone (0.7 – 1mg/kg/day) for 5-7 days

### *Anticholinesterases*

- should always be tried in severe neurotoxic envenoming, especially when no specific antivenom is available, e.g. bites by Malayan krait and coral snakes. The drugs have a variable but potentially useful effect.
- give test dose of IV edrophonium chloride (Tensilon) (0.25mg/kg, adult 10mg) with IV atropine sulphate (50µg/kg, adult 0.6mg)
- if patients respond convincingly, maintain with IV neostigmine methylsulphate (50-100µg/kg) and atropine, four hourly by continuous infusion

### *Supportive/ancillary treatment*

- clean wound with antiseptics
- give analgesia to relief pain (avoid aspirin). In severe pain, morphine may be administered with care. Watch closely for respiratory depression
- give antibiotics if the wound looks contaminated or necrosed  
e.g. IV crystalline penicillin +/- gentamicin, amoxicillin/clavulanic acid, erythromycin or a third generation cephalosporin
- respiratory support – respiratory failure may require assisted ventilation.
- watch for compartment syndrome – pain, swelling, cold distal limbs and muscle paresis. Get early orthopaedic/surgical opinion. Patient may require urgent fasciotomy. Correct coagulation abnormalities with fresh frozen plasma and platelets before any surgical intervention.
- desloughing of necrotic tissues should be carried out as required.
- for oliguria and renal failure, e.g. due to sea snake envenomation, measure daily urine output, serum creatinine, urea and electrolytes. If urine output fails to increase after rehydration and diuretics (e.g. frusemide), start renal dose of dopamine (2.5µg/kg/minute IV infusion) and place on strict fluid balance. Dialysis is rarely required.

### **Pitfalls in management**

- *giving antivenom 'prophylactically' to all snakebite victims.* Not all snakebites by venomous snakes will result in envenoming. On average, 30% bites by cobra, 50% by Malayan pit vipers and 75% by sea snakes DO NOT result in envenoming. Antivenom is expensive and carries the risk of causing severe anaphylactic reactions (as it is derived from horse or sheep serum). Hence, it should be used only in patients in whom the benefits of antivenom are considered to exceed the risks.
- *delaying in giving antivenom in district hospitals until victims are transferred to referral hospitals.* Antivenom should be given as soon as it is indicated to prevent morbidity and mortality. District hospitals should stock important antivenoms and must be equipped with facilities and staff to provide safe monitoring and care during the antivenom infusion.
- *giving polyvalent antivenom for envenoming by all type of snakes.* Polyvalent antivenom does not cover all types of snakes, e.g. Sii polyvalent (imported from India) is effective in cobra and some kraits envenoming but is not effective against Malayan pit viper. Refer to manufacturer drug insert for details.
- *giving smaller doses of antivenom for children.* The dose should be the same as for adults. Amount given depends on the amount of venom injected rather than the size of victim.
- *giving pretreatment with hydrocortisone / antihistamine for snakebite victims.* Snakebites do not cause allergic or anaphylactic reactions. These medications may be considered in those who are given ANTIVENOM.



## COMMON POISONS

### Principles in approach to poisoning

- there is no role for the use of emetics in the modern treatment of poisoning.
- the use of activated charcoal for reducing drug absorption should be considered if patient presents within 1 hour of ingestion. A single dose of 1g/kg body wt can be given by mouth or nasogastric tube within 1 hour of ingestion of a well charcoal absorbed poison and > 1 hour in the case of a slow release drug preparation.
- gastric lavage not recommended unless patient has ingested a potentially life threatening amount of poison and procedure can be done within 1 hour of ingestion
- when in doubt about the nature of poison, contact the poison centre for help.

### Laboratory investigations

- a careful history may obviate the need for blood tests
- blood glucose should be taken in all cases
- blood gas analysis in any patient with respiratory insufficiency, hyperventilation or metabolic acid base disturbance is suspected
- electrolyte estimation may be useful as hypokalaemia may occur in acute poisoning
- routine measurement of paracetamol level should be performed in deliberate poisoning in the older child
- radiology may be used to confirm ingestion of metallic objects, iron salts
- ECG is of limited diagnostic value although prolonged PR and QRS in an unconscious patient should prompt a diagnosis of Tricyclic Antidepressant poisoning

### PARACETAMOL

Paracetamol is also called acetaminophen. Poisoning occurs when > 150mg/kg ingested. Fatality is unlikely if < 225mg/kg is ingested.

### Clinical Manifestations

- Clinical staging:

*Table 1. Clinical staging in paracetamol poisoning*

Stage 1 - nausea vomiting within 12-24 hours, some asymptomatic

Stage 2 - liver enzymes ↑ by 24 hours after ingestion; symptoms often abate

Stage 3 - liver enzymes abnormalities peak at 48-72 hours

- symptoms of nausea and vomiting, anorexia return

- clinical course results in recovery or hepatic failure

- there may be renal impairment

Stage 4 - recovery phase lasts 7-8 days

- most serious effect is liver damage which may not be apparent for the first 2 days

### Management

- communicating the diagnosis is preferably handled in private by a senior medical officer or specialist who is familiar with the natural history, genetic aspect and management of Down syndrome.
- careful examination to look for associated complications.
- investigations: 1. echocardiogram by 2 weeks (if clinical examination or ECG were abnormal) or 6 weeks. 2. Chromosomal analysis. 3. T4 /TSH at birth or by 1-2 weeks of life.

## Management

- measure plasma paracetamol level at 4 hours after ingestion and then 4 hourly.  
Other investigations: RBS/LFT/PT/PTT/RFT daily for 3 days
- initiation of N-Acetylcysteine (NAC) within 10 hours of ingestion; it is still beneficial up to 24 hours of ingestion
  - IV NAC if 4 hour plasma paracetamol level > 150µg/ml.  
Give 150mg in 200mls D5 over 15 min,  
followed by 50mg/kg in 500mls D5 over 4 hours,  
then 100mg/kg in 500mls D5 over 16 hours.
  - NAC is less effective if given > 15 hours after ingestion. Decision is based on the Rumack- Matthew nomogram (Figure 1). Plot the serum level of paracetamol drawn at least 4 hours following ingestion.
  - for patients who are already taking enzyme-inducing drugs, they should be given NAC if the levels are 50% or more of the standard reference line.
- If no blood levels are available, start treatment based on clinical history. Therapy can be stopped once level obtained is confirmed in the non toxic range.
- ensure NAC is appropriately diluted and patient does not become fluid overloaded
- if PT ratio > 3.0, give IM Vitamin K 1- 10mg. Fresh frozen plasma or clotting factor concentrate may be necessary.
- treat complications of acute hepatorenal failure.

## Prognosis

- Without treatment,  $\frac{2}{3}$  will develop severe liver and/or renal damage and 5 % will die
- If treatment given within 15 hours of ingestion, prognosis is excellent

## SALICYLATE

Ingestion of > 0.15 mg/kg will cause symptoms; fatal dose is 0.2 - 0.5g/kg.

Its main effects are as a metabolic poison causing metabolic acidosis and hyperglycaemia.

- clinical features
  - general: hyperpyrexia, profuse sweating and dehydration
  - CNS: delirium, seizures, cerebral oedema, coma, Reye's syndrome
  - respiratory: hyperventilation
  - gastrointestinal: epigastric pain, nausea, vomiting, upper gastrointestinal bleeding, acute hepatitis
  - renal: acute renal failure
  - metabolic: hyper/hypoglycaemia, anion gap metabolic acidosis, hypokalaemia
  - cardiovascular: non-cardiogenic pulmonary oedema
- investigations
  - FBC, PCV; BUSE/Serum creatinine; LFT/PT/PTT, RBS; ABG
  - serum salicylate level at least 6 hours after ingestion

## Management

- use activated charcoal and alkalinisation to enhance elimination.  
Dose of activated charcoal is 1-2g/kg/dose 4-8 hourly.
- Correct dehydration, hypoglycaemia, hypokalaemia, hypothermia, metabolic acidosis
- Give vitamin K if there is hypoprothrombinaemia.
- Plot the salicylate level on the normogram (Figure 2)
- Forced alkaline diuresis - see Table 2.
- haemodialysis if :
  - severe cases, blood level > 100mg/dl
  - refractory acidosis
  - renal failure
  - non-cardiogenic pulmonary oedema
  - severe CNS symptoms e.g. seizures

## Prognosis

The presence of coma, severe metabolic acidosis together with plasma salicylate concentrate > 900mg/L indicate a poor prognosis even with energetic treatment.

**Table 2. Forced alkaline diuresis**

- Indication:** for moderate to severe cases (salicylate level > 35 mg/dl 6 hrs after ingestion)  
*Needs close monitoring as it is potentially dangerous*
1. give 30mls/kg in 1st hour  
( $\frac{1}{2}$  saline/D5% + 1ml/kg 8.4% NaHCO<sub>3</sub>).
  2. continue at 10mls/kg/hr till the salicylate level is at the therapeutic range.
  3. give IV frusemide (1mg/kg/dose) after 1st hr and then 8hrly.
  4. add 1g KCl to each 500mls drip solution, to the above regime (discontinue KCl if serum K<sup>+</sup> > 5mmol/L).
  5. aim for plasma pH of >7.5 and urine output of > 3-6ml/kg/h.
  6. monitor BUSE/RBS/ABG every 6 hrs.
  7. treat hypoglycaemia (5ml/kg of 10% dextrose)

## IRON

Dangerous dose of iron can be as small as 30mg/kg. The toxic effect of iron is due to unbound iron in the serum.

- Clinical features

*Table 3. Clinical staging in iron poisoning*

Stage 1 (6-12 hrs)	gastrointestinal bleeding, vomiting, abdominal pain, diarrhoea, hypotension, dehydration, acidosis and coma
Stage 2 (8-16 hrs)	symptom free period but has nonspecific malaise
Stage 3 (16-24 hrs)	profound hemodynamic instability and shock
Stage 4 (2-5 wks)	liver failure and gastrointestinal scarring with pyloric obstruction

## Management

- ingestion < 30mg/kg - patients are unlikely to require treatment
- ingestion > 30mg/kg - perform an abdominal XRay:
  - if pellets seen then use gastric lavage with wide bore tube
  - if pellets seen in small bowel then whole bowel irrigation with polyethylene glycol
    - volume to use: 500ml/h in children < 6 yrs, or 1000ml/h in children 6-12 yrs. or 1500 – 2000ml/h in children >12 yrs old
- (contraindications: paralytic ileus, significant hematemesis and hypotension)
- blood should be taken at 4 hrs after ingestion
  - if level < 55µmol/l : unlikely to develop toxicity
  - if level 55-90µmol/l, observe for 24 - 48 hrs.
    - Chelate if symptomatic (haematemesis or melaena)
  - if level > 90µmol/l or significant symptoms, chelate with IV Desferrioxamine 15 mg/kg till max of 80 mg/kg in 24 hours

### Notes:

1. If serum iron is not available, severe poisoning is indicated by nausea , vomiting, leucocytosis  $>15 \times 10^9$  and hyperglycaemia  $> 8.3 \mu\text{mol/l}$
2. Administer Desferrioxamine with caution because of hypotension and pulmonary fibrosis. Continue chelation therapy till serum iron normal, metabolic acidosis resolved and urine colour returns to normal.
3. Critical care management: Focus on cardiopulmonary failure, hypotension, severe metabolic acidosis, hypoglycaemia or hyperglycaemia, anaemia, gastrointestinal bleeding, liver and renal failure.

## Prognosis

Gastrointestinal bleeding, hypotension, metabolic acidosis, coma and shock are poor prognostic features.

## KEROSENE AND HYDROCARBON INGESTION

- **strict contraindication** to doing gastric lavage and emesis: it increases risk of chemical pneumonitis.
- admit the child for observation for respiratory distress and treat symptomatically.
- cerebral effects may occur from hypoxia secondary to massive inhalation.
- antibiotics and steroids may be useful in lipoid pneumonia (esp. liquid paraffin).
- chest X-ray

## TRICYCLIC ANTIDEPRESSANTS

- clinical features
  - anticholinergic effects: fever, dry mouth, mydriasis, urinary retention, ileus
  - central nervous system: agitation, confusion, convulsion, drowsiness, coma
  - respiratory system: respiratory depression
  - cardiovascular system: sinus tachycardia, hypotension, complex arrhythmias

### Management

- there is no specific antidote. Give activated charcoal 1-2 g/kg/dose 4-8 hourly.
- continuous ECG monitoring. Meticulous monitoring required: If no QRS widening, cardiac conduction abnormality, hypotension, altered sensorium or seizures within the 6 hours; it is unlikely the patient will deteriorate.
- treatment should be instituted for prolonged QRS and wide complex arrhythmias. QRS > 100ms (seizures) and QRS > 160ms (arrhythmia).
- correct metabolic acidosis. Give bicarbonate (1-2mmol/kg) to keep pH 7.45 - 7.55 when QRS is widened or in the face of ventricular arrhythmias. Administration of NaHCO<sub>3</sub> is targeted at narrowing the QRS and is titrated accordingly by bolus or by infusion. Watch out for hypokalemia and treat accordingly.
- convulsions should be treated with diazepam.
- use propranolol to treat life-threatening arrhythmias.
- if *torsades de pointes* occurs treat with MgSO<sub>4</sub>
- treat hypotension with Norepinephrine. Dopamine is not effective.
- haemodialysis/PD is not effective as tricyclics are protein bound
- important to avoid the use of flumazenil for reversal of co-ingestion of benzodiazepines as this can precipitate tricyclic induced seizure activity

## ORGANOPHOSPHATES

- clinical features:
  - cholinergic effects: miosis, sweating, lacrimation, muscle twitching, urination, excessive salivation, vomiting, diarrhoea
  - central nervous system: convulsions, coma
  - respiratory system: bronchospasm, pulmonary oedema, respiratory arrest
  - cardiovascular system: bradycardia, hypotension

### Management

- Remove contaminated clothing and wash exposed areas with soap and water.
- gastric lavage and give activated charcoal.
- resuscitate the patient. Protect the airway by early intubation. Use only non depolarising neuromuscular agents
- IV atropine 0.05mg/kg every 15 minutes till fully atropinized. Atropine administration is guided by drying of secretions rather than heart rate or pupil size.
- keep patient well atropinized for the next 2-3 days.
- a continuous infusion of atropine can be started at 0.05mg/kg/hr and titrated.
- give IV pralidoxime 25-50mg/kg over 30 min, repeated in 1-2 hrs and at 10-12 hr intervals as needed for symptom control (max 12g/day) till nicotinic signs resolves.
- treat convulsions with diazepam.
- IV furosemide for pulmonary congestion after full atropinisation.
- a rapid sequence intubation involves the potential for prolonged paralysis.

## PARAQUAT

- clinical features:
  - ulcers in the mouth and oesophagus
  - diarrhoea and vomiting
  - jaundice and liver failure
  - renal failure

## Management

- remove contaminated cloth and wash with soap and water.
- gastric lavage till clear.
- to give Fuller's earth in large amount.
- general supportive care.

## CHRONIC LEAD POISONING

This is an important diagnosis to be considered in any child who has raised intracranial pressure or encephalopathy.

- clinical features:
  - usually no history of ingestion
  - colicky abdominal pain, constipation, lethargy, anaemia, drowsiness, vomiting, headache, fits, coma due to encephalopathy.
  - behavioural change
- investigations
  - increase blood lead levels  $> 80\mu\text{g}/100\text{ml}$ .
  - lead lines (lines of increased density) at growing ends of long bones.
  - basophilic stippling of red cells.
  - increased coproporphyrin urinary excretion.

## Management

- identify source and prevent further ingestion.
- decrease cerebral oedema. Use dexamethasone  $0.2\text{--}0.4\text{mg}/\text{kg} \pm \text{IV mannitol}$ .
- chelating agents:

The 2 agents used are IV EDTA ( $50\text{mg}/\text{kg}/\text{day}$  in divided 4 hourly doses) and oral 2,3 dimercaptosuccinic acid (DMSA ).

(Older agents (BAL and penicillamine) are rarely used now)
- when to treat:
  - if blood level  $> 750\mu\text{g}/\text{l}$  admit to PICU for urgent chelation
  - if blood level  $> 450\mu\text{g}/\text{l}$  treat with oral DMSA
  - if blood level  $< 450\mu\text{g}/\text{l}$  treatment has no effect on outcome

## ANAPHYLAXIS

### Definition

Anaphylaxis is a systemic allergic reaction which involves the respiratory and/or cardiovascular systems. Food allergy is the most common cause of anaphylaxis in children.

**Table 1. Diagnostic criteria for Anaphylaxis**

**Anaphylaxis** is highly likely when any one of the following criteria are fulfilled:

1. Acute onset (within minutes to hours) with involvement of skin, mucosal tissue or both *AND* at least one of the following:
  - respiratory compromise e.g. dyspnoea, stridor, bronchospasm
  - reduced BP or associated end organ dysfunction e.g. hypotonia, syncope
2. Two or more of the following that occur rapidly after allergen exposure (within minutes to hours):
  - skin and mucosal involvement
  - respiratory compromise
  - reduced blood pressure or associated symptoms
  - persistent gastrointestinal symptoms e.g. abdominal cramps, vomiting
3. Reduced blood pressure (BP) after known allergen exposure  
(*Infants and children: low systolic BP (age specific) or >30% decrease in systolic BP*)

### Management

#### *Treatment of the acute episodes*

- first line treatment: IM Adrenaline 0.01mg/kg given every 5-15 minutes as necessary (maximum dose 0.5 mg 1:1000 concentration)
  - injection into lateral aspect of thigh achieves higher and faster peak levels.
  - in severe hypotension refractory to fluid support, start intravenous infusion of adrenaline at 0.1 microgram /kg/min.
  - If patient is on  $\beta$ -blockers, the effect of adrenaline may be blocked. In these patients administer iv glucagon 20-30  $\mu$ g/kg, max 1 mg over 5 mins followed by i infusion at 5-15 $\mu$ g/min.
- place patient in supine position.
- intravenous fluid resuscitation at 20ml/kg for cardiovascular support.
- airway support and oxygen
- inhaled  $\beta_2$  agonist may be a useful adjunct to relieve bronchospasm
- antihistamine and corticosteroids:  
(*there is lack of agreement on their use in acute treatment*)
  - antihistamine is useful for pruritus and urticaria but is unable to relieve shock and other symptoms.
  - steroids has a slow onset of action.

Continue observation for 6 – 24 hours depending on the severity of reaction because of the risk of biphasic reaction and the wearing off of adrenaline dose.

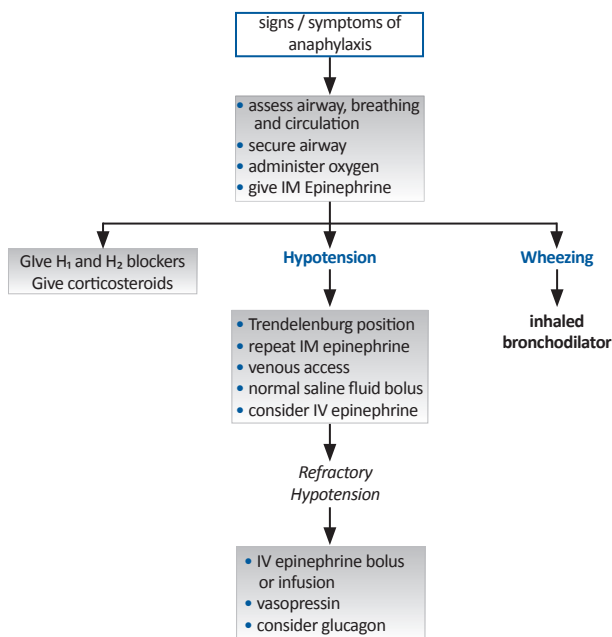
## Discharge planning

- all patients who had experienced an anaphylactic reaction should receive advice about trigger avoidance (if known) and follow up appointment.
- an adrenaline auto-injector should be prescribed as severe reactions are followed by a subsequent severe reaction in about 71% of subjects.
- an auto injector may be considered if there is a history of systemic allergic reaction without anaphylaxis AND one of the following risk factors for fatal anaphylaxis e.g. poorly controlled asthma, peanut/tree nut allergy and remote location.
- education on recognition of signs and treatment and how to use the auto-injector should be given supported by a personalised anaphylaxis action plan.

## Long term management and risk minimisation

- prevention of future episodes by avoiding triggers. However, accidental exposures may occur.
- education of patients and their carers in recognition and treatment
- management of co-morbidities that increases the risks associated with anaphylaxis

Figure 1. Algorithm for the approach to a child with anaphylaxis





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# PROCEDURES

**99** Sedation

**100** Ward Procedures



## SEDATION FOR DIAGNOSTIC AND THERAPEUTIC PROCEDURES

### Definitions

- *Sedation* – reduces state of awareness but does not relieve pain
- *Analgesia* – reduces the perception of pain

### Levels of sedation

- Procedural sedation means minimal or moderate sedation / analgesia.
- *Minimal* sedation (anxiolysis) – drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions are unaffected.
- *Moderate* sedation / analgesia – drug-induced depression during which patient respond to verbal commands either alone or accompanied by light tactile stimulation. The airway is patent and spontaneous ventilation is adequate. Cardiovascular function is adequate.

### Note:

- avoid deep sedation and general anesthesia in which the protective airway reflexes are lost and patients need ventilatory support.
- some children may require general anesthesia even for brief procedures whether painful or painless because of their level of distress.

### Indications

Patients undergoing diagnostic or therapeutic procedures.

### Contra-indications

- blocked airway including large tonsils or adenoids
- increase intracranial pressure
- reduce level of consciousness prior to sedation
- respiratory or cardiovascular failure
- neuromuscular disease
- child too distressed

### Patient selection

The patients should be in class I and II of the ASA classification of sedation risk.

Class I – a healthy patient

Class II – a patient with mild systemic disease, no functional limitation

### Preparation

Consent

Light restraint to prevent self injury

### Facilities

Oxygen source

Resuscitation equipment

ECG monitor

Defibrillator

Suction

Pulse oximeter

Non-invasive BP monitoring

### Personnel

At least a senior medical officer, preferably PALS trained.

A nurse familiar with monitoring and resuscitation

## Fasting

- recommended for all major procedures:
  - Nil orally: no solid food for 6 hours  
no milk feeds for 4 hours
- may allow clear fluids up to 2 hours before, for infants

## Venous access

Vein cannulated after applying local anaesthesia for 60 minutes.

## Sedation for Painless Procedures

- *Non-pharmacologic measures* to reduce anxiety
  - behavioural management, child friendly environment
- *Medication*
  - oral Chloral hydrate (drug 1 in table) may be used.

*Note: - opioids should not be used.*

- *sedatives such as benzodiazepine and dissociative anaesthesia ketamine should be used with caution and only by experienced senior medical officers.*
- *a few children may need general anaesthesia and ventilation even for painless procedure such as MRI brain if the above fails.*

## Sedation for Painful Procedures

- *Non-pharmacologic measures* to reduce anxiety
  - behavioural management, child friendly environment
- *Local anaesthesia*
  - Topical : Lignocaine EMLA ® 5% applied with occlusive plaster for 60 minutes to needle puncture sites, e.g. venous access, lumbar puncture, bone marrow aspiration.
  - subcutaneous Lignocaine infiltrated to the anaesthetised area prior to prolonged needling procedure, e.g. insertion of chest drainage.
- *Medications (refer Table 1)*

Many sedative and analgesic drugs are available; however, it is advisable to use the following frequently used medications:

- narcotics (analgesia) also have sedative effects
  - Morphine
  - Fentanyl
  - Naloxone (narcotic reversal)
    - for respiratory depression\* caused by narcotics.
- Benzodiazepines (sedatives) have no analgesia effects
  - Midazolam
  - Diazepam
  - Flumazenil (benzodiazepine reversal)
    - can reverse respiratory depression\* and paradoxical excitatory reactions

*\*provide bag-mask positive pressure ventilation whilst waiting for reversal agent to take effect.*

- general dissociative anaesthesia
  - Ketamine (to be used by senior doctors preferably in the presence of an anaesthesia doctor)
- adverse effects include
  - o increased systemic, intracranial and intraocular pressures
  - o hallucinogenic emergence reactions (more frequent in older children)
  - o laryngospasm
  - o excessive airway secretions.

*Table 1. Drug dosages used for sedation and analgesia in children*

Drug	Dose	Onset of action	Duration of action
Chloral hydrate	Oral 25 - 50 mg/kg; maximum 2g. For higher doses, i.e. 50 -100 mg/kg, please consult paediatrician or anaesthesiologist.	15 – 30 mins	2 -3 hours
<i>Narcotics</i>			
Morphine	IV 0.05 – 0.1 mg/kg	5 – 10 mins	2 – 4 hours
Fentanyl	IV 1 – 2 mcg/kg	2 – 3 mins	20 -60 mins
<i>Benzodiazepines</i>			
Midazolam	IV 0.05 – 0.1 mg/kg, max single dose 5 mg; may repeat up to max total dose 0.4 mg/kg (10 mg)	1 -2 mins	30 – 60 mins
Diazepam	IV 0.1 - 0.2 mg/kg	2 - 3 mins	30 – 90 mins
Ketamine	IV 0.5 - 2.0 mg/kg	1 – 2 mins	15 – 60 mins
<i>Reversal agents</i>			
Naloxone	Repeated small doses IV 1 - 10 mcg/kg every 1 to 2 mins		
Flumazenil	IV 0.01 – 0.02 mg / kg every 1 -2 minutes up to a maximum dose of 1 mg		

## Post sedation monitoring and discharge

Patient can be discharged when:

- vital signs and SaO<sub>2</sub> normal
- And*
- arousable
  - baseline level of verbal ability and able to follow age-appropriate commands
  - sit unassisted (if appropriate for age)

## References

1. PALS Provider Manual. American Heart Association 2002, Chapter 15, p 379-396.
2. Safe sedation of children undergoing diagnostic and therapeutic procedures. Scottish Intercollegiate Guidelines Network SIGN, May 2004.
3. Guideline statement 2005: Management of procedure-related pain in children and adolescents. Paediatrics & Child Health Division, The Royal Australian College of Physicians.



## WARD PROCEDURES

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### Categories

1. Airway Access – Endotracheal Intubation
2. Blood Sampling & Vascular Access
  - 2.1 Venepuncture & Peripheral Venous Cannulation
  - 2.2 Arterial Blood Sampling & Peripheral Arterial Cannulation
  - 2.3 Intra-Osseous Access
  - 2.4 Neonates
    - 2.4.1 Capillary Blood Sampling
    - 2.4.2 Umbilical Arterial Catheterisation UAC
    - 2.4.3 Umbilical Venous Catheterisation UVC

*[Note: This section is given special emphasis with the intention to prevent iatrogenic vascular complications. Venous access of other sites - External & Internal Jugular, Subclavian, Femoral – refer PALS Provider Manual]*

3. Body Fluid Sampling
  - 3.1. CSF - Lumbar puncture
  - 3.2. Chest tube insertion (open method)
  - 3.3. Heart - Pericardiocentesis
  - 3.4. Abdomen
    - 3.4.1. Gastric lavage
    - 3.4.2. Abdominal paracentesis
    - 3.4.3. Peritoneal dialysis
    - 3.4.4. Suprapubic bladder tap
    - 3.4.5. Bladder catheterisation
  - 3.5 Bone marrow aspiration & trephine biopsy

Selected sedation and pain relief is important before the procedures.  
*(please refer to preceding section on Sedation)*



# 1. AIRWAY ACCESS - ENDOTRACHEAL INTUBATION

(Please request for assistance from an Anaesthesiology Doctor if necessary)

The control of airway and breathing is very important in a patient with respiratory or cardiopulmonary failure or collapse.

## Indications

- when bag and mask ventilation is insufficient
- for prolonged positive pressure ventilation
- direct suctioning of the trachea
- to maintain and protect airway
- diaphragmatic hernia (newborn)

## Contra-indications

- If the operator is inexperienced in intubation, perform bag and mask ventilation till help arrives

## Equipment

- bag and mask with high oxygen flow
- laryngoscope
- blades: straight for infant, curved for older child; size as in Table 3
- scissors and adhesive tape
- sedation ( midazolam or morphine)
- suction catheter and device
- stylet (optional)
- endotracheal tube
  - appropriate size as in Table 2
- pulse oximeter
- muscle relaxant (succinylcholine)

Table 2. Guidelines for Endotracheal tube (ETT) placement

infant weight	ETT size <sup>1</sup>	ETT position (oral) <sup>2,3</sup>
<1000g	2.5	
1000g-2000g	3	7 cm
2000g-3000g	3.5	8 cm
>3000g	3.5-4.0	9 cm

Table 3. ETT blade sizes

ETT blade size	
neonates	0
infants	1
children	2

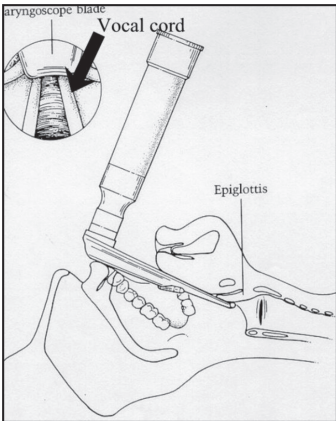
footnote: 1. for children over 1 year: ETT size in mm = 4 + (age in years / 4)

2. in neonates, use weight in kg + 6; in children use 12 + (age in years / 4)

3. for nasal ETT: add 2 cm respectively.

## Technique

1. Position infant with head in midline and slightly extended.
2. Continue bag and mask ventilation with 100% oxygen till well saturated.
3. Sedate the child with
  - IV midazolam (0.1-0.2 mg/kg) or
  - IV morphine (0.1-0.2 mg/kg).Give muscle relaxant if still struggling
  - IV succinylcholine (1-2 mg/kg)
4. Monitor the child's vital signs throughout the procedure.
5. Introduce the blade between the tongue and the palate with left hand and advance to the back of the tongue while assistant secure the head.
6. When epiglottis is seen, lift blade upward and outward to visualize the vocal cord.
7. Suction secretion if necessary.



### Technique (continued)

8. Using the right hand, insert the ETT from the right side of the infant's mouth; a stylet may be required.
9. Keep the glottis in view and insert the ETT when the vocal cords are opened till the desired ETT length while assistant applies cricoid pressure.
10. If intubation is not done within 20 seconds, the attempt should be aborted and re-ventilate with bag and mask.
11. Once intubated, remove laryngoscope and hold the ETT firmly with left hand. Connect to the self-inflating bag and positive pressure ventilation.
12. Confirm the ETT position by looking at the chest expansion, listen to lungs air entry and also the stomach.
13. Secure the ETT with adhesive tape.
14. Connect the ETT to the ventilator.
15. Insert orogastric tube to decompress the stomach.
16. Check chest radiograph.

### Complications and Pitfalls

- oesophageal intubation
- right lung intubation
- trauma to the upper airway
- pneumothorax
- subglottic stenosis (late)
- *relative contra-indications* for succinylcholine are increased intra-cranial pressure, neuromuscular disorders, malignant hyperthermia, hyperkalaemia and renal failure.

Note: The drugs used in Rapid Sequence Intubation are listed in Table 2, pp 362-363 of the PALS Provider Manual year 2002.

## 2. BLOOD SAMPLING & VASCULAR ACCESS

### 2.1. VENEPUNCTURE & PERIPHERAL VENOUS LINE

#### Indications

- blood sampling
- intravenous fluid, medications and blood components

#### Equipment

- alcohol swab
- tourniquet
- topical anaesthetic (TA), e.g lignocaine EMLA® 5%
- catheter or needle; sizes 25, 23, 21 G
- heparinised saline, T-connector, rubber bung for setting an IV line

## Technique

1. Identify the vein for venepuncture. Secure the identified limb and apply tourniquet or equivalent.
2. TA may be applied with occlusive plaster an hour earlier.
3. Clean the skin with alcohol swab.
4. Puncture the skin and advance the needle or catheter in the same direction as the vein at 15-30 degrees angle.
5. In venepuncture, blood is collected once blood flows out from the needle. The needle is then removed and pressure applied once sufficient blood is obtained.
6. In setting an intravenous line, the catheter is advanced a few millimetres further. Once blood appears at the hub, then withdraw the needle while advancing the catheter.
7. Remove the tourniquet and flush the catheter with heparinised saline.
8. Secure the catheter and connect it to either rubber bung or IV drip.
9. Immobilise the joint above and below the site of catheter insertion with restraining board and tape.

## Complications

- haematoma or bleeding
- thrombophlebitis
- extravasation can lead to serious soft tissue injury resulting in limb or digital loss and loss of function. This complication is of concern in neonates, where digital ischaemia, partial limb loss, nerve damage, contractures of skin and across joints can occur

### Extravasation injury:

- *Signs include*
  - pain, tenderness at insertion site especially during infusion or slow bolus drugs
  - redness
  - swelling
  - reduced movement of affected site

*(Note – the inflammatory response can be reduced in neonates, preterm babies)*

- *Observation*

The insertion site should be observed for signs of extravasation:

- at least every 4 hours for ill patients.
- sick preterm in NICU – do observation more often, i.e. every hour.
- each time before, during and after slow bolus or infusion.

*(Consider re-siting the intravenous catheter every 48 to 72 hours)*

- if moderate or serious extravasation occurs, especially in the following situation:
    - preterm babies
    - delay in detection of extravasation
    - hyperosmolar solutions or irritant drugs used (glucose concentration >10% solution, sodium bicarbonate, calcium solution, dopamine, cloxacillin, fusidic acid)
- then:

- refer to plastic surgeon / orthopaedics surgeon.
- consider performing 'subcutaneous saline irrigation' especially for neonates. The drug hyaluronidase is not readily available. Therefore please use normal saline to flush out as much of the irritant drugs as possible

## Pitfalls

- if the patient is in shock, the venous flow back and the arterial flow (in case of accidental cannulation of an artery) is sluggish.
- **BEWARE!** An artery can be accidentally cannulated, e.g. the brachial artery at the cubital fossa and the temporal artery at the side of the head of a neonate and be mistaken as a venous access. If the doctor or nurse continues to use this line, it will lead to disastrous effect to the limb or head of the patient.
- ensure the drug prescribed is given by the proper mode of administration. Some drugs can only be given by slow infusion (e.g. fusidic acid) instead of slow bolus in order to reduce tissue damage from extravasation.

## 2.2. ARTERIAL BLOOD SAMPLING & PERIPHERAL ARTERIAL LINE CANNULATION

### Indications

- arterial blood gases
- invasive blood pressure monitoring
- frequent blood taking

### Contra-indications

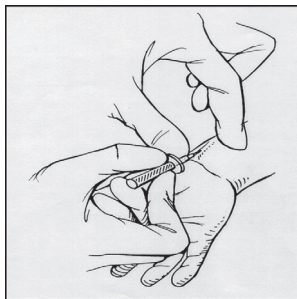
- presence or potential of limb ischaemia
- do not set an arterial line if close monitoring cannot be done

## Equipment

- alcohol swab
- arterial catheter size 25
- topical anaesthetic (TA)  
e.g. lignocaine EMLA® 5%
- needle size 27
- heparinised saline in 5cc syringe, T-connector
- heparinised saline (1 u/ml) for infusion

## Technique

1. Check the ulnar collateral circulation by modified Allen test.
2. The radial pulse is identified. Other sites that can be used are posterior tibial and dorsalis pedis artery.
3. TA may be applied with occlusive plaster an hour before procedure.
4. Clean the skin with alcohol swab.
5. Dorsiflex the wrist slightly. Puncture the skin and advance the catheter in the same direction as the radial artery at a 30-40 degrees angle.
6. The catheter is advanced a few millimetres further when blood appears at the hub, then withdraw the needle while advancing the catheter.
7. Aspirate to ensure good flow, then flush with heparinised saline.
8. Peripheral artery successfully cannulated.
  - ensure that the arterial line is functioning. The arterial pulsation is usually obvious in the tubing
  - connect to T-connector and 3-way stop-cock (red colour) to a syringe pump.
  - label the arterial line and the time of the setting.



## Technique (cont.)

9. Run the heparinised saline at an appropriate rate:
  - 0.5 to 1.0 mL per hour for neonates
  - 1.0 mL (preferred) or even up till 3.0 mL per hour for invasive BP line (to avoid backflow in bigger paediatrics patients)
10. Immobilize the joint above and below the site of catheter insertion with restraining board and adhesive tape.

## Complications and Pitfalls

- arteriospasm which may lead to ischaemia and gangrene.
- neonates especially – digital and limb ischaemia which can lead to partial and complete limb loss

**Precaution:** prevention of digital & limb ischaemia and gangrene

- **Avoid end arteries** e.g. brachial (in cubital fossa) and temporal artery (side of head) in babies (**Beware** - both these arteries can be accidentally cannulated and mistaken as 'veins')
- test for *collateral circulation*
  - if a radial artery is chosen, please perform Allen's test (to confirm the ulnar artery collateral is intact) before cannulation.
  - if either the posterior tibial or dorsalis pedis artery on one foot is chosen, ensure that these 2 arteries are palpable before cannulation.
- *circulation chart*

Perform observations and record circulation of distal limb every hour in the NICU and PICU, and whenever necessary to detect for signs of ischaemia, namely:

- colour - pale, blue, mottled
- cold, clammy skin
- capillary refill > 2 seconds
- *treatment* of digital / limb ischaemia
  - this is difficult as the artery involved is of small calibre
  - refer vascular surgeon if available / orthopaedic surgeon
  - consider warming the contralateral unaffected leg to induce reflex vasodilatation if part of one leg is affected (see section on UAC)
  - anticoagulant drugs and thrombolytic agents are unlikely to be beneficial
- **Reminder:**
  - **Prevention** of limb ischaemia is of utmost importance.
  - early detection of ischaemia is very important to avoid irreversible ischaemia.
  - if the patient is in shock, the risk of limb ischaemia is greater.
  - small and preterm babies are at greater risk for ischaemia.
  - the risk of limb ischemia is greater with fast infusion rate (e.g. > 1 ml per hour).
  - no fluid or medication other than heparinized saline can be given through arterial line. This mistake can occur if the line is not properly labelled, or even wrongly labelled and presumed to be a venous line.

## 2.3. INTRAOSSEOUS ACCESS

### Introduction

- intraosseous (IO) infusion can be used for all age groups
- the most common site for IO cannulation is the anterior tibia (all age groups)  
Alternate sites include:
  - infant: distal femur
  - child: anterior superior iliac spine, distal tibia.
  - adolescent or adult: distal tibia, medial malleolus, anterior superior iliac spine, distal radius, distal ulna.
- all the fluids and medications can be given intraosseously.
- intraosseous infusion is not recommended for use longer than a 24 hour period.

#### Indications

- emergency access for IV fluids and medications when other methods of vascular access have failed
- in certain circumstances, e.g. severe shock with severe vasoconstriction or cardiac arrest, IO access may be the INITIAL means of vascular access attempted

#### Contra-indications

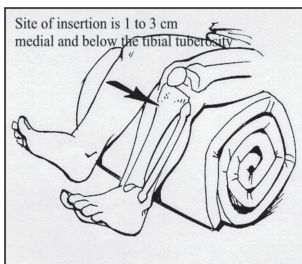
- fractures, crush injuries near the access site
- conditions in which the bone is fragile e.g. osteogenesis imperfecta
- previous attempts to establish access in the same bone
- infection over the overlying tissues

### Equipment

- sterile dressing set
- intraosseous needle
- syringes for aspiration
- local anaesthesia

### Technique

1. Immobilize the lower limb.
2. Support the limb with linen
3. Clean and draped the area
4. Administer LA at the site of insertion
5. Insert the IO needle 1-3 cm below and medial to the tibial tuberosity caudally
6. Advance needle at a 60-90° angle away from the growth plate until a 'give' is felt
7. Remove the needle trocar stylet while stabilizing the needle cannula
8. Withdraw bone marrow with a 5cc syringe to confirm access
9. Infuse a small amount of saline and observe for swelling at the insertion site or posteriorly in the extremity opposite the insertion site. Fluid should flow in freely and NO swelling must be seen. (Swelling indicates that the needle has penetrated into and through the posterior cortical bone. If this happens remove the needle.)
10. Connect the cannula to tubing and IV fluids. Fluid should flow in freely
11. Monitor for any extravasation of fluids.



### Complications

- cellulitis
- osteomyelitis
- extravasation of fluids/compartment syndrome
- damage to growth plate

## 2.4. NEONATES

### 2.4.1. CAPILLARY BLOOD SAMPLING

#### Indications

- capillary blood gases
- capillary blood glucose
- serum bilirubin

#### Equipment

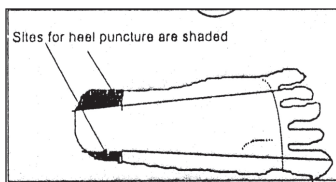
- stilltete
- alcohol swab

#### Technique

1. Either prick the medial or lateral aspect of the heel
2. For the poorly perfused heel, warm with gauze soaked in warm water.
3. Clean the skin with alcohol swab
4. Stab the sterile stilltete to a depth of 2.5mm, then withdraw it. Intermittently squeeze the heel gently when the heel is re-perfused until sufficient blood is obtained.

#### Complications

- cellulitis
- osteomyelitis



### 2.4.2. UMBILICAL ARTERY CATHETERISATION (UAC)

#### Indications

- repeated blood sampling in ill newborn especially those on a ventilator
- occasionally used for continuous BP monitoring

#### Contra-indications

- local vascular compromise in lower extremities
- peritonitis, necrotising enterocolitis
- omphalitis

#### Prior to setting

1. Examine infant's lower extremities and buttocks for signs of vascular insufficiency.
2. Palpate femoral pulses for their presence and equality.
3. Evaluate the infant's legs, feet, and toes for any asymmetry in colour, visible bruising, or vascular insufficiency.
4. Document the findings for later comparison. Do not set if there is any sign of vascular insufficiency

#### Equipment

- umbilical artery catheter, appropriate size
- 5 cc syringes filled with heparinized saline
- heparinized saline (1u/ml) for infusion
- UAC/UVC set
- three-way tap

**Size of UAC in mm:** size 3.5 for weight <1.25 kg; size 5.0 for weight 1.25 - 3.5 kg

#### Technique

1. Clean the umbilicus and the surrounding area using standard aseptic technique. In order to observe for limb ischaemia during umbilical arterial insertion, consider exposing the feet in term babies if the field of sterility is adequate.
2. Catheterise the umbilical artery to the desired position. The formula for UAC is:
  - (body weight in kg x 3) + 9 + 'stump length' in cm (*high position - recommended*)
  - weight in kg + 7 cm (*low position*)

3. Cut the umbilicus horizontally leaving behind a 1cm stump. There are usually 2 arteries and 1 vein. The artery is smaller, white and harder in consistency. Use the curved artery forceps to hold the umbilicus stump upright and taut. Use the probe to dilate the vessel. Insert the catheter to the desired distance
4. Ensure the successful and correct cannulation of one of the umbilical arteries.

- Tips for successful catheterisation of the umbilical artery:

- in a fresh and untwisted umbilical stump, the two arteries can be clearly distinguished from the vein
- the blood withdrawn is bright red
- visible arterial pulsations can be seen in the column of blood withdrawn into the catheter. This pulsation may not be seen in very preterm babies and babies in shock, using the closed system.

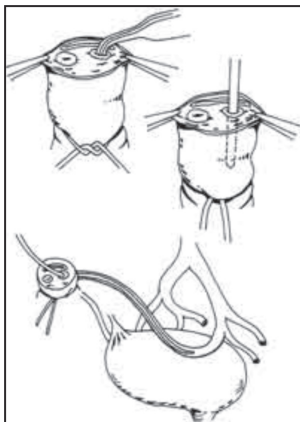
- In *accidental cannulation* of the umbilical vein, the catheter tip can be in the left atrium (via the foramen ovale from the right to left atrium) or in the left ventricle

- Stick the label of the catheter onto the patient's folder for future reference (brand and material of catheter)

5. Observe for signs of arterial occlusion (colour, cold skin, capillary refill delayed, poor dorsalis pedis and posterior tibial pulses) during and after the procedure. Check the circulation of both the legs & buttocks (circulation chart) every 15 minutes during the procedure. This will necessitate the frequent lifting of the edge of the drape by an assistant to observe the lower limbs circulation without compromising the sterility field.
6. If there are no complications (limb ischaemia – see pitfalls), secure the UAC to avoid accidental dislodgement
7. Perform a chest and abdominal X-ray to ascertain the placement of the UAC tip
  - between T 6-9 vertebra (*high position*) - **preferred**
  - at the L 3-4 vertebra (*low position*)

Withdraw the catheter to the correct position if necessary.

8. Monitor the lower limbs and buttock area for ischaemic changes 2-4 hourly
9. Infuse heparinised saline continuously through the UAC at 0.5 to 1 U/hr to reduce the risk of catheter occlusion & thrombotic events
10. Note the catheter length markings every shift and compare with the procedure note at the time of insertion ( to check for catheter migration)
11. Remove the UAC as soon as no longer required to reduce the incidence of thrombus formation and long line sepsis





## Complications

- bleeding from accidental disconnection and open connection.
- embolisation of blood clot or air in the infusion system.
- vasospasm or thrombosis of femoral artery leading to limb ischaemia. A partial or even complete limb loss is an extremely distressing complication. (See chapter on “Management of arterial spasm and thrombosis”)
- thrombosis of renal artery (hypertension, haematuria, renal failure), mesenteric artery (gut ischaemia, necrotising enterocolitis)
- vascular perforation of umbilical arteries, haematoma, retrograde arterial bleeding
- infection

## 2.4.3. UMBILICAL VEIN CATHETERISATION (UVC)

### Indications

- for venous access in :
  - neonatal resuscitation
  - preterm babies especially ELBW babies
  - sick babies in shock with peripheral vasoconstriction
  - exchange transfusion in severe neonatal jaundice

### Contra-indications

- omphalitis, omphalocoele
- necrotising enterocolitis
- peritonitis

## Equipment

- umbilical artery catheter, appropriate size
- 5 cc syringes filled with heparinized saline
- heparinized saline (1u/ml) for infusion
- UAC/UVC set
- three-way tap

**Size of UVC in mm:** size 5.0 for weight <2 kg; size 8.0 for 2-3.5 kg; size 10.0 for > 3.5 kg

## Technique

1. Clean umbilicus and its surroundings using standard procedures. In order to observe for limb ischaemia during insertion (in the event of accidental arterial catheterisation), consider exposing the feet in term babies if field of sterility is adequate.

2. Formula for insertion length of UVC:

- $[0.5 \times \text{UAC cm (high position)}] + 1 \text{ cm.}$   
(Refer to information in UAC).

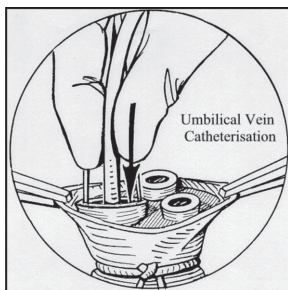
**Or**

- $2 \times \text{weight in kg} + 5 + \text{stump length in cm}$

3. Perform the umbilical venous cannulation

- Tips for successful UV catheterisation:

- in a fresh (first few hours of life) and untwisted umbilical stump, the umbilical vein has a thin wall, is patulous and is usually sited at the 12 o'clock position. The two umbilical arteries which have a thicker wall and in spasm, and sited at the 4 and 8 o'clock positions. However, in a partially dried umbilical cord, the distinction between the vein and arteries may not be obvious.
- the venous flow back is sluggish and without pulsation (in contrast to the arterial pulsation of UAC)
- the blood is dark red in colour



- Central venous pressure
    - the UVC tip is sited in the upper IVC (inferior vena cava) or even within the lower portion of the right atrium. The right atrial pressure in a term relaxed baby range from -2 to + 6 mmHg (i.e. - 3 cm to + 9 cm water).
  - Negative intrathoracic pressure and air embolism
    - in a crying baby, the negative intrathoracic pressure can be significant during deep inspiration
    - ensure that no air embolism occurs during the procedure especially in the presence of negative pressure when the catheter tip is in the right atrium. Air embolism can occur if the baby takes a deep inspiration when the closed UVC circuit is broken.
  - Stick the label of the catheter onto the patient's folder for future reference (brand and material of catheter)
4. If there are no complications, secure the UVC to avoid accidental migration of the catheter.
  5. If the UVC is for longer term usage such as for intravenous access / TPN, perform chest and abdominal radiograph to ascertain the tip of the catheter is in the inferior vena cava above the diaphragm or just inside the right atrium.
  6. Consider removing the UVC after 7 days to reduce incidence of line sepsis or thrombus forming around the catheter.

### Complications

- infections
- thrombo-embolic – lungs, liver, even systemic circulation
- pericardial tamponade, arrhythmias, hydrothorax
- portal vein thrombosis and portal hypertension (manifested later in life)

### Pitfalls

- the umbilical artery can be mistakenly cannulated during umbilical venous catheterisation
- if you suspect that the umbilical artery was wrongly cannulated resulting in limb ischaemia, please refer to section on UAC.

### 3. BODY FLUID SAMPLING

#### 3.1. LUMBAR PUNCTURE

##### Indications

- suspected meningitis / encephalitis
- intrathecal chemotherapy for oncology patients
- in selected patients being investigated for neurometabolic disorders

##### Contra-indications

- increased intracranial pressure (signs and symptoms, raised blood pressure, fundoscopic signs)
- bleeding tendency: platelets  $<50,000/\text{mm}^3$  or prolonged PT and APTT
- skin infection over the site of lumbar puncture

##### Equipment

- sterile set
- sterile bottles for CSF, bottle for RBS (random blood sugar)
- spinal needle 20-22 G, length 1.5 in with stylet; length 3.5 in for children  $>12$  yrs

##### Technique

1. Give sedation (midazolam), apply local anaesthetic
2. Place child in lateral recumbent position with neck, body, hips and knees flexed. Monitor oxygen saturation continuously
3. Visualise a vertical line between the highest point of both iliac crests and its transection with the midline of the spine (at level between vertebrae L 3-4)
4. Clean area using standard aseptic techniques: povidone-iodine and 70% alcohol.
5. Gently puncture skin with spinal needle at the identified mark and point towards the umbilicus. The entry point is distal to the palpated spinous process L4.
6. Gently advance a few millimetres at a time until there is a backflow of CSF (there may be a 'give' on entering the dura mater before the CSF backflow). Collect the CSF in the designated bottles.
7. Gently withdraw needle, spray with op-site, cover with gauze and bandage
8. Take a random blood sugar sample (RBS)
9. Ensure that the child lies supine for the next 4 to 6 hours, continue monitoring child till he or she recovers from the sedation

##### Complications

- headache or back pain following the procedure (from arachnoiditis)
- brain herniation associated with raised ICP
- bleeding into CSF, or around the cord (extraspinal haematoma)

##### Pitfall

- Do not perform a LP on a patient with hypertensive encephalopathy

## 3.2 CHEST TUBE INSERTION

### Indications

- pneumothorax with respiratory distress
- significant pleural effusion
- empyema

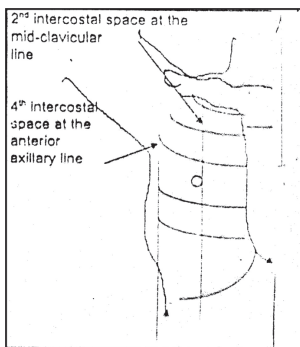
### Equipment

- suturing set
- chest tube, appropriate size
- suction pump – optional
- local anaesthetic +/- sedation
- underwater seal with sterile water

### Technique

*In an open method, after making the skin incision, continue to dissect the tissues till the pleura is seen.*

1. Sedate the child.
2. Position the child with ipsilateral arm fully abducted.
3. Clean and drape the skin.
4. Infiltrate LA into the skin at 4th ICS, AAL or mid axillary line.
5. Make a small incision just above the rib down to the subcutaneous tissue.
6. Place the tip of the chest tube at the incision, point the tip anteriorly for drainage of air and posteriorly for drainage of empyema. Slowly advance the chest tube with introducer, exerting a firm, continuous pressure until a 'give' is felt.
7. Remove the introducer and advance the chest tube till the desired length.
8. Connect the tube to underwater seal. The water should bubble ( if pneumothorax) and the fluid moves with respiration if chest tube is in the pleural space.
9. Secure the chest tube with pulse string sutures.
11. Connect the underwater seal to suction pump if necessary.
10. Confirm the position with a chest X-ray



### NEEDLE THORACOTOMY

1. Indicated in *tension pneumothorax* as an emergency measure to decompress the chest until a chest tube is inserted.
2. Done under strict aseptic technique. Attach a 5ml syringe to a 16 to 20 gauge angiocatheter. Gently insert catheter perpendicularly through the second intercostal space, over the top of the third rib, at the midclavicular line while applying a small negative pressure as the needle is advanced. Air will be aspirated on successful needle thoracotomy. When this happens, remove the needle while leaving the branula in situ to allow the tension pneumothorax to decompress. Insert a chest tube as described above as soon as feasible.

### Complications

- bleeding
- subcutaneous emphysema
- injury to the nearby structures e.g. lung, heart, large vessels, liver
- nerve injury
- infection

## 3.2 PERICARIOCENTESIS

### Indications

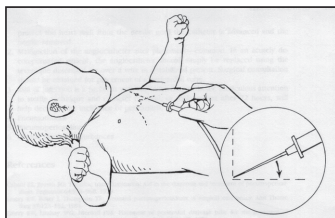
- symptomatic collection of air
- blood or other fluids / empyema in pericardial sac

### Equipment

- suturing set
- angiocatheter – size 20 G for newborn, 18 G for older children
- T-connector
- 3-way stopcock

### Technique

1. Place patient on supine position and on continuous ECG monitoring.
2. Clean and drape the subxiphoid area.
3. Prepare the angiocatheter by attaching the T connector to the needle hub and connect the other end of the T-connector to a 3-way stopcock which is connected to a syringe.
4. Insert the angiocatheter at about 1cm below the xiphoid process at angle of 20-30° to the skin and advance slowly, aiming at the tip of the left shoulder while applying light negative pressure with the syringe. Stop advancing the catheter if there is cardiac arrhythmia
5. Once air or fluid returns in the T connector stop advancing the catheter and aspirate a small amount to confirm positioning.
6. Remove the T connector from the angiocatheter and rapidly hold your finger over the needle hub.
7. Advance the catheter further while removing the needle.
8. Reattach the T connector and resume aspiration of the air or fluid required.
9. Send any aspirated fluid for cell count, biochemistry and culture.
10. Suture the angiocatheter in place. Perform CXR to confirm positioning and look for any complication.
11. The catheter should be removed within 72 hours. If further aspiration is required, placement of a pericardial tube is an option.  
*Do not hesitate to **consult** cardiothoracic surgeon.*



### Complications

- perforation of heart muscle leading to cardiac tamponade.
- haemo / pneumo – pericardium
- cardiac arrhythmias.
- pneumothorax

## 3.4 ABDOMEN

### 3.4.1. GASTRIC LAVAGE

#### Indications

- removal of toxins
- removal of meconium from stomach for newborns

#### Equipment

- nasogastric tube size 8-12
- sterile water
- syringes- 5 cc for neonate, 25-50 cc for older children

#### Technique

1. Put the child on left semiprone position.
2. Estimate the length of tube inserted by measuring the tube from the nostril and extending it over and around the ear and down to the epigastrium.
3. Lubricate the tip of the tube with KY jelly. Insert the tube gently.
4. Confirm position by aspirating stomach contents. Re-check by plunging air into stomach whilst listening with a stethoscope, or check acidity of stomach contents.
5. Perform gastric lavage until the aspirate is clear.
6. If indicated, leave activated charcoal or specific antidote in the stomach.

#### Complications

- discomfort
- aspiration of stomach contents
- trauma to upper gastrointestinal tract

### 3.4.2. ABDOMINAL PARACENTESIS

#### Indications

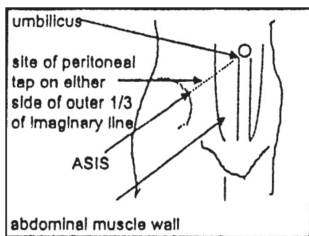
- diagnostic procedure
- drain ascites

#### Equipment

- dressing set
- cannula size 21,23 G
- 10 cc syringes

#### Technique

1. Supine position. Catheterize to empty the bladder. Clean and drape abdomen.
2. Site of puncture is at a point in the outer 1/3 of a line drawn from the umbilicus to the anterior superior iliac spine.
3. Insert the catheter, connected to a syringe, into the peritoneal cavity in a 'Z' track fashion.
4. Aspirate while advancing the catheter until fluid is seen in the syringe. Remove the needle and reconnect the catheter to the syringe and aspirate the amount required. Use a three-way tap if large amounts need to be removed.
5. Once complete, remove the catheter. Cover puncture site with sterile dry gauze.



#### Complications

- infection
- perforation of viscus
- leakage of peritoneal fluid
- hypotension if excessive amount is removed quickly.

### 3.4.3. PERITONEAL DIALYSIS (See protocol on Acute Peritoneal Dialysis)

### 3.4.4. SUPRAPUBIC BLADDER TAP

#### Indications

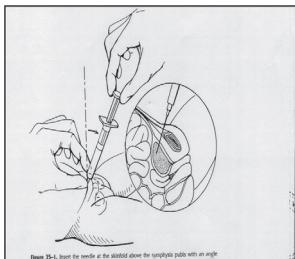
- urine culture in young infant

#### Equipment

- dressing set
- needle size 21, 23
- syringe 5cc
- urine culture bottle

#### Technique

1. Make sure bladder is palpable.  
If needed, encourage patient to drink half to 1 hour before procedure.
2. Position the child in supine position. Clean and drape the lower abdomen.
3. Insert the needle attached to a 5cc syringe perpendicular or slightly caudally to the skin, 0.5 cm above the suprapubic bone.
4. Aspirate while advancing the needle till urine is obtained.
5. Withdraw the needle and syringe.
6. Pressure dressing over the puncture site.
7. Send urine for culture.



#### Complications

- microscopic haematuria
- infection
- viscus perforation

### 3.4.5. BLADDER CATHETERIZATION

#### Indications

- monitor urine output
- urinary retention
- micturating cystourethrogram (MCUG)<sup>2</sup>
- urine culture

#### Bladder catheter sizes

- < 3 kg: size 4
- > 3kg: size 6
- older children:  
Foley's catheter 6-10

1. Patients for MCUG should receive a stat dose of IV gentamicin, or trimethoprim 2 mg/kg bd for 48 hours.

#### Equipment

- dressing set
- urinary catheter
- local anaesthesia / lubricant (e.g. K-Y jelly)
- syringe and water for injection

#### Technique

1. Position the child in a frog-leg position. Clean and drape the perineum.
2. In female, separate the labia majora with fingers to expose the urethra opening.
3. In male, hold the penis perpendicular to the body.
4. Pass catheter in gently till urine is seen then advance a few centimetres further.
5. Secure the catheter with adhesive tape to the body.
6. Connect the catheter to the urine bag.

#### Complications

- infection
- trauma which leads to urethral stricture

### 3.5. BONE MARROW ASPIRATION & TREPHINE BIOPSY

#### Indications

- examination of the bone marrow in a patient with a known or suspected haematology or oncology disorder

#### Contra-indications

- a bleeding tendency, or
- platelet count  $< 50,000 / \text{mm}^3$   
*Consider transfusion of platelet concentrate prior to procedure.*

#### Equipment

- bone marrow set (Islam) 16 – 18G

#### Technique

1. Sedate child, monitor continuously with pulse oximeter.
2. Position child - either as for lumbar puncture or in a prone position.
3. Identify site for aspiration - posterior iliac crest preferred, upper anterior-medial tibia for child  $< 3$  months old.
4. Clean skin using standard aseptic technique with povidone-iodine and 70% alcohol.
5. Make a small skin nick over the PSIS (posterior superior iliac spine). Hold the trocar firmly and gently enter the cortex by a twisting action. A 'give' is felt as the needle enters the bone marrow.
6. Trephine biopsy is usually done before marrow aspiration.
7. Withdraw needle, spray with op-site, cover with gauze and crepe bandage.
8. Lie child supine for the next 4 to 6 hours and observe for blood soaking the gauze in a child with bleeding diathesis.

#### Complications

- bleeding, haematoma
- infection

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# APPENDICES

- i Drug Doses
- ii Growth Charts



## DRUG DOSES

The drug doses in the following pages are reproduced from the 15 th edition (2010) of **Drug Doses**, courtesy of **Professor Frank Shann**, from the Intensive Care Unit, Royal Children's Hospital, Parkville, Victoria 3052, Australia

### DRUGS ARE LISTED BY GENERIC NAME

1/100=1%=10mg/ml, 1/1000=1mg/ml, 1/10000=0.1mg/ml

**Abacavir.** 8mg/kg (adult 300mg) 12H oral.

**Abacavir + lamivudine.** 600mg/300mg tab, >12yr (NOT/kg): 1tab daily oral.

**Abacavir + lamivudine + zidovudine.**

300mg/150mg/300mg tab, ≥18yr (NOT/kg): 1tab 12H oral.

**Abarelix.** Adult (NOT/kg): 1 vial (delivers 100mg) IM on day 1, 15 and 29, and then every 28 days.

**Abatacept.** NOT/kg: 500mg (40-60kg) 750mg (60-100 kg) 1g (>100kg) IV over 30min day 1, 2wk, 4wk, then every 4wk.

**Abciximab.** 0.25mg/kg IV stat 10min before angioplasty, then 0.2mcg/kg/min (max 10mcg/min) IV for 12hr.

**Acamprosate calcium.** Adult (NOT/kg). <60kg: 666mg mane, 333mg noon and nocte oral. >60kg: 666mg 8H.

**Acarbose.** 1-4mg/kg (adult 50-200mg) 8H oral.

**Acebutolol.** 4-8mg/kg (adult 200-400mg) 8-24H oral.

**Aceclofenac.** 2mg/kg (adult 100mg) 12H oral.

**Acemetacin.** 1.2mg/kg (adult 60mg) 8-12H oral.

**Acenocoumarol.** See nicoumalone.

**Acetaminophen.** See paracetamol.

**Acetazolamide.** 5-10mg/kg (adult 100-250mg) 6-8H (daily for epilepsy) oral.

**Acetohydroxamic acid.** 5mg/kg (adult 250mg) 6-8H oral.

**Acetylcholine chloride.** Adult (NOT/kg): 1% instil 0.5-2ml into anterior chamber of the eye.

**Acetylcysteine.** Paracetamol poisoning (regardless of delay): 150mg/kg in 5%D IV over 1hr; then 10mg/kg/hr for 20hr (delay <10hr), 32hr (delay 10-16hr), 72hr (delay >16hr) and longer if still encephalopathic; oral 140mg/kg stat, then 70 mg/kg 4H for 72hr. Monitor serum K+. Give if paracetamol >1000umol/L (150mg/L) at 4hr, >500umol/L 8hr, >250umol/L 12hr. Lung disease: 10% soltn 0.1ml/kg (adult 5ml) 6-12H nebulised or intratracheal.

Meconium ileus equivalent: 5ml (NOT/kg) of 20% soltn 8H oral; 60-100ml of 50mg/ml for 45 min PR. CF: 4-8mg/kg 8H oral. Eye drop 5% + hypro-mellose 0.35%: 1 drop/eye 6-8H.

**Acetylsalicylic acid.** See aspirin.

**Acetyl sulfisoxazole.** 1.16g=1.0g sulphafurazole (qv).

**Aciclovir.** Neonate - 12wk: 20mg/kg IV over 1hr daily (<30wk gest), 18H (30-32wk), 12H (1st wk life), 8H (2-12wk) for 2wk (3wk and CSF PCR -ve if herp enceph). age >12wk: EBV, herpes enceph, immunodef, varicella: 500mg/m2 (12wk-12 yr) 10mg/kg (>12yr) 8H IV over 1hr. Cutaneous herpes 250 mg/m2 (12wk-12yr) 5mg/kg (>12yr) 8H IV over 1hr. Genital herpes (>12yr NOT/kg): 200mg oral x5/day for 10 days, then 200mg x2-3/day for 6mo if reqd. Zoster (>12yr NOT/kg): 400 mg (<2yr) or 800mg (≥2yr) oral x5/day for 7 days. Cold sores: 5% cream x5/day. Eye: 3% oint x5/day.

**Acipimox.** 5mg/kg (adult 250mg) 8-12H oral.

**Acitretin.** 0.5-1mg/kg (adult 25-50mg) daily oral.

**Acriflavine hydrochloride.** 0.1% soltn: apply 12-24H.

**Acrivastine.** 0.15mg/kg (adult 8mg) 8H oral.

**Actinomycin D.** See dactinomycin.

**Activated charcoal.** See charcoal, activated.

**Adalimumab.** Adult (NOT/kg): 40mg every 1-2wk SC.

**Adapalene.** 0.1% gel: apply once/day before bed

**Adefovir.** Adult (NOT/kg): 10mg daily oral.

**Adenosine.** Arrhythmia: 0.1mg/kg (adult 3mg) stat by rapid IV push, incr by 0.1mg/kg (adult 3mg) every 2min to max 0.5 mg/kg (adult 18mg). Pul hypertension: 50mcg/kg/min (3 mg/ml at 1ml/kg/hr) into central vein.

**Adrenaline.** Croup: 1% 0.05 ml/kg diluted to 4ml, or 1/1000 0.5ml/kg (max 6ml) by inhaltn. Cardiac arrest (repeat if reqd): 0.1ml/kg of 1/10,000 IV or intracardiac; via ETT 0.1 ml/kg of 1/1000.

Anaphylaxis: IV 0.05-0.1ml/kg of 1/10,000, rpt if reqd; IM into thigh: 0.01mg/kg (0.01ml/kg of 1/1000) up to 0.1mg/kg, x3 doses 20min apart if reqd. IV infn 0.3 mg/kg in 50ml 5%D-hep at 0.5-10ml/hr (0.05-1mcg/kg/min).

**Adrenaline 0.1% + fluorouracil 3.33%.**

Gel: inject into each wart x1/wk for up to 6wk.

**Adrenocorticotrophic hormone (ACTH).** See cortico-trophin.

**Agalsidase beta.** 0.2-1mg/kg every 2wk IV over 40min

**Agar + paraffin 65%.** NOT/kg: 6mo-2yr 5ml, 3-5yr 5-10ml, >5yr 10ml 8-24H oral.

**Agar + paraffin + phenolphthalein (Agarol).** NOT/kg: 6mo-2yr 2.5ml, 3-5yr 2.5-5ml, >5yr 5ml 8-24H oral.

**Alatrofloxacin.** 4mg/kg (adult 200mg) daily IV over 60min. Severe infn: 6mg/kg (adult 300mg) daily IV over 90min.

**Albendazole.** Pinworm, threadworm, roundworm, hook-worm, whipworm: 20mg/kg (adult 400mg) oral once (may repeat after 2wk). Strongyloides, cutaneous larva migrans, Taenia, H.nana, O.viverrini, C.sinesis: 20mg/kg (adult 400mg) daily for 3 days, repeated in 3wk. 7.5mg/kg (adult 400mg) 12H for 8-30 days (neurocysticercosis); 12H for three 28 day courses 14 days apart (hydatid).

**Albumin.** 20%: 2-5ml/kg IV. 4%: 10-20ml/kg. If no loss from plasma: dose (ml/kg) =  $5 \times (\text{increase g/L}) / (\% \text{ albumin})$ .

**Aldometasone.** 0.05% cream/ointment: apply 8-12H.

**Aldesleukin (synthetic IL-2).** Malignancy: constant IV infsn less toxic than bolus injtn: 3,000,000-5,000,000u/m<sup>2</sup>/day for 5 days, if tolerated repeat x1-2 with 5 day interval.

**Alefacept.** Adult (NOT/kg): 7.5mg IV, 15mg IM weekly for 12wk.

**Alemtuzumab.** Adult (NOT/kg): 3mg daily IV over 2hr for 2-3 days, 10mg daily 2-3 days, then 30mg x3/wk for up to 12wk.

**Alendronate.** 0.5mg/kg (adult 40mg) daily oral.

**Alendronate 70mg + vitamin D3 2800u.** 1 tab each wk oral.

**Alfacalcidol.** 0.05mcg/kg (max 1mcg) daily oral or IV, ad-justed according to response.

**Alfentanil.** 10mcg/kg IV, IM stat, then 5mcg/kg prn. Theatre (ventilated): 30-50mcg/kg IV over 5min, then 15mcg/kg prn or 0.5-1mcg/kg/min. ICU: 50-100mcg/kg IV over 10min, then 0.5-4mcg/kg/min.

**Alfuzosin.** Adult (NOT/kg): 10mg daily oral.

**Alginate acid (Gaviscon single strength).** <1yr: liquid 2ml with feed 4H. 1-12yr: liquid 5-10ml, or 1 tab after meals. >12yr: liquid 10-20ml, or 1-2 tab after meals.

**Alglucerase.** Usual initial dose is 60u/kg every 2wk IV over 2hr, adjusted according to response; reduce every 3-6mo.

**Alimemazine.** See trimeprazine.

**Aliskiren.** Adult (NOT/kg): 150mg (max 300mg) daily oral.

**Alitretinoin.** 0.1% gel: apply 6-12H.

**Allopurinol.** 10mg/kg (adult 300mg) 12-24H oral. Chemo-therapy: 50-100mg/m<sup>2</sup> 6H IV, oral.

**Almotriptan.** Adult (NOT/kg): 6.25-12.5mg oral, repeat in 2hr if reqd (max 2 doses in 24hr).

**Alosetron.** Adult (NOT/kg): 1mg daily oral, incr if reqd after 4wk to 1mg 12H (stop if no response after 4wk).

**Alpha, proteinase inhibitor.** See alpha, antitrypsin.

**Alpha, antitrypsin.** 60mg/kg once wkly IV over 30min

**Alpha tocopheryl acetate.** One alpha-tocopheryl (at) equivalent = 1mg d-at = 1.1mg d-at acetate = 1.5mg dl-at acetate = 1.5u vit E. Abetalipoproteinemia: 100mg/kg (max 4g) daily oral. Cystic fibrosis: 45-200mg (NOT/kg) daily oral. Newborn (high dose, toxicity reported): 10-25mg/kg daily IM or IV, 10-100mg/kg daily oral.

**Alprazolam.** 0.005-0.02mg/kg (adult 0.25-1mg) 8H oral. Slow rel: 0.5-1mg daily, incr to 3-6mg (max 10mg) daily oral.

**Alprenolol.** 1-4mg/kg (max 200mg) 6-12H oral.

**Alprostadil (prostaglandin E1, PGE1).** Maintain PDA: 60 mcg/kg in 50ml 0.9% saline 0.5-3ml/hr (10-60ng/kg/min).

**Alteplase (tissue plasminogen activator).**

0.1-0.6mg/kg/hr IV for 6-12hr (longer if no response); keep fibrinogen >100mg/dL (give cryoprecipitate 1bag/5kg), give heparin 10u/kg/hr IV, give fresh frozen plasma (FFP) 10ml/kg IV daily in infants. Local IA infsn: 0.05mg/kg/hr, give FFP 10ml/kg IV daily. Blocked central line: 0.5mg/2ml (<10kg) 2mg/2ml (>10kg) per lumen left for 2-4hr, withdraw drug, flush with saline; rpt once in 24hr if reqd.

**Altretamine.** 150-300mg/m<sup>2</sup> daily oral.

**Aluminium acetate.** 13% soltn (Burrow's lotion): for wet compresses, or daily to molluscum contagiosum.

**Aluminium chloride hexahydrate.** 20% lotion: x 1-2/wk.

**Aluminium hydroxide.** 25mg/kg (adult 0.5-1g) 4-6H oral. Gel (64mg/ml) 0.1ml/kg 6H oral.

**Aluminium hydroxide 40mg/ml, Mg hydroxide 40mg/ml, simethicone 4mg/ml (Mylanta, Gelusil).** 0.5-1ml/kg (adult 10-20ml) 6-8H oral. ICU: 0.5ml/kg 3H oral if gastric pH <5.

**Aluminium sulphate.** 20% soltn: apply promptly to sting

**Alverine.** 1-2mg/kg (adult 60-120mg) 8-12H oral.

**Amantadine hydrochloride.** 2mg/kg (adult 100mg) 12-24H oral. Flu A prophylaxis (NOT/kg): 100mg daily (5-9yr), 100mg 12H (>9yr).

**Ambrisentan.** Adult (NOT/kg): 5mg (max 10mg) dly oral

**Amcinonide.** 0.1% lotion, cream, ointment: apply 8-12H.

**Amethocaine.** Gel 4% in methylcellulose: 0.5g to skin, apply occlusive dressing, wait 30-60min, remove gel. 0.5%, 1%: 1 drop/eye.

**Amifostine.** 910mg/m<sup>2</sup> IV over 15min daily 30min before chemotherapy; reduce to 740mg/m<sup>2</sup> if severe side effects.

**Amikacin.** Single daily dose IV or IM. Neonate: 15mg/kg stat, then 7.5mg/kg (<30wk) 10mg/kg (30-35wk) 15mg/kg (term <1wk) daily. 1wk-10yr: 25mg/kg day 1, then 18mg/kg daily. >10yr: 20mg/kg day 1, then 15mg/kg (max 1.5g) daily. Trough level <5.0mg/L.

**Amiloride.** 0.2mg/kg (adult 5mg) 12-24H oral.

**Aminoacridine hydrochloride.** See aminacrine.

**Aminacrine hydrochloride.** 0.02% 1 drop/eye 2-4H.

**Aminobenzoic acid.** 60mg/kg (max 3g) 6H oral.

**Aminocaproic acid.** 3g/m<sup>2</sup> (adult 5g) over 1hr IV, then 1g/m<sup>2</sup>/hr (adult 1-1.25g/hr).

Prophylaxis: 70mg/kg 6H IV, oral.

**Aminogluthethimide.** Adult (NOT/kg): 250mg daily oral, incr over 4wk to 250mg 6H.

**Aminohippuric acid (PAHA).** 6-10mg/kg stat, then 0.2-0.5 mg/kg/min IV gives 2mg/100ml in plasma.

**Aminolevulinic acid.** 20% soltn: apply to lesions, expose to 400-450nm blue light for 1000sec (10 J/cm<sup>2</sup>) next day; repeat after 8wk if reqd.

**Aminophylline** (100mg = 80mg theophylline).

Load: 10 mg/kg (max 500mg) IV over 1hr.

Maintenance: 1st wk life 2.5mg/kg IV over 1hr 12H; 2nd wk life 3mg/kg 12H; 3wk-12 mo ((0.12 x age in wk) + 3) mg/kg 8H; >12mo and <35kg, 55 mg/kg in 50ml 5%dex-hep at 1ml/hr (1.1mg/kg/hr) or 6mg/kg IV over 1hr 6H; >35kg and <17yr, or >17yr and smoker, 25 mg/ml at 0.028ml/kg/hr (0.7mg/kg/hr) or 4mg/kg IV over 1hr 6H; >17yr non-smoker 25mg/ml at 0.02ml/kg/hr (0.5mg/kg/hr) or 3mg/kg IV over 1hr 6H; Level 60-80umol/L (neonate), 60-110 (asthma) (x0.18=mcg/ml).

**Aminosalicylic acid (4-Aminosalicylic acid, ASA, 4-ASA, para-ASA, PAS).** 50-100mg/kg (adult 4g) 8H oral.

**5-Aminosalicylic acid.** See mesalazine.

**Amiodarone.** IV: 15mg/kg in 50ml 5% dex (no heparin) at 5ml/hr (25mcg/kg/min) for 4hr, then 1-3ml/hr (5-15mcg/kg/min, max 1.2g/24hr). Oral: 4mg/kg (adult 200mg) 8H 1 wk, 12H 1 wk, then 12-24H. After starting tablets, taper IV infsn over 5 days. Reduce dose of digoxin and warfarin. Pulseless VF or VT: 5mg/kg IV over 3-5 min.

**Amsulpride.** 1-6mg/kg (adult 50-300mg) daily oral; acute psychosis 5-15mg/kg (adult 300-800mg) 12H.

**Amitriptyline.** Usually 0.5-1mg/kg (adult 25-50mg) 8H oral. Enuresis: 1-1.5mg/kg nocte.

**Amlodipine.** 0.05-0.2mg/kg (adult 2.5-10mg) daily oral.

**Amlodipine + olmesartan (5mg/20mg, 5/40, 10/20, 10/40).** Adult (NOT/kg): 1 tablet daily oral.

**Amlodipine + valsartan (5mg/160mg, 5mg/320, 10/160, 10/320).** Adult (NOT/kg): 1 tablet daily oral.

**Amodiaquine.** Treatment: 10mg/kg daily for 3 days oral. Prophylaxis: 5mg/kg once a wk.

**Amorolfine.** Nail lacquer 5%: apply x1-2/wk.

**Amoxapine.** 0.5-2mg/kg (adult 25-100mg) 8H oral.

**Amoxycillin.** 10-25mg/kg (adult 0.25-1g) 8H IV, IM or oral; or 20mg/kg 12H oral. Severe infn: 50mg/kg (adult 2g) IV 12H (1st wk life), 6H (2-4 wk), 4-6H or constant infsn (4+ wk).

**Amoxycillin + clavulanic acid.** Dose as amoxycillin. 4:1 (non-Duo products) 8H, 7:1 (Duo) 12H, 16:1 (XR) 12H oral.

**Amphotericin B (Fungizone).** Usually 1.5mg/kg/day (up to 2mg/kg/day) by continuous infsn IV. Central line: 1.5mg/kg in 50ml 5%dex-hep at 2ml/hr (up to 46kg); 1.5 mg/kg in 1.2 ml/kg 5%dex-hep (1.25mg/ml) at 0.05ml/kg/hr (over 46kg). Peripheral IV: usually 1.5mg/kg in 12ml/kg 5% dex-hep at 0.5ml/kg/hr (higher concentrations may cause thrombo-phleb-itis). Oral (NOT/kg): 100mg 6H, 50mg 6H prophylaxis. Bladder washout: 25 mcg/ml. Cream, oint- 3%: apply 6-12H.

**Amphotericin, colloidal dispersion (Amphocil, Amphotec).** Usually 3-4mg/kg (up to 6mg/kg for aspergillus) daily IV at 2.5mg/kg/hr.

**Amphotericin, lipid complex (Abelcet).**

2.5-5mg/kg daily over 2hr IV, typically for 2-4wk.

**Amphotericin, liposomal (AmBisome).**

3-6mg/kg (up to 15 mg/kg if severe infn) daily over 1-2hr IV, typically for 2-4wk.

**Ampicillin.** 10-25mg/kg (adult 0.25-1g) 6H IV, IM or oral. Severe infn: 50mg/kg (max 2g) IV 12H (1st wk life), 6H (2-4 wk), 3-6H or constant infsn (4+wk).

**Ampicillin + flucloxacillin.** NOT/kg. 125mg/125mg or 250/250 (child), 250/250 or 500/500 (adult) 6H oral, IM or IV.

**Ampicillin 1g + sulbactam 0.5g.** 25-50mg/kg (adult 1-2g) of ampicillin 6H IM or IV over 30min.

**Amprenavir.** Age ≥ 4yr. Soltn (max 2.8g/day): 22.5 mg/kg 12H, or 17mg/kg 8H oral. Caps (max 2.4g/day): 20mg/kg 12H, or 15mg/kg 8H oral.

**Amrinone.** <4wk old: 4mg/kg IV over 1hr, then 3-5mcg/kg/min. >4wk: 1-3mg/kg IV over 1hr, then 5-15mcg/kg/min.

**Amsacrine.** 400-600mg/m<sup>2</sup> IV over 2hr dly x3-5 days

**Amylase.** See pancreatic enzymes.

**Amylobarbitone.** 0.3-1mg/kg (adult 15-50mg) 8-12H, or 2-4mg/kg (adult 200-400mg) at night, oral.

**Anagrelide.** Adult (NOT/kg): 0.5mg 12H, incr slowly if reqd to max 2.5mg 6H oral.

**Anakinra.** Adult (NOT/kg): 100mg daily SC.

**Anastrozole.** Adult (NOT/kg): 1mg daily oral.

**Ancestim (human stem cell factor).** 20mcg/kg/d SC

**Aneurine.** See thiamine.

**Anidulafungin.** 2-4mg/kg (adult 100-200mg) oral day 1, then 1-2mg/kg (adult 50-100mg) daily.

**Anistreplase.** Adult (NOT/kg): 30u IV over 5min.

**Anthraquinone.** See sennoside.

**Antihæmophilic factor.** See factor 8.

**Anti-inhibitor coagulant complex.** See factor 8 inhibitor bypassing fraction.

**Antilymphocyte globulin.** See immunoglobulin, antilymphocyte.

**Antithrombin III.** No. IU = (desired - actual level) x Wt / 2.2.

**Antithymocyte globulin.** See immunoglobulin, antilymphocyte.

**Antivenom to Australian box jellyfish, snakes (black, brown, death adder, sea, taipan, tiger).**

Dose depends on amount of venom injected, not size of patient. Higher doses for multiple bites, severe symptoms or delayed administration. Give adrenaline 0.005mg/kg (0.005ml/kg of 1 in 1000) SC. Initial dose usually 1-2 amp diluted 1/10 in Hartmann's soltn IV over 30min. Monitor PT, PTT, fibrinogen, platelets; give repeatedly if symptoms or coagulopathy persist.

**Antivenom to coral snake (USA).** 3-6 vials IV over 1-2hr, repeat if signs progress. Premedicate with diphenhydramine 5mg/kg (adult 300mg) IV, have adrenaline available.

**Antivenom to Crotalidae (pit vipers - USA).**

4-6 vials, with higher dose for more severe envenomation, diluted 1/10 in saline IV over 1hr, rptd 1hr later if reqd; then 2 vials 6H for 3 doses.

**Apomorphine.** Adult (NOT/kg): usually 2.4-3.6mg/dose (max 6mg) prn to max 50mg/day SC. Infns: 0.02-0.08 mg/kg/hr (max 200mg/day) SC.

**Apraclonidine.** 1 drop/eye 8H (0.5%), 12H (1%).

**Aprepitant.** Adult (NOT/kg): 125mg oral 1hr before chemo, then 80mg on days 2 and 3.

**Aprotinin** (1kiu = 140ng = 0.00056peu, 1mg = 7143kiu). 1,200,000 kiu/m<sup>2</sup> IV over 1hr (plus 1,200,000 kiu/m<sup>2</sup> in prime), then 300,000 kiu/m<sup>2</sup>/hr; half for "low dose". Adult (NOT/kg): 2,000,000kiu IV over 1hr (plus 2,000,000 kiu in prime), then 500,000 kiu/hr; half for "low dose". Prophylaxis: 4000 kiu/kg, then 2000 kiu/kg 6H IV.

**Arachis oil.** 130ml enema as required.

**Arachis oil 57% + chlorbutol 5% + dichlorobenzene 16% (Cerumol).** 5 drops to ear 15-30min before syringing.

**Arformoterol.**

NOT/kg: 15mcg in 2ml 12H by nebulisation.

**Argatroban.** 2mcg/kg/min; adjust to maintain APTT x1.5-3.

**Arginine hydrochloride.** Dose (mg) = BE x Wt(kg) x 70; give half this IV over 1hr, then rpt if reqd.

**Arginine vasopressin.** See vasopressin.

**Aripiprazole.** Adult (NOT/kg): 10-15mg daily oral, incr if reqd after 2wk to max 30mg daily.

**Artemether, oily soltn.** 3.2mg/kg IM stat, then 1.6mg/kg daily until oral therapy possible.

**Artemether 20mg + lumefantrine 120mg.** NOT/kg: 1 tab (10-14kg), 2 tab (15-24kg), 3 tab (25-34kg), 4 tab (>34kg) at 0hr, 8hr, 24hr, 36hr, 48hr, 60hr. Rpt dose if vomits within 1hr of ingestion.

**Artemisinin.** 25mg/kg oral day 1; then 12.5mg/kg dly for 2 days (with mefloquine 15-25mg/kg on day 2), or for 4-6 days if mefloquine resistance.

**Artesunate.** Oral: 5mg/kg day 1; then 2.5mg/kg dly for 2 days (with mefloquine 15-25mg/kg on day 2), or for 4-6 days if mefloquine resistance. IM, or IV over 1-2min: 2mg/kg stat, then 1mg/kg in 6hr if hyperparasitic, then 1mg/kg daily until oral therapy possible.

**Articane 40mg/ml + adrenaline 1:100,000.**

Adult (NOT/kg) avge dose 1.7ml (max 7mg/kg = 0.175ml/kg) by injection.

**Ascorbic acid.**

Burn (NOT/kg): 200-500mg daily IV, IM, SC, oral. Metabolic dis (NOT/kg): 250mg (<7yr) 500mg (>7yr) daily oral. Scurvy (NOT/kg): 100mg 8H oral for 10 days. Urine acidification: 10-30mg/kg 6H.

**Asparaginase.** See colaspase.

**Aspirin.** 10-15mg/kg (adult 300-600mg) 4-6H oral. Antiplatelet: 3-5mg/kg (max 100mg) daily. Kawasaki: 10mg/kg 6H (low dose) or 25mg/kg 6H (high dose) for 2wk, then 3-5 mg/kg daily. Arthritis: 25mg/kg (max 2g) 6H for 3 days, then 15-20mg/kg 6H. Salicylate level (arthritis) midway between doses 0.7-2.0 mmol/L (x13.81 = mg/100ml).

**Aspirin 25mg + dipyridamole 200mg.**

Adult (NOT/kg) 1 sustained rel cap 12H oral.

**Astemizole.** 0.2mg/kg (adult 10mg) daily oral.

**Atazanavir.** >16yr (NOT/kg): 400mg daily oral.

**Atenolol.** Oral: 1-2mg/kg (adult 50-100mg) 12- 24H. IV: 0.05 mg/kg (adult 2.5mg) every 5 min if reqd (max 4 doses), then 0.1-0.2mg/kg (adult 5-10mg) over 10min 12-24H.

**Atomoxetine.** 0.5mg/kg (>70kg 40mg) daily oral, incr after at least 3 days to max 1.2mg/kg (>70kg 100mg) as single daily dose or divided 12H.

**Atorvastatin.** 0.2mg/kg (adult 10mg) dly, incr if reqd every 4wk to max 1.6mg/kg (adult 80mg) dly.

**Atosiban.** Adult (NOT/kg): 6.75mg IV over 1min, then 300 mcg/min for 3hr, then 100mcg/min for max 45hr.

**Atovaquone, micronised.** Pneumocystis: 3-24mo 45mg/kg, >24mo 30mg/kg (max 1500mg) dlyoral.

**Atovaquone 250mg + proguanil 100mg (Malarone).** Malaria treatment: 20mg/kg of atovaquone (adult 1g) daily for 3 days oral; prophylaxis: 5mg/kg of atovaquone (adult 250mg) daily.

**Atovaquone 62.5mg + proguanil 25mg (Malarone paediatric).** Malaria prophylaxis: 5mg/kg (adult 250mg) daily oral.

**Atracurium besylate.** 0.3-0.6mg/kg stat, then 0.1-0.2mg/kg when reqd or 5-10mcg/kg/min IV.

- Atropine.** 0.02mg/kg (max 0.6mg) IV or IM, then 0.01mg/kg 4-6H. Organophosphate poisoning: 0.05-1mg/kg (adult 2mg) IV, then 0.02-0.05mg/kg (adult 2mg) every 15-60min until atropinised, then 0.02-0.08mg/kg/hr for several days.
- Atropine 25mcg + diphenoxylate 2.5mg tab (Lomotil).** Adult (NOT/kg): 1-2 tab 6-8H oral.
- Attapulgite.** Adult (NOT/kg): 0.6-1.2g 3-6H oral.
- Auranofin.** 0.1mg/kg (adult 6mg) daily oral, incr if reqd to max 0.05mg/kg (adult 3mg) 8H.
- Aurothioglucose.** 0.25mg/kg weekly IM, incr to 1mg/kg (max 40mg) weekly for 20wk, then every 1-4wk.
- Azaciditidine.** 75mg/m<sup>2</sup> SC dly for 7 days, rptd every 4wk; incr if reqd after 2 cycles to 100mg/m<sup>2</sup> daily.
- Azapropazone.** 10mg/kg (max 600mg) 12H oral. Acute gout: 6H (day 1), 8H (day 2), then 12H.
- Azatadine.** NOT/kg: 0.5-1mg (child >6yr), 1-2mg (adult) 12-24H oral.
- Azathioprine.** 25-75mg/m<sup>2</sup> (approx 1-3mg/kg) daily oral, IV.
- Azelaic acid.** 20% cream, 15% gel: apply 12H.
- Azelastine.** 0.1% spray, >5yr: 0.15ml to each nostril 12H.
- Azidothymidine (AZT).** See zidovudine.
- Azithromycin.** Oral (only 40% bioavailable): 15mg/kg (adult 500mg) on day 1 then 7.5mg/kg (adult 250mg) days 2-5, or 15mg/kg (adult 500mg) dly for 3 days; trachoma 20 mg/kg (adult 1g) wkly x3; MAC prophylaxis (adult) 1.2g wkly; Gp A strep 20mg/kg dly x3. IV: 15mg/kg (adult 500mg) day 1, then 5mg/kg (adult 200mg) dly. 1% eye drops: 1 drop 12H for 2 days, then dly for 5 days.
- Aztreonam.** 30mg/kg (adult 1g) 8H IV. Severe infn: 50mg/kg (adult 2g) 12H (1st wk life), 8H (2-4 wk), 6H or infns (4+ wk).
- Bacampicillin.** 15-25mg/kg (adult 400-800mg) 12H oral.
- Bacillus Calmette-Guerin (BCG) vaccine (CSL).** Live. Intradermal (1mg/ml): 0.075ml (<3mo) or 0.1ml (>3mo) once. Percutaneous (60mg/ml suspension): 1 drop on skin, inoculated with Heaf apparatus, once.
- Bacillus Calmette-Guerin (BCG) suspension, about 5 x 10<sup>8</sup> cfu/vial.** Adult: 1 vial (OncoTICE) or 3 vials (Immu-Cyst) left in bladder for 2hr each wk for 6wks, then at 3, 6, 12, 18 and 24mo.
- Bacitracin 500u/g + polymyxin B 10,000u/g.** Eye ointment: apply x2-5/day.
- Bacitracin 400u/g + polymyxin B 5000u/g + neomycin 5mg/g (Neosporin).** Ointment or eye ointment: apply x2-5/day. Powder: apply 6-12H (skin infn), every few days (burns). Eye drops: see gramicidin.
- Baclofen.** 0.2mg/kg (adult 5mg) 8H oral, incr every 3 days to 1mg/kg (adult 25mg, max 50mg) 8H. Intrathecal infns: 2-20mcg/kg (max 1000mcg)/24hr.
- Balsalazide.** Adult (NOT/kg): 2.25g 8H oral (= 2.34g -mesalazine daily).
- Bambuterol.** 0.2-0.4mg/kg (adult 10-20mg) nocte oral
- Basiliximab.** 12mg/m<sup>2</sup> (max 20mg) IV 2hr preop, repeated 4 days later.
- BCG vaccine.** See Bacillus Calmette-Guerin vaccine.
- Beclomethasone dipropionate.** Rotacap or aerosol (NOT /kg): 100-200mcg (<8yr), 150-400mcg (>8yr) x2/day (rare-ly x4/day). Nasal (NOT/kg): aerosol or pump (50mcg /spray): 1spray 12H (<12yr), 2spray 12H (>12yr).
- Bemiparin.** Surgery (adult, NOT/kg): 2500u (orthopaedics 3500u) SC 2hr pre-op or 6hr post-op, then daily for 7-10 days. DVT: 115u/kg daily 5-9 days (or until oral anticoag).
- Benazepril.** 0.2-0.4mg/kg (adult 10-20mg) 12-24H oral.
- Bendroflumethiazide.** See bendrofluazide.
- Bendrofluazide.** 0.1-0.2mg/kg (adult 5-10mg) dly oral.
- Benflumetol (lumefantrine).** See artemether.
- Benorylate.** 30mg/kg (adult 1.5g) 8H oral.
- Benperidol.** 5-15mcg/kg (adult 0.25-1.5mg) 12-24H oral.
- Benserazide.** See levodopa + benserazide.
- Benazathine penicillin.** See penicillin, benzathine.
- Benzbromarone.** Adult (NOT/kg): 50-300mg daily oral, or 20-25mg with allopurinol.
- Benzhexol.** >3yr: 0.02mg/kg (adult 1mg) 8H, incr to 0.1-0.3 mg/kg (adult 1.5-5mg) 8H oral.
- Benzoic acid.** 1%-20% topical: usually applied 4-6H.
- Benzoic acid + cetylpyridinium.** Mouth wash (Cepacaine): apply 3H prn, do not swallow.
- Benzocaine + phenazone 5.4% (Auralgin).** 3 drops per ear 3 times a day for 2-3 days.
- Benzoic acid 6% + salicylic acid 3%.** Whitfield's ointment: apply 12H.
- Benzonatate.** 2-4mg/kg (adult 100-200mg) 8H oral.
- Benzoil peroxide.** Liq, gel 2.5%-10%: apply x 1-3/d
- Benzoquinamide.** IM: 0.5-1mg/kg (adult 50mg) stat and repeat in 1hr if needed, then 3-4H prn. IV over 1-5min: 0.2-0.4mg/kg (adult 25mg) once.
- Benztiazide 25mg + triamterene 50mg.** Adult (NOT/kg): 1-2 tab on alternate days, oral.
- Benztropine.** >3yr: 0.02mg/kg (adult 1mg) stat IM or IV, may repeat in 15min. 0.02-0.06mg/kg (adult 1-3mg) 12-24H oral.
- Benzyd benzoate.** 25% lotion. Scabies: apply from neck down after hot bath, wash off after 24hr; repeat in 5days. Lice: apply to infected region, wash off after 24hr; repeat in 7days.



**Benzylpenicillin.** See penicillin G.

**Bepiridil.** 4-8mg/kg (adult 200-400mg) daily oral.

**Beractant (bovine surfactant, Survanta).**

25mg/ml soltn. 4ml/kg intratracheal 2-4 doses in 48hr, each dose in 4 parts: body inclined down with head to right, body down head left, body up head right, body up head left.

**Beta carotene.** Porphyria: 1-5mg/kg (adult 30-300mg) daily.

**Betahistine.** 0.15-0.3mg/kg (adult 8-16mg) 8H oral.

**Betaine hydrochloride.** Usually 60mg/kg (adult 3g) 12H oral, max 100mg/kg (adult 5g) 12H.

**Betamethasone.** 0.01-0.2mg/kg daily oral. Betamethasone has no mineralocorticoid action, 1mg = 25mg hydrocortisone in glucocorticoid action. Gel 0.05%; cream, lotion, ointment, 0.02%, 0.05%, 0.1%: apply sparingly 8-24H. Eye 0.1%: initially 1 drop/eye 1-2H, then 6H; or 0.6cm oint 8-12H.

**Betamethasone 0.1% + neomycin 0.5%.**

1 drop/eye 4-8H.

**Betamethasone acetate 3mg/ml + betamethasone sodium phosphate 3.9mg/ml (Celestone Chronodose).** Adult: 0.25-2ml (NOT/kg) IM, intra-articular, or intralesional injection.

**Betamethasone dipropionate 0.064% + calcipotriol 0.005% (Dovonex).** Ointment: apply daily to no more than 30% of body for up to 4wk (max 100g/wk in adult).

**Betaxolol.** 0.4-0.8mg/kg (adult 20-40mg) daily oral. Eye drops 0.25%-0.5%: 1 drop/eye 12H.

**Bethanecol.** Oral: 0.2-1mg/kg (adult 10-50mg) 6-8H. SC: 0.05-0.1mg/kg (adult 2.5-5mg) 6-8H.

**Bevacizumab.** 5mg/kg IV every 14 days.

**Bexarotene.** 300mg/m<sup>2</sup> (range 100-400mg/m<sup>2</sup>) daily oral.

**Bezafibrate.** 4mg/kg (adult 200mg) 8H oral with food.

**Bicalutamide.** Adult (NOT/kg): 50-150mg daily oral.

**Bicalutamide + goserelin.** Adult (NOT/kg): 50mcg daily oral, + goserelin 10.8mg implant 4 wkly or 10.8mg SC every 3mo.

**Bicarbonate.** Slow IV: dose (mmol) = BE x Wt/4 (<5kg), BE x Wt/6 (child), BE x Wt/10 (adult). These doses correct half the base deficit. Alkalise urine: 0.25mmol/kg 6-12H oral.

**Bifonazole.** 1% cream: apply daily for 2-4wk.

**Bimatoprost.** 0.03% drops: 1 drop/eye/evening.

**Bimatoprost 0.3mg/ml + timolol 5mg/ml.** 1 drop/eye daily.

**Biotin (coenzyme R, vitamin H).**

NOT/kg: 5-20mg daily IV, IM, SC or oral.

**Biperiden hydrochloride.** 0.02-0.04mg/kg (adult 1-2mg) 8-12H oral. IM or slow IV: 0.05-0.1mg/kg (adult 2.5-5mg), max x4/day.

**Bisacodyl.** NOT/kg: <12mo 2.5mg PR, 1-5yr 5mg PR or 5-10mg oral, >5yr 10mg PR or 10-20mg oral. Enema: half daily (6mo-3yr), 1 enema daily (>3yr).

**Bisacodyl 10mg + docusate sodium 100mg.**

<2yr half suppos, 1-11yr half to 1 suppos, >11yr 1 suppos daily.

**Bismuth subsalicylate.** 5mg/kg (adult 240mg) 12H oral 30min before meal. H.pylori (adult, NOT/kg): 107.7mg x4/day with meals and nocte for 2wk + tetracycline 500mg x4/day + metronidazole 200mg with meals and 400mg nocte; see also omeprazole + bismuth.

**Bisoprolol.** 0.2-0.4mg/kg (adult 10-20mg) dly oral.

**Bitolterol.** Resp soltn (0.2%): 1ml diluted to 4ml 3-6H (mild), 2ml diluted to 4ml 1-2H (moderate), undiltd -con-stant (severe, in ICU). Aerosol 370mcg/puff: 1-2 puff 4-6H.

**Bivalirudin.** 0.75-1mg/kg IV stat, then 1.75-2.5mg/kg/hr for 4hr, then stop or give 1.75-2mg/kg/hr for 14-20hr.

**Bleomycin sulfate.** 10-20u/m<sup>2</sup> IM, SC or IV over 15min x1-2/wk. Max total dose 250u/m<sup>2</sup>.

**Bortezomib.** 1.3mg/m<sup>2</sup> on days 1, 4, 8, 11; then 10 day rest (21 day cycle, average 6 cycles). Stop if toxicity, then use 1 mg/m<sup>2</sup>/dose; stop if toxicity recurs, then use 0.7mg/m<sup>2</sup>/dose.

**Bosentan.** 1mg/kg (adult 62.5mg) 12H oral for 1-4wk, then 2mg/kg (adult 125mg) 12H. IV: half oral dose.

**Botulinum toxin type A.** NOT/kg: 1.25-2.5u/site (max 5u/site) IM, max total 200u in 30 days. Oesoph achalasia: 100u per session divided between 4-6 sites. Hyperhidrosis: 50u/2ml intradermal per axilla (given in 10-15 sites).

**Botulinum toxin type B.** NOT/kg: usual total dose 2,500-10,000u, rptd every 3-4 mo if reqd.

**Bretylium tosylate.** 5mg/kg IV in 1hr, then 5-30 mcg/kg/min.

**Brimonidine.** 0.2%: 1 drop/eye 12H.

**Brimonidine 0.2% + timolol 0.5%.** 1 drop/eye 12H.

**Brinzolamide.** 1%: 1 drop/eye 8-12H.

**Bromazepam.** 0.02-0.1mg/kg (adult 1-3mg) 8H oral

**Bromhexine.** 0.3mg/kg (adult 16mg) 8H oral for 7 days, then 0.15mg/kg (adult 8mg) 8H.

**Bromocriptine.** 0.025mg/kg (adult 1.25mg) 8-12H, incr wkly to 0.05-0.2mg/kg (adult 2.5-10mg) 6-12H oral. Inhibit lactation, NOT/kg: 2.5mg 12H for 2wk.

**Brompheniramine.** 0.1-0.2mg/kg (adult 5-10 mg) 6-8H oral, SC, IM or slow IV.

**Bucizine.** 0.25-1mg/kg (adult 12.5-50mg) 8-24H oral

**Budesonide.** Metered dose inhaler (NOT/kg): <12yr 50-200 mcg 6-12H, reducing to 100-200mcg 12H; >12yr 100-600 mcg 6-12H, reducing to 100-400mcg 12H.

Nebuliser (NOT/kg): <12yr 0.5-1mg 12H, reducing to 0.25-0.5mg 12H; >12yr 1-2mg 12H, reducing to 0.5-1mg 12H. Croup: 2mg (NOT/kg) nebulised. Nasal spray, aerosol (NOT/kg): 64-128 mcg/ nostril 12-24H. Crohns dis, adult (NOT/kg): 9mg daily for 8wk, then reduce over 4wk.

**Budesonide + formoterol.** NOT/kg: 80mcg / 4.5mcg or 160mcg/4.5mcg, two inhalations 12H.

**Bumetanide.** 25mcg/kg (adult 1mg) daily oral, may incr to max 50mcg/kg (adult 3mg) 8-12H.

**Bupivacaine.** Max dose: 2-3mg/kg (0.4-0.6ml/kg of 0.5%). With adrenaline: max dose: 3-4mg/kg (0.6-0.8ml/kg of 0.5%). Intrathecal: 1mg/kg (0.2ml/kg of 0.5%). Epidural: 2mg/kg (0.4ml/kg of 0.5%) stat intraop, then 0.25mg/kg/hr (0.2ml/kg/hr of 0.125%) postop. Intrapleural: 0.5% 0.5ml/kg (max 20ml) 8-12H, or 0.5ml/kg (max 10ml) stat then 0.1-0.25 ml/kg/hr (max 10ml/hr). Epidural in ICU: 25ml 0.5% + 1000 mcg (20ml) fentanyl + saline to 100ml at 2-8ml/hr in adult.

**Buprenorphine.** Adult (NOT/kg): 200-800mcg 6-8H sublin-gual, IM or slow IV.

**Bupropion.** 2-3mg/kg (adult 100-150mg) 8-12H oral

**Burrow's solution.** See aluminium acetate soltn.

**Buserelin.** Adult, NOT/kg. Intranasal: 100mcg 4H, or 150 mcg each nostril 8H.

**Buspirone.** 0.1mg/kg (adult 5mg) 8-12H oral, incr to max 0.3mg/kg (adult 15mg) 8-12H.

**Busulfan.** Induction: 0.06mg/kg (max 4mg) daily oral if leucocytes >20,000/mm<sup>3</sup> and platelets >100,000/mm<sup>3</sup>. Maintenance: 0.01-0.03mg/kg (max 2mg) daily.

**Butalbital.** 1-2mg/kg (adult 50-100mg) 8-24H oral.

**Butenafine.** 1% cream: apply 12-24H for 1-4wk.

**Butobarbitone.** 2-4mg/kg (adult 100-200mg) nocte oral.

**Butoconazole nitrate.** 2% vaginal cream: 5g (NOT/kg) nocte.

**Butorphanol.** IM: 0.02-0.1mg/kg (adult 1-4mg)

3-4H. IV: 0.01-0.05mg/kg (adult 0.5-2mg) 3-4H.

**C1 esterase inhibitor.** 1u = activity 1ml plasma. 10-50u/kg IV over 1hr once (prophylaxis), 12-24H (treatment).

**Cabergoline.** 10mcg/kg/wk (adult 0.5mg) in 1-2 doses, incr if reqd mthly by 10mcg/kg/wk to usu. 20mcg/kg/wk (adult 1mg) in 1-4 doses, max 90mcg/kg/wk (adult 4.5mg). Inhibit lactation: 1 mg oral stat.

**Caffeine citrate.** 2mg citrate = 1mg base. 1-5mg/kg (adult 50-250mg) of citrate 4-8H oral, PR. Neonate: 20mg/kg stat of citrate, then 5mg/kg daily oral or IV over 30min; weekly level 5-30mg/L midway between doses.

**Calcifediol (25-OH D3).** Deficiency: 1-2mcg/kg daily oral.

**Calciferol (Vitamin D2).** See ergocalciferol.

**Calcipotriol.** 50mcg/g (0.005%) ointment: apply 12-24H. See also betamethasone + calcipotriol ointment.

**Calcitonin.** Hypercalcaemia: 4u/kg 12-24H IM or SC, may incr up to 8u/kg 6-12H. Paget's: 1.5-3u/kg (max 160u) x3/wk IM or SC. Nasal spray: 200u daily.

**Calcitriol (1,25-OH vitamin D3).** Renal failure, vit D resistant rickets: 0.02mcg/kg daily oral, incr by 0.02mcg/kg every 4-8wk according to serum Ca (adult usually 0.25mcg 12H).

**Calcium (as carbonate, lactate or phosphate).** NOT/kg. Neonate: 50mg x4-6/day; 1mo-3yr: 100mg x2-5/day oral; 4-12yr: 300mg x2-3/day; >12yr: 1000mg x1-2/day.

**Calcium carbimide.** 1-2mg/kg (adult 50-100mg) 12H oral.

**Calcium carbonate.** Adult NOT/kg: 1250-1500mg (500-600 mg calcium) 8H oral with meals for hyperphosphataemia.

**Calcium chloride.** 10% soltn (0.7mmol/ml Ca): 0.2ml/kg (max 10ml) slow IV stat. Requirement <16yr 2ml/kg/day IV. Inotrope: 0.03-0.12 ml/kg/hr (0.5-2mmol/kg/day) via CVC.

**Calcium edetate (EDTA).** See sodium calciumedetate

**Calcium folinate.** NOT/kg: 5-15mg oral, or 1mg IM or IV daily. Rescue starting up to 24hr after methotrexate: 10-15 mg/m<sup>2</sup> 6H for 36-48hr IV. Methotrexate toxicity: 100-1000mg/m<sup>2</sup> 6H IV. Before a fluorouracil dose of 370 mg/m<sup>2</sup>: 200mg/m<sup>2</sup> IV daily x5, repeat every 3-4wk.

**Calcium gluconate.** 10% soltn (0.22mmol/ml Ca): 0.5ml/kg (max 20ml) slow IV stat. Requirement <16yr 5ml/kg/day IV. Inotrope: 0.5-2mmol/kg/day (0.1-0.4ml/kg/hr) via CVC.

**Calcium levofolinate.** ½ the dose of calcium folinate.

**Calcium leucovorin.** See calcium folinate.

**Calcium polystyrene sulfonate (Calcium Resonium).** 0.3-0.6g/kg (adult 15-30g) 6H NG (+ lactulose), PR.

**Calfactant.** 35mg/ml phospholipids, 0.65mg/ml proteins: 1.5 ml/kg intratracheal gradually over 20-30 breaths during inspiration with infant lying on one side, then another 1.5 ml/kg with infant lying on other side.

**Candesartan.** 0.1-0.3mg/kg (adult 4-16mg) dly oral.

**Canrenoate.** 3-8mg/kg (adult 150-400mg) daily IV.

**Capecitabine.** 1250mg/m<sup>2</sup> 12H oral for 2wk then 1wk off, in 3wk cycles.

**Capreomycin sulphate.** 20mg/kg (adult 1g) IM daily, decr after 2-4mo to 2-3 times per wk.

**Capsaicin.** Cream 0.025%, 0.075%. Apply 6-8H. wash off after 24hr; repeat in 7days.

- Captopril.** Beware hypotension. 0.1mg/kg (adult 2.5-5mg) 8H oral, incr if reqd to max 2mg/kg (adult 50mg) 8H. Less hypotension if mixed with NG feeds given continuously (or 1-2H).
- Carbachol.** 0.01%: max 0.5ml in ant. chamber (eye)
- Carbamazepine.** 2mg/kg (adult 100mg) 8H oral, may incr over 2-4wk to 5-10mg/kg (adult 250-500mg) 8H. Bipolar dis-order (adult, NOT/kg): 200mg as slow-rel cap 12H oral, incr if reqd to max 800mg 12H. Level 20-40umol/L ( $\times 0.24 = \text{mg/l}$ ).
- Carbaryl.** 0.5% lotion: rub into hair, leave 12hr, wash
- Carbenicillin.** 382mg tab, adult (NOT/kg): 1-2 tab 4H oral.
- Carbenoxolone sodium.** Adult (NOT/kg): 20-50mg 6H oral. Mouth gel 2%, or 2g granules in 40ml water, apply 6H.
- Carbetocin.** Adult (NOT/kg): 100mcg IV over 1 min; IM
- Carbidopa.** See levodopa + carbidopa.
- Carbimazole.** 0.4mg/kg (adult 20mg) 8-12H oral for 2wk, then 0.1mg/kg (adult 5-10mg) 8-24H.
- Carbinoxamine.** NOT/kg: 2mg (1-3yr), 2-4mg (3-6yr), 4-8mg (>6yr) 6-8H oral.
- Carbocisteine.** 10-15mg/kg (adult 500-750mg) 8H oral
- Carboplatin.** 300-400mg/m<sup>2</sup> IV over 60min every 4wk
- Carglumic acid.** 50mg/kg 12H oral, incr to 6H if reqd
- Carisoprodol.** 7mg/kg (adult 350mg) 6H oral.
- Carmustine (BCNU).** 200mg/m<sup>2</sup> IV over 2hr every 6wk ( $\downarrow$  if wbc <3000/mm<sup>3</sup> or plt <75,000/mm<sup>3</sup>).
- Carnitine, L form.** IV: 5-15mg/kg (max 1g) 6H. Oral: 25mg/kg 6-12H (max 3g/day).
- Carob bean gum.** NOT/kg: 1 scoop (1.8g) in 100ml water, give 10-20ml by spoon; or add  $\frac{1}{2}$  scoop to every 100-200ml of milk.
- Carteolol.** 0.05-0.2mg/kg (adult 2.5-10mg) daily oral. 1%, 2%: 1drop/eye 12H.
- Carvedilol.** 0.08mg/kg (adult 3.125mg) 12H oral; if tolerated incr by 0.08mg/kg (adult 3.125mg) every 1-2wk to max 0.5-0.75mg/kg (adult 25mg) 12H.
- Casanthranol + docusate sodium.** Cap 30mg/100mg (NOT/kg): adult 1-2cap 12-24H oral. Syrup 2mg/4mg per ml (NOT/kg): child 5-15ml bedtime, adult 15-30ml 12-24H.
- Caspofungin.** 70mg/m<sup>2</sup> (max 70mg) day 1, then 50 mg/m<sup>2</sup> (usu. max 50mg, up to 70mg) dly IV over 1h
- Cefaclor.** 10-15mg/kg (adult 250-500mg) 8H oral. Slow release tab 375mg (adult, NOT/kg): 1-2 tab 12H oral.
- Cefadroxil.** 15-25mg/kg (adult 0.5-1g) 12H oral.
- Cefamandole.** See cephamandole.
- Cefazolin.** See cephalazolin.
- Cefdinir.** 14mg/kg (adult 600mg) daily (or in 2 divided doses) oral.
- Cefditoren.** 4-8mg/kg (adult 200-400mg) 12H oral.
- Cefepime hydrochloride.** 25mg/kg (adult 1g) 12H IM or IV. Severe infn: 50mg/kg (adult 2g) IV 8-12H or constant infnsn.
- Cefixime.** 5mg/kg (adult 200mg) 12-24H oral.
- Cefodizime.** 25mg/kg (max 1g) 12H IV or IM.
- Cefonicid.** 15-50mg/kg (adult 0.5-2g) IV or IM dly
- Cefoperazone.** 25-60mg/kg (max 1-3g) 6-12H IV in 1hr or IM.
- Cefotaxime.** 25mg/kg (adult 1g) 12H (<4wk), 8H (4+wk) IV. Severe infn: 50mg/kg (adult 2-3g) IV 12H (preterm), 8H (1st wk life), 6H (2-4 wk), 4-6H or constant infnsn (4+ wk).
- Cefotetan.** 25mg/kg (adult 1g) 12H IM, IV. Severe infn: 50mg/kg (max 2-3g) 12H or constant infnsn.
- Cefoxitin.** 25-60mg/kg (adult 1-3g) 12H (1st wk life), 8H (1-4wk), 6-8H (>4wk) IV.
- Cefpirome.** 25-50mg/kg (adult 1-2g) 12H IV.
- Cefpodoxime.** 5mg/kg (adult 100-200mg) 12H oral.
- Cefprozil.** 15mg/kg (adult 500mg) 12-24H oral.
- Ceftazidime.** 15-25mg/kg (adult 0.5-1g) 8H IV or IM. Severe infn, cystic fibrosis: 50mg/kg (max 2g) 12H (1st wk life), 8H (2-4 wk), 6H or constant infnsn (4+ wk).
- Ceftibuten.** 10mg/kg (adult 400mg) daily oral.
- Ceftizoxime.** 25-60mg/kg (adult 1-3g) 6-8H IV.
- Ceftriaxone sodium.** 25mg/kg (adult 1g) 12-24H IV, or IM (in 1% lignocaine). Severe infn: 50mg/kg (max 2g) dly (1st wk life), 12H (2+ wk). Epiglottitis: 100mg/kg (max 2g) stat, then 50mg/kg (max 2g) after 24hr. Meningococ proph (NOT/kg): child 125mg, >12yr 250mg IM in 1% lignocaine once.
- Cefuroxime.** Oral (as cefuroxime axetil): 10-15mg/kg (adult 250-500mg) 12H. IV: 25mg/kg (adult 1g) 8H. Severe infn: 50mg/kg (max 2g) IV 12H (1st wk life), 8H (2nd wk), 6H or constant infnsn (>2wk).
- Celecoxib.** Usually 2mg/kg (adult 100mg) 12H, or 4mg/kg (adult 200mg) daily oral.
- Celiprolol.** 5-10mg/kg (adult 200-400mg) daily oral.
- Cephalexin.** 7.5mg/kg (adult 250mg) 6H, or 15mg/kg (adult 500mg) 12H oral.
- Cephalothin.** 15-25mg/kg (adult 0.5-1g) 6H IV or IM. Severe infn: 50mg/kg (max 2g) IV 4H or constant infnsn. Irrigation fluid: 2g/L (2mg/ml).
- Cephmandole.** 15-25mg/kg (adult 0.5-1g) 6-8H IV over 10min or IM. Severe infn: 40mg/kg (adult 2g) IV over 20min 4-6H or constant infnsn.
- Cephazolin.** 10-15mg/kg (adult 0.5g) 6H IV or IM. Severe infn: 50mg/kg (adult 2g) IV 4-6H or constant infnsn. Surgical proph: 50mg/kg IV at induction.
- Cephadrine.** Oral: 10-25mg/kg (adult 0.25-1g) 6H. IM or IV: 25-50mg/kg (adult 1-2g) 6H.
- Certoparin.** Prophylaxis: 60u/kg (adult 3000u) 1-2hr preop, then daily SC.

**Cetirizine.** NOT/kg: 2.5mg (6mo-2yr), 2.5-5mg (2-5yr), 5-10mg (>5yr) daily oral.

**Cetrimide.** See chlorhexidine.

**Cetrorelix (GnRH antagonist).** Adult (NOT/kg): 0.25 mg SC on stimulation day 5, then dly till hCG given.

**Cetuximab.** 400mg/m<sup>2</sup> IV over 2hr, then 250mg/m<sup>2</sup> wklly.

**Cetylpyridinium.** See benzocaine + cetylpyridinium.

**Cevimeline.** 0.6mg/kg (adult 30mg) 8H oral.

**Charcoal, activated.** Check bowel sounds present. 1-2g/kg (adult 50-100g) NG; then 0.25g/kg hrly if reqd. Laxative: sorbitol 1g/kg (1.4ml/kg of 70%) once NG, may repeat x1.

**Chenodeoxycholic acid.** 5-10mg/kg 12H oral.

**Chloral betaine.** 1.7mg = 1mg chloral hydrate.

**Chloral hydrate.** Hypnotic: 50mg/kg (max 2g) stat (ICU up to 100mg/kg, max 5g). Sedative: 8mg/kg 6-8H oral or PR.

**Chlorambucil.** Typically 0.1-0.2mg/kg daily oral.

**Chloramphenicol.** Severe infn: 40mg/kg (max 2g) stat IV, IM or oral; then 25mg/kg (max 1g) daily (1st wk life) 12H (2-4 wk) 8H (>4wk) x5 days, then 6H. Eye drop, oint: apply 2-6H. Ear: 4drop 6H. Serum level 20-30mg/L 2hr, <15mg/L trough.

**Chlordiazepoxide.** 0.1mg/kg (adult 5mg) 12H oral, may incr to max 0.5mg/kg (adult 30mg) 6-8H.

**Chlorhexidine.** 0.1%: catheterisation prep, impetigo. 0.2%: mouthwash. 1%: skin disinfection. 2-4%: hand wash.

**Chlorhexidine 0.5% + alcohol 70%.** Skin disinfection.

**Chlorhexidine 1.5% + cetrimide 15%.** 1/50 in water: cleaning tissues, wounds or equipment. 140ml in 1 L water: disinfecting skin, equipment (soak 2 min, rinse in sterile water).

**Chlorhexidine + cetrimide.** 0.05%/0.5%, 0.1%/1%, 0.15%/0.15% soltn: wound cleaning.

**Chlorhexidine 1% + hexamidine 0.15%.** Powder: wounds.

**Chlormethiazole.** IV (edisylate 0.8%): 1-2ml/kg (8-16 mg/kg) over 15min, then 0.5-1ml/kg/hr (4-8 mg/kg/hr). Caps 192 mg base, adult (NOT/kg): 2-4 cap stat (may rpt in 1-2hr), then 1-2cap 8H, oral.

**Chlormezanone.** 5mg/kg (adult 200mg) 6-8H, or 10mg/kg (adult 400mg) at night oral.

**Chlorophyllin copper complex.** 2mg/kg 8-24H oral.

**Chloroprocaine.** Max 11mg/kg (max 800mg). With adrenaline (1/200,000) max 14mg/kg (max 1000mg).

**Chloroquine, base.** Oral: 10mg/kg (max 600mg) daily x3 days. IM: 4mg/kg (max 300mg) 12H for 3 days. Prophylaxis: 5mg/kg (adult 300mg) oral x1/wk. Lupus, rheu arth: 12mg/kg (max 600mg) daily, reduce to 4-8mg/kg (max 400mg) daily.

**Chlorothiazide.** 5-20mg/kg (adult 0.25-1g) 12-24H oral, IV.

**Chlorphenasin. 1% ointment:** apply 12H.

**Chlorpheniramine.** 0.1mg/kg (adult 4mg) 6-8H oral.

**Chlorpheniramine 1.25mg + phenylephrine 2.5mg in 5ml.** Syr (NOT/kg): 1.25-2.5ml (0-1yr), 2.5-5ml (2-5yr), 5-10ml (6-12yr), 10-15ml (>12yr) 6-8H oral.

**Chlorpromazine.** Oral or PR: 0.5-2mg/kg (max 100mg) 6-8H; up to 20mg/kg 8H for psychosis. IM (painful) or slow IV (beware hypotension): 0.25-1mg/kg (usual max 50mg) 6-8H.

**Chlorpropamide.** Adult (NOT/kg): initially 125-250mg oral, max 500mg daily.

**Chlorquinaldol.** 5% paste: apply 12H.

**Chlortetracycline.** 3% cream, ointment: apply 8-24H.

**Chlortetracycline 115.4mg + demeclocycline 69.2mg + tetracycline 115.4mg.** NOT/kg. >12yr: 1 tab 12H oral.

**Chlorthalidone.** 2mg/kg (max 100mg) 3 x /wk oral.

**Chlorzoxazone.** 5-15mg/kg (max 250-750mg) 6-8H oral

**Cholecalciferol (Vitamin D3).** 1 mcg = 40u = 1mcg ergocalciferol (qv). Osteodys-trophy: 0.2mcg/kg (hepatic) 15-40mcg/kg (renal) daily oral.

**Cholera, whole cell plus toxin b subunit recombinant vaccine (Dukoral).** Inactivated. Dissolve granules in 150ml water. 2-6yr: give 75ml x3 doses 1wk apart oral, boost after 6mo. >6yr: give 150ml x2 doses 1wk apart, boost after 2yr.

**Cholestyramine.** NOT/kg. 1g (<6yr) 2-4g (6-12yr) 4g (>12yr) dly oral, incr over 4wk to max 1-2x initial dose 8H.

**Choline magnesium trisalicylate.** See aspirin.

**Choline salicylate, mouth gel (Bonjela).** Apply 3H pm

**Choline theophyllinate** (200mg = theophylline 127mg). See theophylline.

**Choriogonadotropin alfa.** Adult(NOT/kg):250mcg SC

**Chorionic gonadotrophin.** NOT/kg.

Cryptorchidism all ages: 500-1000u x1-2/wk for 5wk. After FSH: 10,000iu IM once. Men: 7000iu IM x2/wk, with 75iu FSH and 75iu LH IM x3/wk.

**Chymopapain.** Adult (NOT/kg): 2000-4000 picokatal units / disc, max 10,000 picokatal units per patient.

**Ciclesonide.** Inhaltn (adult): 160mcg in the evening, reducing to 80mcg if possible.

**Ciclopirox.** 1% cream or lotion: apply 12H.

**Cidofovir.** 5mg/kg over 1hr IV on day 0, 7, then every 14 days (with probenecid). Papilloma: inject 6.25 mg/ml soltn (max total 0.6mg/kg) at ≥2wk intervals

**Cilazapril.** Usu. 0.02-0.1mg/kg (adult 1-5mg)dly oral. Renal hypertension: 0.005-0.01mg/kg dly oral.

**Cilostazol.** Adult (NOT/kg): 100mg 12H oral.

**Cimetidine.** Oral: 5-10mg/kg (adult 300-400mg) 6H, or 20 mg/kg (adult 800mg) nocte. IV: 10-15mg/kg (adult 200mg) 12H (newborn), 6H (>4wk).

- Cinacalcet.** Adult (NOT/kg) 30mg daily oral, incr every 2-4wk (to max 180mg) to control parathyroid hormone level. Parathyroid carcinoma: 30mg 12H, incr every 2-4wk if reqd to control serum Ca to max 90mg 6H oral.
- Cinnarizine.** 0.3-0.6mg/kg (adult 15-30mg) 8H oral. Periph vasculitis: 1.5mg/kg (adult 75mg) 8H oral.
- Cinchocaine.** Max dose 2mg/kg (0.4ml/kg of 0.5%) by injection. Oint 0.5% with hydrocortisone 0.5%: apply 8-24H.
- Cinoxacin.** 10mg/kg (adult 500mg) 12H oral.
- Ciprofibrate.** 2-4mg/kg (adult 100-200mg) daily oral.
- Ciprofloxacin.** 5-10mg/kg (adult 250-500mg) 12H oral, 4-7mg/kg (adult 200-300mg) 12H IV. Severe infn, or cystic fibrosis: 20mg/kg (max 750mg) 12H oral, 10mg/kg (max 400mg) 8H IV; higher doses used occasionally. Meningococcus prophylaxis: 15mg/kg (max 500mg) once oral.
- Ciprofloxacin, eye drops. 0.3%.** Corneal ulcer: 1 drop/15min for 6hr then 1 drop/30 min for 18hr (day 1), 1drop 1H (day 2), 1drop 4H (day 3-14). Conjunctivitis: 1 drop 4H; if severe 1 drop 2H when awake for 2 days, then 6H.
- Ciprofloxacin, eye ointment. 0.3%.** Apply 1.25cm 8H for 3 days, then 12H for 3 or more days.
- Cisatracurium.** 0.1mg/kg (child) or 0.15mg/kg (adult) IV stat, then 0.03mg/kg if reqd or 1-3mcg/kg/min. ICU: 0.15 mg/kg stat, then (1-10mcg/kg/min) IV.
- Cisplatin.** 60-100mg/m<sup>2</sup> IV over 6hr every 3-4wk x6 cycles.
- Citalopram.** 0.4mg/kg (adult 20mg) dly, incr if reqd over 4wk to max 0.4mg/kg (adult 60mg) dly oral.
- Citric acid 0.25g + potassium citrate 1.5g.** Urine alkalinisation >6yr (NOT/kg): 2 tab 8-12H oral.
- Cladribine.** Hair cell leuk: usually 0.09mg/kg/day for 7 days by continuous IV infn. Ch lymph leuk: 0.12mg/kg/day over 2hr IV on days 1-5 of 28 day cycle, max 6 cycles.
- Clarithromycin.** 7.5-15mg/kg (adult 250-500mg) 12H oral. Slow rel tab, adult (NOT/kg): 0.5g or 1g dly.
- Clavulanic acid.** See amoxycillin, ticarcillin.
- Clemastine.** 0.02-0.06mg/kg (adult 1-3mg) 12H oral
- Clenbuterol.** Adult (NOT/kg): 20mcg (up to 40mcg) 12H oral.
- Clinidium.** 0.05-0.1mg/kg (adult 2.5-5mg) 6-8H oral.
- Clindamycin.** 6mg/kg (adult 150-450mg) 6H oral. IV over 30 min, or IM: 5mg/kg 12H (prem <1wk old), 5mg/kg 8H (prem >1wk, term <1wk), 7.5mg/kg 8H (term >1wk), >28 days 10mg/kg (adult 600mg) 8H. Severe infn (>28 days): 15-20 mg/kg (adult 900mg) 8H IV over 1hr. Acne soltn 1%: 12H.
- Clioquinol.** 10mg/g cream, 100% powder: apply 6-12H
- Clobazam.** 0.1mg/kg (adult 10mg) daily oral, incr if reqd to max 0.4mg/kg (adult 20mg) 8-12H oral.
- Clobetasol.** 0.05% spray, cream, ointment, gel, solution, foam, lotion, shampoo: apply 12H.
- Clobetasone.** 0.1% soltn: 1drop/eye 1-6H.
- Clodronate.** 10-30mg/kg (adult 0.6-1.8g) IV over 2hr every 2mo; or 6mg/kg (adult 300mg) IV over 2hr daily x7 days, then 15-30mg/kg (adult 0.8-1.6g) 12H oral.
- Clofarabine.** 52mg/m<sup>2</sup> IV over 2hr for 5 days every 2-6wk.
- Clofazimine.** 2mg/kg (adult 100mg) daily oral. Lepa reaction: up to 6mg/kg (max 300mg) daily for max 3 months
- Clofibrate.** 10mg/kg 8-12H oral.
- Clomethiazole.** Equivalent action: cap 192mg base, tab 500mg edisylate, syrup 250mg edisylate in 5ml. Adult (NOT/kg): 1-2 cap or tab, or 5-10ml syrup, at bedtime oral.
- Clomiphene.** Adult (NOT/kg): 50mg dly for 5d oral, incr to 100mg dly for 5d if no ovulation.
- Clomipramine.** 0.5-1mg/kg (adult 25-50mg) 12H oral, incr if reqd to max 2mg/kg (adult 100mg) 8H.
- Clonazepam.** 1 drop = 0.1mg. 0.01mg/kg (max 0.5mg) 12H oral, slowly incr to 0.05mg/kg (max 2mg) 6-12H oral. Status (may be rptd if ventilated), NOT/kg: neonate 0.25mg, child 0.5mg, adult 1mg IV.
- Clonidine.** Hypertension: 1-5mcg/kg slow IV, 1-6mcg/kg (adult 50-300mcg) 8-12H oral. Migraine: start 0.5mcg/kg (adult 50-75mcg) 12H oral. Analgesia: 2.5mcg/kg premed oral, 0.3 mcg/kg/hr IV, 1-2mcg/kg local block; ventild 0.5-2 mcg/kg/hr (<12kg 1mcg/kg/hr is 50mcg/kg in 50ml at 1ml/hr, >12kg 25 mcg/kg in 50ml at 2ml/hr) + midazolam 1mcg/kg/min (3 mg/kg in 50ml at 1ml/hr).
- Clopidogrel.** 1.5mg/kg (adult 75mg) daily oral.
- Clorazepate.** 0.3-2mg/kg (adult 15-90mg) nocte oral, or 0.1-0.5mg/kg (adult 5-30mg) 8H
- Clostridia antitoxin.** See gas gangrene antitoxin.
- Clotrimazole.** Topical: 1% cream or solution 8-12H. Vaginal (NOT/kg): 1% cream or 100mg tab daily for 6 days, or 2% cream or 500mg tab daily for 3 days.
- Cloxacillin.** 15mg/kg (adult 500mg) 6H oral, IM or IV. Severe infn: 25-50mg/kg (adult 1-2g) IV 12H (1st wk life), 8H (2-4wk), 4-6 H (>4wk) or constant infn (>4wk).
- Clozapine.** 0.5mg/kg (adult 25mg) 12H oral, incr over 7-14 d to 2-5mg/kg (adult 100-300mg) 8-12H; later reducing to 2mg/kg (adult 100mg) 8-12H.
- Coagulation factor, human (Prothrombinex).** Factors 2, 9, 10; 250U/10ml. 1ml/kg slow IV daily. Risk of thrombosis in acute liver failure.
- Coal tar, topical.** 0.5% incr to max 10%, applied 6-8H.
- Cocaine.** Topical: 1-3mg/kg.

- Codeine phosphate.** Inactive in  $\approx 10\%$  of adults, poor activity in children  $< 5$  yrs. Analgesic: 0.5–1 mg/kg (adult 15–60 mg) 4H oral, IM, SC. Cough: 0.25–0.5 mg/kg (adult 15–30 mg) 6H.
- Co-danthramer, co-danthrusate.** See dantron.
- Co-dergocrine mesylate.** Adult (NOT/kg): usually 3.0–4.5 mg daily before meal oral or sublingual; 300 mcg daily IM, SC or IV infns.
- Coenzyme Q10.** See ubiquinone.
- Colaspase.** Test 2–50 u intradermal. Typical dose 6000 u/m<sup>2</sup> every 3rd day x9 IV over 4 hr, IM, SC.
- Colchicine.** Acute gout: 0.02 mg/kg (adult 1 mg) 2H oral (max 3 doses/day). Chronic use (gout, FMF): 0.01–0.04 mg/kg (adult 0.5–2 mg) daily oral.
- Colesevelam.** 625 mg tab. Adult (NOT/kg): 3 tab 12H oral, or 6 tab dly. With statin: 4–6 tab/day (in 1–2 doses).
- Colestipol hydrochloride.** 0.1–0.2 g/kg (adult 5–10 g) 8H oral.
- Colfosceril palmitate (Exosurf Neonatal).** Soln 13.5 mg/ml. Prophylaxis: 5 ml/kg intratracheal over 5 min straight after birth, and at 12 hr and 24 hr if still ventilated. Rescue: 5 ml/kg intratracheal over 5 min, repeat in 12 hr if still ventilated.
- Colistimethate.** See colistin sulfomethate sodium.
- Colistin 3 mg/ml + neomycin 3.3 mg/ml.** Otic: 4 drops 8H.
- Colistin sulphomethate sodium.** 2.6 mg = 1 mg colistin base = 30,000 u. IM, or IV over 5 min: 40,000 u/kg (adult 2 million u) 8H, or 1.25–2.5 mg/kg of colistin base 12H. Oral or inhaled: 30,000–60,000 u/kg (adult 1.5–3 million u) 8H.
- Colonic lavage, macrogol-3350 and macrogol-4000 (polyethylene glycol) 105 g/L.** Poisoning, severe constipation: if bowel sounds present, 25 ml/kg/hr (adult 1.5 L/hr) oral or NG for 2–4 hr (until rectal effluent clear). Before colonoscopy: clear fluids only to noon, 1 whole 5 mg bisacodyl tab per 10 kg (adult 4 tab) at noon, wait for bowel motion (max 6 hr), then macrogol 4 g/kg (adult 200 g) in 40 ml/kg fluid (adult 2 L) over 2 hr oral or NG.
- Colony stimulating factors.** See anastroline, epoetin, filgrastim, lenograstim, molgramostim, sargramostim.
- Coloxyl.** See docusate sodium.
- Conivaptan.** Adult (NOT/kg): 20 mg over 30 min IV, then 20 mg (max 40 mg) over 24 hr by IV infusion.
- Conjugated oestrogens (CO) + medroxyprogesterone (MP).** NOT/kg. CO (NOT/kg): 0.625 mg (0.3–1.25 mg) daily continuously, with MP 10 mg (up to 20 mg) daily oral for last 10–14 days of 28 day cycle.
- Co-cyprindiol.** See cyproterone acetate + ethinylloestradiol.
- Corticorelin.** 1–2 mcg/kg (max 100 mcg) IV.
- Corticotrophin releasing factor, hormone.** See corticorelin.
- Cortisone acetate.** 1–2.5 mg/kg 6–8 H oral. Physiological: 7.5 mg/m<sup>2</sup> 8H. Cortisone acetate 1 mg = hydrocortisone 1.25 mg in mineralo- and gluco-corticoid action.
- Cosyntropin (ACTH subunit).** NOT/kg:  $< 2$  yr 0.125 mg,  $> 2$  yr 0.25–0.75 mg IM, IV, or infused over 4–8 hr.
- Cotrimoxazole (trimethoprim 1 mg + sulphamethoxazole 5 mg).** TMP 1.5–3 mg/kg (adult 80–160 mg) 12H IV over 1 hr or oral. Renal proph: TMP 2 mg/kg (max 80 mg) daily oral. Pneumocystis: proph TMP 5 mg/kg daily on 3 days/wk; treatment TMP 250 mg/m<sup>2</sup> stat, then 150 mg/m<sup>2</sup> 8H ( $< 11$  yr) or 12H ( $> 10$  yr) IV over 1 hr; in renal failure dose interval (hr) = serum creatinine (mmol/l)  $\times$  135 (max 48 hr); 1 hr post-infns serum TMP 5–10 mcg/ml, SMX 100–200 mcg/ml. IV infns: TMP max 1.6 mg/ml in 5% dext.
- Coumarin.** Oral: 1–8 mg/kg (adult 50–400 mg) daily. Cream 100 mg/g: apply 8–12 H.
- Cromolyn, sodium.** See sodium cromoglycate.
- Crotamiton.** 10% cream or lotion: apply x2–3/day.
- Cryoprecipitate.** Low factor 8: 1 u/kg incr activity 2% (t  $\frac{1}{2}$  = 12 hr); usu. dose 5 ml/kg or 1 bag/4 kg 12H IV for 1–2 infns (muscle, joint), 3–6 infns (hip, forearm, retroperitoneal, oropharynx), 7–14 infns (intracranial). Low fibrinogen: usually 5 ml/kg or 1 bag/4 kg IV. Bag usu. 20–30 ml: factor 8  $\approx$  5 u/ml (100 u/bag), fibrinogen  $\approx$  10 mg/ml (200 mg/bag).
- Cyanocobalamin (Vit B12).** 20 mcg/kg (adult 1000 mcg) IM daily for 7 d then wkly (treatment), monthly (prophylaxis). IV dangerous in megaloblastic anaemia. Maintenance treatment (adult NOT/kg): 2 mg daily oral, 500 mcg wkly nasal.
- Cyclizine.** 1 mg/kg (adult 50 mg) 8H oral, IM or IV.
- Cyclizine 30 mg + dipipanone 10 mg.** Adult (NOT/kg): 1 tab 6H oral, incr dose by half tab if reqd, to max 3 tab 6H.
- Cyclobenzaprine.** 0.2–0.4 mg/kg (adult 5–15 mg) 8H oral. Extended-release (adult, NOT/kg): 15 mg or 30 mg daily oral.
- Cyclopenthiiazide.** 5–10 mcg/kg (adult 250–500 mcg) 12–24 H.
- Cyclopentolate.** 0.5%, 1%: 1 drop/eye, repeat after 5 min. Pilocarpine 1% speeds recovery.
- Cyclophosphamide.** A typical regimen is 600 mg/m<sup>2</sup> IV over 30 min dly  $\times$  3 d, then 600 mg/m<sup>2</sup> IV wkly or 10 mg/kg twice wkly (if leucocytes  $> 3000/\text{mm}^3$ ).
- Cycloserine.** 5–10 mg/kg (adult 250–500 mg) 12H oral. Keep plasma conc  $< 30$  mcg/ml.
- Cyclosporin.** 1–3 mcg/kg/min IV for 24–48 hr, then 5–8 mg/kg 12H reducing by 1 mg/kg/dose each mth to 3–4 mg/kg/dose 12H oral. Eczema, juvenile arthritis, nephrotic, syndrome, psoriasis: 1.5–2.5 mg/kg 12H.



**Cyclosporin.** (cont.)

Usual target trough levels by Abbott TDx monoclonal specific assay ( $\times 2.5$  = non-specific assay level) on whole blood: 100-250 ng/ml (marrow), 300-400 ng/ml first 3mth then 100-300 ng/ml (kidney), 200-250 first 3mo then 100-125 (liver), 100-400ng/ml (heart, lung).

**Cyclosporin ophthalmic.** 0.05% 1 drop each eye 12H.

**Cyproheptadine.** 0.1mg/kg (adult 4mg) 6-8H oral.

Migraine 0.1mg/kg (adult 4mg), rpt in 30min if reqd.

**Cyproterone acetate.** 1mg/kg (adult 50mg)

8-12H oral. Prec puberty: 25-50mg/m<sup>2</sup> 8-12H

oral. Hyperandrogenism: 50-100mg daily days 5-14, with oestradiol valerate 1mg daily days 5-25.

**Cyproterone acetate + ethinylestradiol.**

(2mg/35mcg)  $\times$  21 tab, + 7 inert tab. In females for acne, contraception, or hirsutism: 1 tab daily, starting 1st day of menstruation.

**Cysteamine bitartrate.** 0.05mg/m<sup>2</sup> 6H oral, incr over 6wk to 0.33mg/m<sup>2</sup>/dose (<50kg) or 0.5mg/kg/dose (>50kg) 6H.

**Cytarabine.** 100mg/m<sup>2</sup> daily for 10 days by IV injn or constant infsn. Intrathecal: 30mg/m<sup>2</sup> every 4d until CSF normal (dissolve in saline not diluent).

**Dacarbazine.** 250mg/m<sup>2</sup> IV daily for 5 d every 3wk.

**Daclizumab.** 1mg/kg IV over 15min every 2wk  $\times$  5

**Dactinomycin.** 400-600mcg/m<sup>2</sup> IV daily for 5 days, repeat after 3-4wk.

**Dalfopristin 350mg + quinupristin 150mg (Synercid IV 500mg vial).** 7.5mg/kg (combined) 8H IV over 1hr.

**Dalteparin sodium.** Proph (adult): 2500-5000u SC 1-2hr preop, then daily. Venous thrombosis: 100u/kg 12H SC, or infuse 200u/kg/day IV (anti-Xa 0.5-1u/ml 4hr post dose). Haemodialysis: 5-10u/kg stat, then 4-5u/kg/hr IV (acute renal failure, anti-Xa 0.2-0.4u/ml); 30-40u/kg stat, then 10-15u/kg/hr (chronic renal failure, anti-Xa 0.5-1u/ml).

**Danaparoid.** Preventn: 15u/kg (adult 750u) 12H SC. Heparin induced thrombocytopenia: 30u/kg stat IV, then 1.2-2u/kg/hr to maintain anti-Xa 0.4-0.8u/ml.

**Danazol.** 2-4mg/kg (adult 100-200mg) 6-12H oral.

**Dantrolene.** Hyperpyrexia: 1mg/kg/min until improves (max 10mg/kg), then 1-2mg/kg 6H for 1-3day IV or oral. Spasticity: 0.5mg/kg (adult 25mg) 6H, incr over 2wk if reqd to 3mg/kg (adult 50-100mg) 6H oral.

**Dantron + docusate (co-danthrusate).** NOT/kg. 50/60mg cap: 7-12yr 1cap, adult 1-3cap at night. 50/60mg in 5ml: 1-6yr 2.5ml, 7-12yr 5ml, adult 5-15ml at night.

**Dantron + poloxamer 188 (co-danthramer).** NOT/kg. 25/200mg cap: 7-12yr 1cap, adult 1-3cap at night. 25/200mg in 5ml: 1-6yr 2.5ml, 7-12yr 5ml, adult 5-15ml at night.

**Dapsone.** 1-2mg/kg (adult 50-100mg) daily oral.

Derm herpet: 1-6mg/kg (adult 50-300mg) daily oral.

**Dapsone 100mg + pyrimethamine 12.5mg (Maloprim).** 1-4yr qtrr tab wkly, 5-10yr half tab, >10yr 1 tab.

**Daptomycin.** 4mg/kg IV over 30min daily.

**Darbepoetin alfa.** Incr/reduce dose if reqd by 25 % every 4wk. Renal failure: 0.45mcg/kg wkly (0.75mcg/kg wkly if not on dialysis) SC or IV. Cancer: 6.75mcg/kg every 3wk, or 2.25mcg/kg every wk, SC or IV

**Darifenacin.** Adult (NOT/kg): 7.5-15mg daily oral.

**Darunavir.** Adult (NOT/kg): 600mg 12H oral.

**Dasatinib.** Adult (NOT/kg): 70mg (up to 100mg) 12H oral.

**Daunorubicin.** 30mg/m<sup>2</sup> wkly slow IV, or 60-90 mg/m<sup>2</sup> every 3wk. Max total dose 500mg/m<sup>2</sup>.

**DDAVP.** See desmopressin.

**Decitabine.** 15mg/m<sup>2</sup> IV over 3hr 8H for 3 days, rpt every 6wk (minimum of 4 cycles).

**Deferasirox.** 20mg/kg (15-30mg/kg) daily oral.

**Deferiprone.** 25mg/kg 8H (max 100mg/kg/day) oral

**Deflazacort.** Usu. 0.1-1.5mg/kg (adult 5-90mg) 24-48H oral. 1.2 mg = 1mg prednisolone in glucocorticoid activity.

**Delavirdine.** Adult (NOT/kg): 400mg 8H, or 600mg 12H oral.

**Demecarium bromide.** 0.125%, 0.25% ophthalmic soltn. Glaucoma: 1 drop  $\times$  2/day to  $\times$  2/wk. Strabismus: 1 drop daily for 2wk, then 1 drop alternate days for 2-3wk.

**Demeclocycline.** >8yr: 3mg/kg (adult 150mg) 6H, or 6mg/kg (adult 300mg) 12H oral

**Denileukin diftitox.** 9-18mcg/kg daily IV over 15min for 5 consecutive days every 21 days.

**Dequalinium.** NOT/kg: one 0.25mg pastile 4H oral.

**Deserpidine.** 0.005-0.02mg/kg (adult 0.25-1mg) daily oral.

**Desferrioxamine.** Antidote: 10-15mg/kg/hr IV for 12-24hr (max 6g/24hr) if Fe >60-90umol/l at 4hr or 8hr; some also give 5-10g (NOT/kg) once oral. Thalassaemia (NOT/kg): 500mg per unit blood; and 5-6 nights/wk 1-3g in 5ml water SC over 10hr, 0.5-1.5g in 10ml water SC over 5min.

**Desirudin.** 0.3mg/kg (adult 15mg) 12H SC.

**Desloratadine.** 0.1mg/kg (adult 5mg) daily oral.

**Desmopressin (DDAVP).** 1u = 1mcg. Nasal (NOT/kg): 5-10mcg (0.05-0.1ml) per dose 12-24H; enuresis 10-40mcg nocte. IV: 0.5-2mcg in 1L fluid, and replace urine output + 10% hrly (but much better to use vasopressin). Haemophilia, von Willebrand's: 0.3mcg/kg (adult 20mcg) IV over 1hr 12-24H. More potent, longer acting than vasopressin.

**Desogestrel.** Contraception: 75mcg daily oral, starting 1st day of menstruation.

**Desogestrel + ethinyloestradiol (150mcg/30mcg, 150/20) x21 tab, + 7 inert tab.** Contraception: 1 tab daily, starting 1st day of menstruation.

**Desonide.** 0.05% cream, ointment, lotion: apply 8-12H

**Desoxymethasone.** 0.05% or 0.25% cream, oint, gel: apply 12H.

**Desoxyribonuclease.** See fibrinolysin.

**Dexamethasone.** 0.1-0.25mg/kg 6H oral, IM or IV. BPD: 0.1mg/kg 6H for 3 days, then 8H 3 days, 12H 3 days, 24H 3 days, 48H 7 days. Cerebral oedema: 0.25-1mg/kg (adult 10-50mg) stat, then 0.1-0.2mg/kg (adult 4-8mg) 4H IV reducing over 3-5 days to 0.05mg/kg (adult 2mg) 8-12H. Congen ad hypopl: 0.27mg/m2 daily oral. Severe croup, extubtn stridor: 0.6mg/kg (max 12mg) IV or IM stat, then prednisolone 1mg/kg 8-12H oral. Eye drops 0.1%: 1 drop/eye 3-8H. Dexamethasone has no mineralocorticoid action; 1mg = 25mg hydrocortisone in glucocorticoid action.

**Dexamethasone 0.5mg/ml (0.05%) + framycetin 5mg/ml (0.5%) + gramicidin 0.05mg/ml (0.005%) (Sofradex).** Eye 1 drop 1-3H, ear 2-3 drops 6-8H, ointment 8-12H.

**Dexamethasone 0.1% + neomycin 0.35% + polymyxin 6000u/g.** 1 drop/eye 6-8H.

**Dexamethasone 0.1% + tobramycin 0.3%.** 1 drop/eye 4-6H; up to 2H for 2 days after surgery if reqd.

**Dexamethasone 20mcg + tramazoline 120mcg per dose.** Aerosol: 1 puff in each nostril 4-8H.

**Dexchlorpheniramine maleate.** 0.05mg/kg (adult 2mg) 6-8H oral. Repetab (adult NOT/kg): 6mg 12H oral.

**Dexfenfluramine.** Adult: 15mg (NOT/kg) 12H oral.

**Dexibuprofen.** Adult (NOT/kg): 400mg 12H (max 8H) oral

**Dexketoprofen.** Adult (NOT/kg): 12.5mg 4-6H, or 25mg 8H (max 75mg/day) oral.

**Dexmedetomidine.** ICU: 1mcg/kg IV over 15min, then 0.2-0.7mcg/kg/hr for max 24hr.

**Dexmethylphenidate.** NOT/kg, given as two doses/day 4hr apart: 2.5mg/dose oral, incr if reqd to 10mg/dose. Use half the dose of racemic methylphenidate.

**Dexpanthenol.** 5-10mg/kg (adult 250-500mg) IM. 5% cream: apply 12-24H

**Dexrazoxane.** 10mg for each 1mg doxorubicin IV. Extravasation of anthracyclines: within 6hr give 1g/m<sup>2</sup> (max 2g) IV over 2hr, repeated after 24hr; then 0.5g/m<sup>2</sup> 48hr after first dose.

**Dextran 1 (Promit).** 15% soltn. 0.3ml/kg IV 1-2min before giving dextran 40 or dextran 70.

**Dextran 40.** 10% soltn: 10ml/kg x1-2 on day 1, then 10ml/kg/day IV. Half life about 3hr.

**Dextran 70.** 6% soltn: 10ml/kg x1-2 on day 1, then 10ml/kg/day IV. Half life about 12hr.

**Dextromethorphan hydrobromide.** 0.2-0.4mg/kg (adult 10-20mg) 6-8H oral.

**Dextromoramide.** 0.1mg/kg (adult 5mg) 8H, may incr to 0.5mg/kg (adult 20mg) 8H oral or PR.

**Dextropropoxyphene.** Hydrochloride 1.3mg/kg (adult 65mg) or napsylate 2mg/kg (adult 100mg) 6H oral.

**Dextrose.** Infant sedation (NOT/kg): 1ml 50% D oral. Hypoglycaemia: 0.5ml/kg 50%D or 2.5ml/kg 10%D slow IV, then incr maintenance infns rate. Hyperkalaemia: 0.1u/kg insulin + 2ml/kg 50%D IV. Neonates: 6g/kg/day (about 4mg/kg/min) day 1, incr to 12 g/kg/day (up to 18g/kg/day with hypoglycaemia). Infns rate (ml/hr) = (4.17 x Wt x g/kg/day) / %D = (6 x Wt x mg/kg/min) / %D. Dose (g/kg/day) = (ml/hr x %D) / (4.17 x Wt). Dose (mg/kg/min) = (ml/hr x %D) / (6 x Wt). Dose (g/kg/day) = g/kg/day / 1.44. 0.5ml/kg/hr of 50% = 6g/kg/day

**Dextrose-heparin (dex-hep).** Dextrose soltn (usually 5%) with heparin 1u/ml.

**Dextrothyroxine.** Adult (NOT/kg): 1-2mg daily oral, incr monthly if reqd to max 4-8mg daily.

**Dezocine.** IM: 0.1-0.4mg/kg (adult 5-20mg) 3-6H. IV: 0.05-0.2mg/kg (adult 2.5-10mg) 2-4H.

**3,4-Diaminopyridine.** Adult (NOT/kg): 10mg 6-8H oral, incr if reqd to max 20mg x5/day.

**Diamorphine.** Adult (NOT/kg): 5-10mg 4H IV, IM, SC, oral.

**Diazepam.** 0.1-0.4mg/kg (adult 10-20mg) IV or PR. 0.04-0.2 mg/kg (adult 2-10mg) 8-12H oral. Do not give by IV infns (binds to PVC); emulsion can be infused. Premed: 0.2-0.4mg/kg oral, PR. 2-3mg = 1mg midazolam.

**Diazoxide.** Hypertension: 1-3mg/kg (max 150mg) stat by rapid IV injection (severe hypotension may occur) repeat once if reqd, then 2-5mg/kg IV 6H. Hyperinsulinism: <12mo 5mg/kg 8-12H oral; >12mo 30-100mg/m2 per dose 8H oral.

**Dibromopropamide.** 0.15% cream on dressing pm.

**Dibucaine.** See cinchocaine.

**Dichloralphenazone 100mg + isometheptene mucate 65mg + paracetamol 325mg (Midrin).** Adult (NOT/kg): 2 capsules stat, then 1/hr if reqd (max 5 cap in 12hr).

**Dichlorphenamide.** 2-4mg/kg (adult 100- 200mg) stat, then 2mg/kg (adult 100mg) 12H until response then 0.5-1mg/kg (adult 50mg) 8-24H oral.

**Diclofenac.** 1mg/kg (adult 50mg) 8-12H oral, PR. Eye drops 0.1%: preop 1-5 drops over 3hr, postop 1 drop stat, then 1 drop 4-8H. Topical gel 1% (arthritis) 3% (keratoses): apply 2-4g 6-8H. Patch 1.3% (180mg) 10x14cm: apply 12H.



- Diclofenac + misoprostal.** Adult, NOT/kg. 50mg/200mcg tab 8-12H oral; 75mg/200mcg tab 12H oral.
- Dicloxacillin.** 15-25mg/kg (adult 250-500mg) 6H oral, IM or IV. Severe infn: 25-50mg/kg (max 2g) IV 12H (1st wk life), 8H (2-4 wk), 4-6H or constant infsn (>4 wk).
- Dicobalt edetate.** 10mg/kg (adult 300mg) IV over 1-5min, repeat x2 if no response.
- Dicyclomine.** 0.5mg/kg (adult 10-20mg) 6-8H oral.
- Dicycloverine.** See dicyclomine.
- Didanosine.** <90 days: 50mg/m<sup>2</sup> 12H oral. >90 days: 120mg/m<sup>2</sup> (max 200mg) 12H, or 240mg/m<sup>2</sup> (max 400mg) daily oral. CNS disease: 150mg/m<sup>2</sup> 12H oral.
- Dideoxycytidine (ddC).** See zalcitabine.
- Dienoestrol.** 0.01% vaginal cream: 1 applicatorful (5g) 12-24H for 1-2wk, reducing gradually to x1-3/wk.
- Diethylcarbamazine.** 6mg/kg daily for 12 days oral, or a single dose of 6mg/kg rpt every 6-12 mths.
- Diethylpropion hydrochloride.** 6-12yr: 25mg (NOT/kg) 12H oral. >12yr: 25mg (NOT/kg) 6-8H oral.
- Diethylstilboestrol.** See stilboestrol.
- Diflorasone.** 0.05% cream, ointment: apply 6-24H.
- Diffunisal.** 5-10mg/kg (adult 250-500mg) 12H oral.
- Digitoxin.** 4mcg/kg (max 0.2mg) 12H oral for 4d, then 1-6mcg/kg (adult usu. 0.15mg, max 0.3mg) dly.
- Digoxin.** 15mcg/kg stat and 5mcg/kg after 6H, then 3-5 mcg/kg (usual max 200mcg IV, 250mcg oral) 12H slow IV or oral. Level 6hr or more after dose: 1.0-2.5 nmol/L (x0.78=ng/ml).
- Digoxin immune FAB (antibodies).** IV over 30min. Dose (to nearest 40mg) = serum digoxin (nmol/L) x Wt (kg) x 0.3, or mg ingstd x 55. Give if >0.3mg/kg ingested, or level >6.4 nmol/L or 5.0ng/ml.
- Dihydrocodeine.** 0.5-1mg/kg 4-6H oral.
- Dihydroergotamine mesylate.** Adult (NOT/kg): 1mg IM, SC, IV, rpt hrly x2 if needed. Max 6mg/wk.
- Dihydromorphanone.** See hydromorphone.
- Dihydrothachysterol (1-OH vitamin D2).** Renal failure, vit D resis. rickets: 20mcg/kg daily oral, incr by 20mcg/kg every 4-8wk accordg to serum Ca
- Dihydrotestosterone.** See stanolone.
- Dihydroxyacetone.** 5% soltn: apply 1-3 coats 1hr apart, every 1-3 days.
- Diiodohydroxyquin.** See di-iodohydroxyquinoline.
- Di-iodohydroxyquinoline.** 10-13.3mg/kg (adult 650mg) 8H oral for 20 days.
- Diloxanide furoate.** 10mg/kg (adult 500mg) 8H oral.
- Diltiazem.** 1mg/kg (adult 60mg) 8H, incr if reqd to max 3mg/kg (adult 180mg) 8H oral. Slow rel (adult, NOT/kg): 120-240mg dly, or 90-180mg 8-12H oral
- Dimenhydrinate.** 1-1.5mg/kg (adult 50-75mg) 4-6H oral, IM or IV.
- Dimercaprol (BAL).** 3mg/kg (max 150mg) IM 4H for 2 days, then 6H for 1 day, then 12H for 10 days.
- Dimethicone.** Infant colic (NOT/kg): 40mg/ml, 1-2 dropperfuls before each feed. 10%, 15% barrier cream: apply prn.
- Dimethindene.** 0.02-0.04mg/kg (adult 1-2mg) 8H oral.
- Dimethyl sulfoxide (DMSO).** 50% soltn: 50ml in bladder for 15 min every 2wk.
- Dinoprost (Prostaglandin F2 alpha).** Extra-amniotic: 1ml of 250mcg/ml stat, then 3ml 2H. Intra-amniotic: 40mg stat, then 10-40mg after 24hr if required.
- Dinoprostone (Prostaglandin E2).** Labour induction: 1mg into posterior vagina, may rpt dose 1-2mg after 6hr (max 60mcg/kg over 6hr). Maintain PDA: 25mcg/kg 1H (less often after 1wk) oral; or 0.003-0.01mcg/kg/min IV.
- Diocetyl sodium sulphosuccinate.** See docusate sodium.
- Diphenamil methylsulphate.** 20mg/g powder: apply 8-12H.
- Diphenhydramine hydrochloride.** 1-2mg/kg (adult 50-100mg) 6-8H oral.
- Diphenoxylate.** See atropine + diphenoxylate (Lomotil).
- Diphtheria antitoxin (horse).** IM or IV (NOT/kg): 2500u (nasal), 10,000u (unilateral tonsillar), 20,000u (bilateral tonsillar), 30,000u (laryngeal), 50,000u (beyond tonsillar fossa), 150,000u (bullneck). Repeat dose may be needed. See also immunoglobulin, diphtheria.
- Diphtheria vaccine, adult (CSL).** Inactivated. 0.5ml IM stat, 6wk later, and 6mo later (3 doses). Boost every 10yr.
- Diphtheria vaccine, child <8yr (CSL).** Inactivated. 0.5ml IM stat, in 6wk, then 6mo (3 doses). Boost with adult vaccine.
- Diphtheria + hepatitis B + pertussis (acellular) + polio + tetanus [DaPT-HepB-IPV] (Pediarix).** Inactivated. 0.5ml IM at 2mo, 4mo, 6mo (3 doses), and (DaPT) 18mo.
- Diphtheria + hepatitis B + pertussis (acellular) + tetanus vaccine [DaPT-hepB] (Infanrix Hep B).** Inactivated. 0.5ml IM at 2mo, 4mo, 6mo (3 doses), and (without hep B) 18mo.
- Diphtheria + hepatitis B + Hib + pertussis (acellular) + tetanus vaccine [DaPT-hepB-Hib] (Infanrix Hexa).** Inactivated. 0.5ml IM 2mo, 4mo, 6mo (3 doses).
- Diphtheria + Hib + pertussis (acellular) + polio + tetanus [DaPT-Hib-IPV] (Infanrix Penta, Pediacel).** Inactivated. 0.5ml IM at 2mo, 4mo, 6mo (3 doses), and (DaPT) 18mo.
- Diphtheria + pertussis (whole cell) + tetanus vaccine [DPT] (Triple Antigen).** Inactivated. 0.5ml IM at 2mo, 4mo, 6mo, 18mo, 4-5yr age (5 doses).

**Diphtheria + pertussis (acellular) + tetanus vaccine [DaPT] (Tripacel).** Inactivated. 0.5ml IM at 2mo, 4mo, 6mo, 18mo and 4-5yr of age (5 doses).

**Diphtheria + pertussis (acellular) + tetanus vaccine, adult [daPt] (Adacel, Boostrix).**

Inactivated.  $\geq 10$ yr: 0.5ml IM.

**Diphtheria + pertussis (acellular) + polio + tetanus vaccine [DaPT-IPV] (Quadacel).**

Inactivated. 0.5ml IM at 2, 4, 6mo (3 doses).

**Diphtheria + pertussis (acellular) + polio + tetanus vaccine [DaPT-IPV] (Infanrix-IPV).**

Inactivated. 16mo-13yr: 0.5ml IM once as booster.

**Diphtheria + pertussis (acellular) + polio + tetanus vaccine [daPT-IPV] (Repevax).**

Inactivated.  $> 3$ yr: 0.5ml IM once as booster.

**Diphtheria + pertussis (acellular) + polio + tetanus vaccine, adult [daPT-IPV] (Adacel Polio, Boostrix-IPV).** Inactivated.  $\geq 10$ yr: 0.5ml IM once as booster.

**Diphtheria + polio + tetanus vaccine [dT-IPV] (Revaxis).** Inactivated.  $> 6$ yr: 0.5ml IM once as booster

**Diphtheria + tetanus vaccine, adult [dt] (ADT Booster).** Inactivated. 0.5ml IM for revaccination after primary course.

**Diphtheria + tetanus vaccine, child  $< 8$ yr [DT] (CDT).** Inactivated. 0.5ml IM, in 6wk, 6mo later (3 dose). Boost with ADT.

**Dipipanone.** See cyclizine.

**Dipivefrin.** 0.1% soln: 1 drop per eye 12H.

**Diprophylline.** Usually 15mg/kg 6H oral or IM.

**Dipyridamole.** 1-2mg/kg (adult 50-100mg) 6-8H oral. See also aspirin + dipyridamole.

**Dirithromycin.** 10mg/kg (adult 500mg) daily oral.

**Disodium clodronate.** See sodium clodronate.

**Disodium edetate.** See trisodium edetate.

**Disodium etidronate.** See etidronate.

**Disopyramide.** Oral: 1.5-4mg/kg (adult 75-200mg) 6H. IV: 2mg/kg (max 150mg) over 5min, then 0.4mg/kg/hr (max 800mg/day). Level 9-15umol/L ( $\times 0.3395 =$  mcg/ml).

**Distigmine.** Neurogenic bladder, megacolon: 0.01mg/kg (adult 0.5mg) IM daily, 0.1mg/kg (adult 5mg) oral daily. Myasth gravis: 0.1-0.2mg/kg 12-24H (max 20mg/day) oral.

**Disulfiram.** Adult (NOT/kg): 500mg oral daily for 1-2wk, then 125-500mg daily.

**Dithranol.** 0.1%-2% cream, ointment: start with lowest strength, apply daily, wash off after 10min incr to 30min.

**Divalproex.** Dose as for sodium valproate.

**DMSA.** See succimer.

**Dobutamine.**  $< 30$ kg: 15mg/kg in 50ml 0.9% saline with heparin 1u/ml at 1-4ml/hr (5-20mcg/kg/min), CVC or periph IV;  $> 30$ kg: 6mg/kg in 100ml 0.9% saline with hep 1u/ml at 5-20ml/hr (5-20mcg/kg/min).

**Docetaxel.** Initially 75-100mg/m<sup>2</sup> over 1hr IV every 3wk.

**Docosanol.** 10% cream: apply 5 times a day.

**Docusate sodium.** NOT/kg: 100mg (3-10yr), 120-240mg ( $> 10$ yr) daily oral. Enema (5ml 18% + 155ml water): 30ml (newborn), 60ml (1-12mo), 60-120ml ( $> 12$ mo) PR.

**Docusate sodium 50mg + sennoside 8mg, tab.**  $> 12$ yr: 1-4 tab at night oral. See also bisacodyl; casanthranol; dantron.

**Dofetilide.** 10mcg/kg (adult 500mcg) 12H oral, less if renal impairment or increased QTc interval.

**Dolasetron.** Cancer: 1.8mg/kg (adult 100mg) IV 30min before chemo, or 4mg/kg (adult 200mg) oral 1hr before chemo. Surgery: 1mg/kg (adult 50mg) oral at induction, or 0.25mg/kg (adult 12.5mg) IV postop.

**Domperidone.** Oral: 0.2-0.4mg/kg (adult 10-20mg) 4-8H. Rectal suppos: adult (NOT/kg) 30-60mg 4-8H.

**Donepezil.** Adult (NOT/kg): 5mg at night oral, incr to 10mg after 1mo if reqd.

**Dopamine.**  $< 30$ kg: 15mg/kg in 50ml 5%dex-hep at 1-4ml/hr (5-20mcg/kg/min) via CVC;  $> 30$ kg: 6mg/kg in 100ml 5%dex-hep at 5-20ml/hr (5-20mcg/kg/hr).

**Dopexamine.** IV infns 0.5-6mcg/kg/min.

**Doripenem.** 10mg/kg (adult 500mg) 8H IV.

**Dornase alpha (deoxyribonuclease I).** NOT/kg: usually 2.5mg (max 10mg) inhaled daily (5-21yr), 12-24H ( $> 21$ yr).

**Dorzolamide.** 2% drops: 1 drop/eye 8-12H.

**Dorzolamide 2% + timolol 0.5%.** 1 drop/eye 12H.

**Dosulepin hydrochloride.** See dothiepin.

**Dothiepin.** 0.5-1mg/kg (adult 25-50mg) 8-12H oral.

**Doxacurium.** 50-80mcg/kg stat, then 5-10mcg/kg/dose IV.

**Doxapram.** 5mg/kg IV over 1hr, then 0.5-1mg/kg/hr for 1hr (max total dose 400mg).

**Doxazosin.** Usu. 0.02-0.1mg/kg (adult 1-4mg) dly oral

**Doxepin.** 0.2-2mg/kg (adult 10-100mg) 8H oral. 5% cream: apply  $\times 3-4$ /day.

**Doxercalciferol (1,25-OH D2 analogue).** Initially 0.2mcg/kg (adult 10mcg) oral, or 0.08mcg/kg (adult 4mcg) IV,  $\times 3$ /wk at end of dialysis. Aim for blood iPTH 150-300pg/ml.

**Doxorubicin.** 30mg/m<sup>2</sup> IV over 15min wkly, or 30mg/m<sup>2</sup> dly  $\times 2-3$ days every 3-4wk. Max tot. dose 480mg/m<sup>2</sup> (300mg/m<sup>2</sup> if mediastinal irradiation).

**Doxorubicin, liposomal.** Carcinoma: 50mg/m<sup>2</sup> IV every 3wk. Kaposi: 20mg/m<sup>2</sup> IV every 2wk.

**Doxycycline.** Over 8yr: 2mg/kg (adult 100mg) 12H for 2 doses, then daily oral. Severe: 2mg/kg 12H. Malaria proph: 2mg/kg (adult 100mg) daily oral.

**Doxycycline 30mg + 10mg slow rel (Oracea).**

Rosacea in adults (NOT/kg): 1 tab daily oral.

**Doxylamine succinate.** 0.25-0.5mg/kg (adult 12.5-25mg) 8H oral. Hypnotic: 0.5-1mg/kg (adult 25-50mg).**Dronabinol.** Initially 5mg/m<sup>2</sup> 2-4H (max 4-6 doses per day) oral, slow incr by 2.5mg/m<sup>2</sup>/dose to max 15mg/m<sup>2</sup> 4H.**Droperidol.** Antiemetic: postop 0.02-0.05mg/kg (adult 1.25mg) 4-6H IM or slow IV, chemother 0.02-0.1 (adult 1-5mg) 1-6H. Psychiatry, neurolept, analg, IM or slow IV: 0.1 mg/kg (adult 2.5mg) stat, incr to max 0.3mg/kg (adult 15 mg) 4-6H. Psych, oral: 0.1-0.4mg/kg (adult 5-20mg) 4-8H.**Drospirenone + ethinyloestradiol (3mg/30mcg) x 21 tab + 7 inert tab.** Contraception: 1 daily starting 1st day menstruation.**Drospirenone + ethinyloestradiol (3mg/20mcg, 3mg/ 30mcg) x 24 tab, + 4 inert tab.** Contraception: 1 daily starting 1st day of menstruation.**Drospirenone + oestradiol (0.5mg/1mg, 2mg/1mg).** Post-menopause (NOT/kg): 1 tab daily oral.**Drotrecogin alfa (protein C), activated.**

24mcg/kg/hr for 96hr IV. Minor surgery: stop 2hr before, restart straight after. Major surgery: stop 2hr before, restart 12hr after.

**Duloxetine.** Adult, NOT/kg: 20-30mg 12H, or 60mg daily oral.**Dutasteride.** Adult (NOT/kg): 0.5mg daily oral.**Dyclonine hydrochloride.** See dyclocaine hydrochloride.**Dydrogesterone.** 0.2mg/kg (adult 10mg) 12-24H oral**Dydrogesterone + oestradiol (5mg/1mg, 10/1, 10/2).** Adult (NOT/kg). Postmenopausal: 1 tab daily oral.**Dydrogesterone 10mg tab + oestradiol patch (40 or 80 mcg/24hr).** Adult (NOT/kg). Postmenopausal: apply new patch every 3-4 days, 1tab daily oral for last 14days of cycle.**Dyphylline.** See diprophylline.**Econazole nitrate.** Topical: 1% cream, powdr, lotion 8-12H. Vaginal: 75mg cream, 150mg ovule 2x/d**Ecothiopate iodide.** 0.03%, 0.06%, 0.125%, 0.25% soltn: usu. 0.125% 1 drop/eye every 1-2 d bedtime**Eculizumab.** 600mg IV over 35min wkly for 4wk, 900mg the next wk, then 900mg every 2wk.**Edrophonium.** Test dose 20mcg/kg (max 2mg), then 1min later 80mcg/kg (adult 8mg) IV. SVT: 0.15mg/kg (max 2mg) incr to max 0.75mg/kg (max 10mg) IV, with atropine if reqd.**EDTA.** See sodium calciumedetate.**Efalizumab.** 0.7mg/kg stat, then 1mg/kg wkly SC.**Efavirenz.** Dly oral 10-15kg 200mg, 15-20mg 250mg, 20-25 kg 300mg, 25-33kg 350mg, 33-40kg 400mg, >40kg 600mg.**Eflornithine.** 13.9% cream: apply 12H.**Eformoterol.** Caps 12mg (NOT/kg): 1cap (5-12yr) or 1-2 caps (adult) inhaled 12H.**Electrolyte solution.** See glucose electrolyte solution.**Eletriptan.** Adult (NOT/kg): 20-40mg, repeat after 2hr if reqd (max 80mg/day).**EMLA cream.** See lignocaine + prilocaine.**Emedastine.** 0.5mg/ml soltn: 1 drop/eye 12H.**Emtricitabine.** Adult (NOT/kg) 200mg daily oral.**Emtricitabine + tenofovir disoproxil (as fumarate).** 200mg/245mg tab, ≥18yr (NOT/kg): 1tab daily oral.**Enalapril.** 0.1mg/kg (adult 2.5mg) daily oral, incr over 2wk if reqd to max 0.5mg/kg (adult 5-20mg) 12H.**Enalaprilat.** Usually 0.025mg/kg (max 1.25mg) 6H IV, max 0.1mg/kg (max 5mg) 6H.**Enfuvirtide.** Age ≥6yr: 2mg/kg (max 90mg) 12H SC**Enoxacin.** 4-8mg/kg (adult 200-400mg) 12H oral.**Enoxaparin (1mg=100u).** 1.5mg/kg (<2mo), 1mg/kg (2mo-18yr), 40mg (adult) 12H SC (anti-Xa 0.5-1u/ml 4hr post dose). Prophylaxis: 0.75mg/kg 12H (<2mo), 0.5 mg/kg 12H (2mo-18yr), 20-40mg 2-12hr preop, then daily (adult) SC. Haemodialysis: 1mg/kg into arterial line at start 4hr session.**Enoximone.** IV: 5-20mcg/kg/min.

Oral: 1-3mg/kg (adult 50-150mg) 8H.

**Entacapone.** Adult (NOT/kg): 200mg with each l-dopa/DDC inhibitor dose (av 800-1400mg/day, max 2000mg) oral.**Entecavir.** Hepatitis B (adult, NOT/kg): 0.5mg daily oral; 1mg daily if refractory to lamivudine.**Ephedrine.** 0.25-1mg/kg (adult 12.5-60mg) 4-8H oral, IM, SC, IV. Nasal (0.25%-1%): 1drop each nostril 6-8H, max 4 days.**Epinastine.** 0.05% ophthalmic: 1 drop/eye 12H.**Epinephrine.** See adrenaline.**Epirubicin.** Adult: 75-90mg/m<sup>2</sup> IV over 10min every 3wk.**Eplerenone.** 0.5-1mg/kg (adult 25-50mg) 12-24H oral.**Epoetin alfa, beta, delta.** 20-50u/kg x3/wk, incr to max 240 u/kg x1-3/wk SC, IV. When Hb >10g%: 20-100u/kg x2-3/wk.**Epoprostenol (prostacyclin, PGI<sub>2</sub>).** Incompatible with all other drugs. <8kg: 60mcg/kg in 50ml diluent at 0.25-0.75 ml/hr (5-15ng/kg/min) via CVC or periph IV; >8kg: 500mcg in 50ml diluent at 0.03-0.09ml/kg/hr (5-15ng/kg/min). Chronic pul ht: 2ng/kg/min IV, incr to 20-40ng/kg/min.**Eprosartan.** 12mg/kg (adult 600mg) daily, incr if reqd to 6-8mg/kg (adult 300-400mg) 12H oral.**Epsilon aminocaproic acid.** See aminocaproic acid.**Eptacog alfa (recombinant factor 7a).** See factor 7a.

**Eptifibatide.** Adult (NOT/kg): 180mcg/kg stat IV, then 2 mcg/kg/min for up to 72hr.

**Edosteine.** Adult (NOT/kg): 300mg 12H oral.

**Ergocalciferol (Vitamin D2).** 40u = 1mcg = 1mcg cholecalciferol (D3). Cystic fib, cholestasis: 10-20mcg daily oral. Cirrhosis: adult 40-120mcg daily oral. Deficiency: 50-100mcg daily for 2wk oral, then 10-625mcg daily (more if severe malabs); or 2.5-5mg (100,000-200,000u) every 6-8wk. Monitor serum calcium; measure alk phos and parathyroid hormone after 6-8wk. See also doxercalciferol.

**Ergoloid mesylates.** See co-dergocrine mesylate.

**Ergometrine maleate.** Adult (NOT/kg): 250-500 mcg IM or IV; 500mcg 8H oral, sublingual or PR.

**Ergometrine maleate 0.5mg + oxytocin 5u in 1ml.** 1ml IM; may rpt after 2hr, max 3 doses in 24hr.

**Ergonovine maleate.** See ergometrine maleate.

**Ergotamine tartrate.** >10yr (NOT/kg): 2mg subling stat, then 1mg/hr (max 6mg/episode, 10mg/wk). Suppos (1-2mg): 1 stat, may repeat once after 1hr.

**Erlotinib.** Adult (NOT/kg): 150 mg daily oral; reduce to 100mg then 50mg daily if reqd.

**Ertapenem.** 20-40mg/kg (adult 1g) daily IM, IV over 30min.

**Erythromycin.** Oral or slow IV (max 5mg/kg/hr): usually 10 mg/kg (adult 250-500mg) 6H; severe infn 15-25mg/kg (adult 0.75-1g) 6H. Gut prokinetic: 2mg/kg 8H. 2% gel: apply 12H.

**Erythropoietin.** See epoetin.

**Escitalopram.** Adult (NOT/kg): 5mg daily oral, incr if reqd to max 20mg daily.

**Esmolol.** 0.5mg/kg (500mcg/kg) IV over 1min, rpt if reqd. Infsn (undiluted 10mg/ml soltn): 0.15-1.8ml/kg/hr (25-300mcg/kg/min); rarely given for >48hr.

**Esomeprazole.** 0.4-0.8mg/kg (adult 20-40mg) daily oral. H.pylori (adult NOT/kg): 20mg + amoxicillin 1g + clarithromycin 500mg 12H oral for 7 days.

**Estazolam.** 0.02-0.1mg/kg (adult 1-4mg) nocte oral.

**Estradiol.** See oestradiol.

**Estramustine.** 200mg/m<sup>2</sup> 8H oral (avoid milk).

**Eszopiclone.** Adult (NOT/kg): 2mg (1-3mg) nocte oral.

**Etamsylate.** 12.5mg/kg (adult 500mg) 6H oral.

**Etanercept.** 0.4mg/kg (max 25mg) 2x/wk deep SC.

**Ethacrynic acid.** IV: 0.5-1mg/kg (adult 25-50mg) 12-24H. Oral: 1-4mg/kg (adult 50-200mg) 12-24H.

**Ethambutol hydrochloride.** 25mg/kg once daily for 8wk, then 15mg/kg daily oral. Intermittent: 35mg/kg x3/wk. IV: 80% oral dose.

**Etamsylate.** 12.5mg/kg (max 500mg) 6H oral, IM, IV  
**Ethanol, dehydrated (100%).** Vessel sclerosis: inject max of 1ml/kg.

**Ethanolamine oleate.** 5% soltn, adult (NOT/kg): 1.5-5ml per varix (max 20ml per treatment).

**Ethchlorvynol.** 10-20mg/kg (adult 0.5-1g) nocte oral

**Ethinylloestradiol.** 10-50mcg daily for 21 days per month. See also cyproterone; desogestrel.

**Ethinylloestradiol + ethynodiol diacetate (50mcg/0.5mg or 50mcg/1mg) x 21 tab, + 7 inert tab.**

Contraceptn: 1 tab dly, from 1st day of menstruatn

**Ethinylloestradiol + gestodene (30mcg/75mcg, 20/75) x 21 tab + 7 inert tab.**

1 daily, starting 1st day of menstruation.

**Ethinylloestradiol + gestodene (30mcg/50mcg x 6 tab + 40/70 x5 + 30/100 x10 + inert x7).**

1 tab daily, starting 1st day of menstruation.

**Ethinylloestradiol + levonorgestrel (20mcg/90mcg).** Contraception: 1 tab daily (with no hormone-free interval).

**Ethinylloestradiol + levonorgestrel (30mcg/150mcg or 50mcg/125mcg) x 21 tab, + 7 inert tab.**

Contraceptn: 1 tab dly, from 1st day of menstruatn

**Ethinylloestradiol + levonorgestrel (30mcg/50mcg x6 tab + 40/75 x5 + 30/125 x10 + inert x7).**

1 tab daily, starting 1st day of menstruation.

**Ethinylloestradiol + levonorgestrel (30mcg/150mcg) x 84 tab, then either 7 inert tab or 7 tab ethinylloestradiol 10 mcg.**

Contraceptn: 1 tab dly, from 1st day of menstruatn

**Ethinylloestradiol + norelgestromin (20mcg/150mcg, 0.75mg/6mg) patches.** Contraceptn: apply 1 patch wkly x3, wk 4 patch-free.

**Ethinylloestradiol + norethisterone (35mcg/0.25mg, 30/0.5, 35/0.5, 35/0.75, 20/1, 35/1, 30/1.5) x 21 tab, + 7 inert tab.**

Contraceptn: 1 tab dly, from 1st day of menstruatn

**Ethinylloestradiol + norethisterone (20mcg/1mg) x 24 tab, + 4 inert tab.**

Contraceptn: 1 tab dly, from 1st day of menstruatn

**Ethinylloestradiol + norethisterone (35mcg/0.5mg x7tab + 35/1 x14 + inert x7).**

Contraceptn: 1 tab dly, from 1st day of menstruatn

**Ethinylloestradiol + norethisterone (35mcg/0.5mg x7tab + 35/1 x9 + 35/0.5 x5 + inert x7).**

Contraceptn: 1 tab dly, from 1st day of menstruatn

**Ethinylloestradiol + norethisterone (35mcg/0.5mg x7tab + 35/0.75 x7 + 35/1 x7 + inert x7).**

Contraceptn: 1 tab dly, from 1st day of menstruatn

**Ethionamide.** TB: 15-20mg/kg (max 1g) at night oral. Leprosy: 5-8mg/kg (max 375mg) daily.

**Ethoheptazine.** 3mg/kg (adult 150mg) 6-8H oral.

**Ethosuximide.** 10mg/kg (adult 500mg) daily oral, incr by 50% each wk to max 40mg/kg (adult 2g) daily. Trough level 0.3-0.7mmol/L.

- Ethotoin.** 5mg/kg (adult 250mg) 6H oral, incr to max 15mg/kg (adult 750mg) 6H.
- Etidocaine.** 0.5%-1.5% soltn: max 6mg/kg (0.6ml/kg of 1%) parenteral, or 8mg/kg (0.8ml/kg of 1%) with adrenaline.
- Etidronate.** 5-20mg/kg daily oral (no food for 2hr before and after dose) for max 6mo. IV: 7.5mg/kg daily for 3-7 days.
- Etidonate and calcium citrate.** Etidronate 400mg tab daily 14 days, then calcium citrate 500mg daily for 76 days oral.
- Etodolac.** 4-8mg/kg (adult 200-400mg) 6-8H oral.
- Etomidate.** 0.3mg/kg slow IV.
- Etonogestrel.** 68mg sub-dermal implant lasts 3yr.
- Etoposide.** 50-60mg/m<sup>2</sup> IV over 1hr daily for 5 days, rpt after 2-4wk. Oral dose 2-3 times IV dose.
- Etoricoxib.** Adult (NOT/kg). 60-90mg daily oral. Gout: 120 mg daily, max 8 days.
- Etretinate.** 0.25mg/kg 8-12H oral for 2-4wk, then 6H (max 75mg dly) if reqd for 6-8wk, then 12-24H.
- Etynodiol diacetate.** Contraception: 500mcg daily oral, starting 1st day of menstruation.
- Everolimus.** Adult (NOT/kg): 0.75mg 12H oral adjusted to trough level 3-8ng/ml (chromatographic assay).
- Exemestane.** Adult (NOT/kg): 25mg daily oral.
- Exenatide.** Adult, NOT/kg: 5mcg SC before morning and evening meals, incr if reqd to 10mcg/dose after 1mo.
- Ezetimibe.** Adult (NOT/kg): 10mg daily oral.
- Factor 7a, recombinant (rFVIIa).** Usually 90mcg/kg IV 2H until haemostasis, then 3-6H.
- Factor 8 concentrate (vial 200-250u), recombinant-antihaemophilic factor (rAHF).** Joint 20u/kg, psoas 30u/kg, cerebral 50u/kg. 2 x dose(u/kg) = % normal activity, eg 35u/kg gives peak level of 70% normal.
- Factor 8 inhibitor bypassing fraction.** IV max 2u/kg/min: joint 50u/kg 12H, mucous mem 50u/kg 6H, soft tissue 100u/kg 12H, cerebral 100u/kg 6-12H.
- Factor 9.** IV infsn (max 2u/kg/min): minor hge 25u/kg daily, joint 40u/kg 12-24H, surgery 50u/kg stat then 30u/kg 12-24H, major surgery 85u/kg stat then 50u/kg 12-24H. Prophylaxis: 25-40u/kg x2/wk (trough >1u/dl).
- Factor 9 complex (factor 2, 9, 10, and some 7).** 40-60 iu/kg, then 5-10iu/kg 12H IV. Prophylaxis: 10-20iu/kg x1-2/wk. Factor 8 antibodies: 75iu/kg, rpt in 12hr prn.
- Factor 13.** Vial 250u. Prophylaxis: 10u/kg IV every 4wk. Pre-op: up to 3u/kg just before surgery, then 10u/kg daily x5. Severe hge: 10-20u/kg daily.
- Famciclovir.** Zoster, varicella: 5mg/kg (adult 250mg) 8H oral x7 days; immunocompromised 10mg/kg (adult 500mg) 8H for 10 days. Genital herpes (adult, NOT/kg): 125mg 12H oral for 5 days (treatment), 250mg (suppression) 12H; immunocompromised 500mg 12H for 7 days (treatment), 500mg daily (suppression).
- Famotidine.** 0.5-1mg/kg (adult 20-40mg) 12-24H oral. 0.5mg/kg (max 20mg) 12H slow IV
- Fat emulsion 20%.** See lipid emulsion.
- Felbamate.** 5mg/kg 6-8H (max 1200mg/day) oral, incr over 2-3wk to 15mg/kg 6-8H (max 3600mg/d)
- Felodipine.** 0.1mg/kg (adult 2.5mg) daily, incr if reqd to 0.5 mg/kg (adult 10mg) daily oral.
- Fenbufen.** 10mg/kg (adult 450mg) 12H oral.
- Fenfluramine.** Adult (NOT/kg): 60mg daily oral.
- Fenofibrate.** 2mg/kg (adult 100mg) 6-12H oral.
- Fenoldopam.** 0.1mcg/kg/min IV infsn incr gradually if reqd every 15-30min to max 1.6mcg/kg/min
- Fenopropfen.** 4mg/kg (adult 200mg) 6-8H oral, may incr gradually to 12mg/kg/dose (max 800mg).
- Fenoterol.** Oral: 0.1mg/kg 6H. Resp soltn 1mg/ml: 0.5ml diluted to 2ml 3-6H (mild), 1ml diluted to 2ml 1-2H (moderate), undiluted continuous (severe, in ICU). Aerosol (200mcg/puff): 1-2 puffs 4-8H.
- Fentanyl.** Not ventilated: 1-2 mcg/kg (adult 50-100mcg) IM or IV; infsn 2-4mcg/kg/hr (<10kg 100mcg/kg in 50ml 5%dex-hep at 1-2ml/hr; >10kg amp 50mcg/ml at 0.04-0.08ml/kg/hr). Ventilated: 5-10mcg/kg stat or 50mcg/kg IV over 1hr; infuse amp 50mcg/ml at 0.1-0.2ml/kg/hr (5-10 mcg/kg/hr). Patch (lasts 72hr) in adult (NOT/kg): 25 mcg/hr, incr if reqd by 25 mcg/hr every 3 days. Transmucosal tabs (adult, NOT/kg): 100mcg held between cheek and upper gum until dissolved (15-30 min) 4-8H, incr if reqd to max 800mg 4H. Epidural: 0.5 mcg/kg stat, or 0.4mcg/kg/hr.
- Fenticonazole vaginal pessaries.** 600mg nocte once, or 200mg nocte for 3 nights.
- Ferrous salts.** Prophylaxis 2mg/kg/day elemental iron oral, treatment 6mg/kg/day elemental iron oral. Fumarate 1mg = 0.33mg iron. Gluconate 1mg = 0.12mg iron; so Fergon (60 mg/ml gluconate) prophylaxis 0.3ml/kg daily, treatment 1ml/kg daily oral. Sulphate (dry) 1mg = 0.3mg iron; so Ferro-Gradumet (350mg dry sulphate) prophylaxis 7mg/kg (adult 350mg) daily, treatment 20mg/kg (adult 1050mg) daily oral.
- Fexofenadine.** NOT/kg: 30mg 12H (6-11yr), 60mg 12H or 180mg daily (>11yr) oral.
- Fibrin glue.** See thrombin glue.
- Fibrinolysin 8-10u/ml + desoxyribonuclease 500-667 u/ml.** Ointment, soltn: apply topically 6-24H.

- Filgrastim (granulocyte CSF).** Idiopathic or cyclic neutropaenia: 5mcg/kg daily SC or IV over 30min. Cong neutropaenia: 12mcg/kg daily SC or IV over 1hr. Marrow trans: 20-30mcg/kg daily IV over 4-24hr, reduce if neutrophil  $>1 \times 10^9/L$ .
- Finasteride.** Adult (NOT/kg). Alopecia: 1mg dly oral.
- Flavoxate.** 2-4mg/kg (adult 100-200mg) 6-8H, or single dose at bedtime oral.
- Flecainide.** 2-3mg/kg (max 100mg) 12H oral, may incr over 2wk to 7mg/kg (max 200mg) 8-12H. IV over 30min: 0.5-2mg/kg (max 150mg) 12H.
- Floxuridine (FUDR).** 100-300mcg/kg/day by constant intra-arterial infn (400-600mcg/kg/day in hepatic artery). Stop if WCC  $<3500/mm^3$  or platelets  $<100,000/mm^3$ .
- Flucloxacillin.** Oral: 12.5-25mg/kg (adult 250-500mg) 6H. IM or IV: 25mg/kg (adult 1g) 6H. Severe infn: 50mg/kg (adult 2g) IV 12H (1st wk life), 8H (2-4 wk), 6H or constant infn ( $>4$  wk). See also ampicillin + flucloxacillin.
- Fluconazole.** 6mg/kg (adult 200mg) stat, then 3mg/kg (adult 100mg) dly oral or IV. Severe infn: 12mg/kg (adult 400mg) stat, then 6-12mg/kg (adult 200-400mg) daily IV; if haemofiltered 12mg/kg (adult 600mg) 12H.
- Flucytosine (5-fluorocytosine).** 400-1200mg/m<sup>2</sup> (max 2g) 6H IV over 30 min, or oral. Peak level 50-100mcg/ml, trough 25-50mcg/ml ( $\times 7.75 = \mu\text{mol/L}$ ).
- Fludarabine.** 25mg/m<sup>2</sup> daily  $\times 5$  IV over 30min, every 28 days.
- Fludrocortisone acetate.** 150mcg/m<sup>2</sup> daily oral. Fludrocortisone 1mg = hydrocortisone 125mg in mineralocorticoid activity, 10mg in glucocorticoid.
- Flumazenil.** 5mcg/kg every 60sec to max total 40mcg/kg (adult 2mg), then 2-10mcg/kg/hr IV.
- Flunisolide.** Asthma (250mcg/puff): 1-2 puffs 12H. Nasal (25mcg/puff): 1-2 puffs/nostril 8-24H.
- Flunitrazepam.** Adult (NOT/kg): 0.5-2mg nocte oral
- Fluocinolone.** See fluocinonide.
- Fluocinonide.** 0.025%, 0.05% cream, oint: apply 6-12H
- Fluocortolone.** 0.25% cream, ointment: apply 8-12H.
- Fluorescein.** 1%, 2% drops: 1 drop/eye. 10% (100 mg/ml), 25% (250mg/ml): 8mg/kg (max 500mg) IV.
- Fluorescein 0.25% + oxybuprocaine 0.4%.** 1 drop/eye.
- Fluorometholone.** 0.1% soltn: 1 drop/eye 6-12H.
- Fluorouracil.** 15mg/kg (max 1g) IV over 4hr daily until side effects, then 5-10mg/kg wkly. See also adrenaline + fluorouracil; and folic acid.
- Fluoxetine.** 0.5mg/kg (max 20mg) daily, incr to max 1mg/kg (max 40mg) 12H oral. Weekly 90mg cap: 1 per wk.
- Fluoxetine + olanzapine (25mg/6mg, 25mg/12mg, 50mg/6mg, 50mg/12mg).** (NOT/kg): 1cap dly oral
- Fluoxymesterone.** 0.1-0.2mg/kg (adult 5-10mg) daily oral.
- Flupenthixol.** Oral: 0.05-0.2mg/kg (adult 3-9mg) 12H. Depot IM: usually 0.4-0.8mg/kg (up to 5mg/kg, max 300 mg) every 2-4wk (1mg flupenthixol deconate = 0.625mg fluphenazine decanoate = 1.25mg haloperidol).
- Fluphenazine.** 0.02-0.2mg/kg (adult 1-10mg) 8-12H oral.
- Flurandrenolide.** See flurandrenolone.
- Flurandrenolone.** 0.025%, 0.05% cream, ointment or lotion: apply 6-24H. 4mcg/m<sup>2</sup> tape: apply 12H.
- Flurazepam.** Adult (NOT/kg): 15-30mg nocte oral.
- Flurbiprofen.** 1-2mg/kg (adult 50-100mg) 8H oral or PR. 0.03% drops: 1 drop/eye every 30min  $\times 4$
- Flutamide.** Adult (NOT/kg): 250mg 8H oral.
- Fluticasone.** Inhaled (NOT/kg): 50-100mcg (child), 100-500mcg (adult) 12H. 0.05% soltn: 1-4 sprays /nostril dly. 0.05% cream: apply sparingly dly.
- Fluticasone + salmeterol.** NOT/kg. Accuhaler: 100mcg/ 50mcg (child), 250/50 or 500/50 (adult)  $\times 1-2$  inhln 12H. MDI: 50/25 (child), 125/25 or 250/25  $\times 1-2$  inhln 12H.
- Fluvastatin.** 0.4mg/kg (adult 20mg) nocte oral, incr to 0.8 mg/kg (adult 40mg) 12H if reqd. Slow rel: 80mg nocte.
- Fluvoxamine.** 2mg/kg (adult 100mg) 8-24H oral.
- Folic acid.** NOT/kg. Deficiency: 50mcg (neonate), 0.1-0.25mg ( $<4$ yr), 0.5-1mg ( $>4$ yr) daily IV, IM, SC or oral. Metabolic dis: 5mg/day oral. Pregnancy: 0.5mg (high risk 4mg) daily oral.
- Folinic acid.** See calcium folinate.
- Follicle stimulating hormone (FSH).** Adult (NOT/kg), monitor urinary oestrogen. Anovulatn: usu. 50-150iu SC dly for 9-12 days. Superovulatn (2wk after starting GnRH agonist): 100-225iu/kg daily starting day 3 of cycle.
- Follitropin  $\alpha$ ,  $\beta$ .** See follicle stimulating hormone
- Fomivirsen.** Intravitreal injection, adult (NOT/kg). New disease: 165mcg/eye wkly  $\times 3$ , then every 2wk. Previously treatd: 330mcg/eye stat, in 2wk, then every 4wk
- Fondaparin.** Adult (NOT/kg): 2.5mg SC 6hr postop, then daily for 5-9 days.
- Formestane.** Adult (NOT/kg): 250mg 2wkly deep IM
- Formoterol.**  $>4$ yr (NOT/kg). Powder: 12mcg inhalation 12H. Solutn: 20mcg in 2ml nebulised 12H. See also budesonide.
- Fosamprenavir.** Adult (NOT/kg): 0.7g 12H, or 1.4g daily oral.
- Foscarnet.** 20mg/kg IV over 30min, then 200mg/kg/day by constant IV infsn (less if creatinine  $>0.11\text{mmol/l}$ ) or 60 mg/kg 8H IV over 2hr. Chronic use: 90-120mg/kg IV over 2hr daily.



**Fosfestrol.** Adult (NOT/kg) Initial: 0.5g IV over 1hr day 1, then 1g x5 days. Maintenance: 120-240mg 8H oral, later reducing to 120-240mg daily.

**Fosfomycin tromethamine.** One 5.63g (3g base) sachet mixed with water once oral.

**Fosinopril.** 0.2-0.8mg/kg (adult 10-40mg) dly oral

**Fosphenytoin.** 75mg = 50mg phenytoin (qv).

Prescribed / dispensed as phenytoin equivalents.

**Fotemustine.** IV over 1hr, or IA over 4hr: 100mg /m<sup>2</sup> wklly x3, rest 4-5wk, then every 3wk.

**Framycetin sulfate (Soframycin).** Subconjunctival: 500mg in 1ml water daily x3 days. Bladder: 500mg in 50ml saline 8H x10 days. 0.5%: eye 1drop 8H, ear 3drops 8H, ointment 8H.

**Framycetin sulfate 15mg/g + gramicidin 0.05mg/g.**

Cream, ointment (Soframycin topical): apply 8-12H.

See also dexamethasone + framycetin + gramicidin.

**Fresh frozen plasma.** Contains all clotting factors. 10-20 ml/kg IV. 1 bag is about 230ml.

**Frusemide.** Usually 0.5-1mg/kg (adult 20-40mg) 6-24H (daily if preterm) oral, IM, or IV over 20min (max 0.05 mg/kg/min IV). IV infn: 0.1-1mg/kg/hr (<20kg 25 mg/kg in 50ml 0.9% saline with heparin 1u/ml at 0.2-2 ml/hr; >20kg amp 10mg/ml at 0.01-0.1ml/kg/hr); protect from light.

**Fulvestrant.** Adult (NOT/kg): 250mg IM once / mth

**Furazolidone.** 2mg/kg (adult 100mg) 6H oral 7-10 d

**Fusafungine.** 125mcg spray: oral 1spray/10kg (adult 5sprays) x5/d, nasal 1spray/20kg (adult 3sprays) x5/d

**Fusidate, sodium.** See sodium fusidate.

**Fusidic acid.** Fusidic acid (susp) absorption only 70% that of sodium fusidate (tabs). Suspension: 15-20mg/kg (adult 750mg) 8H oral. Eye %: 1drop/eye 12H. For tablets and IV, see sodium fusidate.

**Gabapentin.** Anticonvulsant: 10mg/kg (adult 300mg) once day 1 oral, 12H day 2, 8H day 3 then adjusted to 10-20 mg/kg (adult 300-1200mg) 8H. Premed: 25mg/kg (adult 1200mg) 1hr preop. Analgesia: 2mg/kg (adult 100mg) 8H, incr if reqd to 15mg/kg (adult 800mg) or higher if tolerated.

**Galantamine.** Adult (NOT/kg): 4mg 12H x 4wk, then 8mg 12H, incr aftr 4wk if reqd to 8-12mg 12H oral

**Gallamine.** 1-2mg/kg (adult 50-100mg) IV.

**Gallium nitrate.** 100-200mg/m<sup>2</sup>/day x5days constant IV infn.

**Gamma benzene hexachloride.** See lindane.

**Gamma hydroxybutyrate.** See sodium oxybate.

**Gamolenic acid.** 2-5mg/kg (adult 120-240mg) 12H oral

**Ganciclovir.** 5mg/kg 12H IV over 1hr for 2-3wk; then 5mg/kg IV daily, or 6mg/kg IV on 6 days/wk, or 20 mg/kg (adult 1g) 8H oral.

Congenital CMV: 7.5mg/kg 12H IV over 2hr.

**Ganirelix.** Adult (NOT/kg): 0.25mg daily SC from day 6 of FSH to day of ovulation induction.

**Gas gangrene (Clostridia) antitoxin.** Prophylaxis: 25,000u IM / IV. Treatment: 75,000-150,000u IV over 1hr, rpt x1-2 aftr 8-12hr; if severe give 100,000u IM.

**Gatifloxacin.** 8mg/kg (adult 400mg) dly IV over 1hr. Gonorrh: 8mg/kg (adult 400mg) once. 0.3% ophthalmic: 1 drop/eye 2H when awake days 1-2, then x4/day days 3-7.

**Gaviscon.** See alginate acid.

**Gefitinib.** Adult (NOT/kg): 250mg daily oral.

**Gelatin, succinylated.** 10-20ml/kg (may be repeated). Volume effect lasts 3-4hr.

**Gemcitabine.** 1g/m<sup>2</sup> IV over 30min wklly for 3wk, rest for 1wk, then repeat 4wk cycle.

**Gemeprost (PGE<sub>1</sub> analogue).** Cervical dilatation: 1 pessary (1mg) into posterior vagina 3hr before surgery. Termination: 1 pessary (1mg) into posterior vagina 3H (max 5 pessaries).

**Gemfibrozil.** 10mg/kg (max 600mg) 12H oral.

**Gemifloxacin.** Adult (NOT/kg): 320mg daily oral.

**Gemtuzumab ozogamicin.** 9mg/m<sup>2</sup> IV over 2hr, repeated after 14 days.

**Gentamicin.** IV or IM. 1wk-10yr: 8mg/kg day 1, then 6 mg/kg dly. >10yr: 7mg/kg day 1, then 5mg/kg (max 240-360mg) dly. Neonate, 5mg/kg dose: <1200g 48H (day 0-7 of life), 36H (8-30 days), 24H (>30 days); 1200-2500g 36H (day 0-7 of life), 24H (>7 days); term 24H (0-7 days of life), then as for 1 wk-10yr. Trough level <1.0mg/L.

**Gentamicin, eye drops.** 0.3% 1drop/eye every 15min if severe, reducing to 1drop 4-6H.

**Gestodene.** See ethinyloestradiol + gestodene.

**Gestrinone.** Adult (NOT/kg): 2.5mg x2/wk on day 1 & 4 of menstrual cycle, then same days each wk

**Gestronol.** Adult (NOT/kg): 200-400mg every 5-7d IM

**Ginkgo biloba.** Adult (NOT/kg): 1200mg 12H oral.

**Glibenclamide.** Adult (NOT/kg): initially 2.5mg daily oral, max 20mg daily.

**Glibenclamide + metformin.** Adult (NOT/kg): 1.25mg / 250mg 12-24H oral, incr if reqd to 2.5mg / 500mg or 5mg / 500mg (max 10mg/1000mg) 12H.

**Gliclazide.** Adult (NOT/kg): initially 40mg daily oral, max 160mg 12H.

**Glimepiride.** Adult (NOT/kg): 2-4mg (max 6mg) dly oral

**Glimepiride + pioglitazone (2mg/30mg, 4mg/30mg).** Adult (NOT/kg): 1 tab daily oral.

**Glimepiride + rosiglitazone (1mg/4mg, 2mg/4mg, 4mg/4mg).** (NOT/kg): 1-2 tab dly (max 4mg/8mg) oral.

**Glipizide.** Adult (NOT/kg): 5mg dly oral, max 20mg 12H

**Gliquidone.** 0.25-1mg/kg (adult 15-60mg) 8-12H oral

**Glucagon.** 1u=1mg. 0.04mg/kg (adult 1-2mg) IV / IM stat, then 10-50mcg/kg/hr (0.5mg/kg in 50ml at 1-5ml/hr) IV.  $\beta$ -blocker overdose: 0.1mg/kg IV stat, then 0.3-2 mcg/kg/min.

**Glucose.** See dextrose.

**Glucose electrolyte solution.** Not dehydrated: 1 heaped teaspoon sucrose in large cup of water (4% sucrose = 2% glucose); do NOT add salt. Dehydrated: 1 sachet of Gastro-lyte in 200ml water; give frequent sips, or infuse by NG tube.

**Glutamic acid.** 10-20mg/kg (adult 0.5-1g) oral with meals.

**Glyburide.** See glibenclamide.

**Glycerin.** See sorbolene + glycerin cream.

**Glycerol.** Supp: 0.7-1g infant, 1.4-2g child, 2.8-4g adult.

**Glyceryl trinitrate.** Adult (NOT/kg): subling. tab 0.3-0.9 mg/dose (lasts 30-60min); subling. aerosol 0.4-0.8 mg/dose; slow-release buccal tab 1-10mg 8-12H; trans-dermal 0.5-5cm of 2% ointment, or 5-15mg patch 8-12H. IV infns 0.5-5mcg/kg/min (<30kg 3mg/kg in 50ml 5%dex-hep at 0.5-5ml/hr; >30kg 3mg/kg made up to 100ml in 5%dex-hep at 1-10ml/hr); use special non-PVC tubing.

**Glycopyrrolate.** To reduce secretions or treat bradycardia: 5-10mcg/kg (adult 0.2-0.4mg) 6-8H IV or IM. With 0.05mg/kg neostigmine: 10-15mcg/kg IV. Anticholinergic: 0.02-0.04mg/kg (max 2mg) 8H oral.

**Glycopyrronium bromide.** As for glycopyrrolate.

**GM-CSF.** See sargramostim.

**Gold sodium thiomalate.** See sodium aurothiomalate

**Gonadorelin (GnRH or LHRH).** Pituitary function test, child or adult: 100mcg IV. See also leuporelin.

**Gonadotrophin.** See chorionic gonadtrn, and menotrophin.

**Goserelin.** Adult (NOT/kg): 3.6mg SC every 28 d; implant 10.8mg SC every 12wk. See also bicalutamide.

**Gramicidin 0.025% + neomycin 0.25% + nystatin 100,000 u/g + triamcinolone 0.1%.** Kenacomb ointment: apply 8-12H. Kenacomb otic oint, drops: apply 8-12H (2-3 drops).

**Gramicidin 25mcg/ml + neomycin 2.5mg/ml + polymyxin B 5000u/ml (Neosporin).** Eye drops: 1 drop/eye every 15-30min, reducing to 6-12H. See also dexamethasone.

**Granisetron.** 0.04mg/kg (adult 1mg) IV over 5min daily. Chemo: 0.05mg/kg (adult max 1-3mg) IV over 5min; up to 3 doses/day, at least 10min apart.

**Granulocyte-macrophage colony stimulating factor (GM-CSF).** See lenograstim, sargramostim.

**Griseofulvin (Grisovin, Fulcin).** 10-20mg/kg (adult 0.5-1g) daily oral.

**Griseofulvin, ultramicrosize (Griseostatin).** 5.5-7mg/kg (adult 330-660mg) daily oral.

**Growth hormone.** See somatotropin.

**Guaiphenesin.** 4-8mg/kg (adult 200-400mg) 4H oral

**Guanabenz.** 0.1mg/kg (max 4mg) 12H oral, incr to max 0.6mg/kg (max 32mg) 12H.

**Guanadrel.** 0.1mg/kg (max 5mg) 12H oral, incr to max 0.5mg/kg (max 25mg) 8-12H.

**Guanethidine.** 0.2mg/kg (max 10mg) daily oral, incr to 0.5-6mg/kg (max 300mg) daily. Regnl symp block (adult): cuff 55mmHg >syst BP, 10-20mg in 10-25ml saline (arm) or 15-30mg in 15-50ml (leg) IV, wait 10-20min, release cuff over 5min; >=7 days betw injctns (max 12/yr)

**Guanfacine.** 0.02mg/kg (max 1mg) daily oral, incr over several wks to max 0.06mg/kg (max 3mg) dly.

**Guargum.1g/10kg(adult 5g) 8Horal in fluid 40ml/g gum**

**Haem arginate.** 3-4mg/kg daily IV over 30-60min.

**Haemacel.** See polygeline.

**Haemophilus influenzae type b, vaccines.** Inactivated. <12mo: give diphtheria protein conjugate (HibTITER, ProHIBit), or tetanus conjugate (Act-HIB, Hiberix) 0.5ml IM at 2mo, 4mo, 6mo and 15mo; or meningococcal con-jugate (Pedvax Hib) 0.5ml IM at 2mo, 4mo and 15mo. If 1st dose >18mo: give 1 dose of HibTITER or Pedvax Hib.

**Haemophilus influenzae type b + hepatitis B vaccine (Comvax).** Inactivated. 0.5ml IM 2mo, 4 mo, 12-15 mo (3 doses).

**Haemophilus influenzae type b + meningococcus type c vaccine (Menitorix).** Inactivated. 0.5ml IM 2mo, 3mo, 4mo (3 doses); boost from 12mo.

**Halcinonide.** 0.1% cream: apply sparingly 8-12H.

**Halobetasol.** 0.05% cream, ointmnt: apply 12-24H

**Halofantrine.** 10mg/kg (max 500mg) 6H for 3 doses oral, repeat after 1wk if nonimmune.

**Haloperidol.** 0.01mg/kg (max 0.5mg) daily, incr up to 0.1 mg/kg 12H IV or oral. Acutely disturbed: 0.1-0.2mg/kg (adult 5-10mg) IM. Long-acting decanoate ester: 1-6mg/kg IM every 4wk.

**Hemin.** 1-3mg/kg 12-24H IV over 30min.

**Heparin.** 1mg=100u. Low dose: 75u/kg IV stat, then 500u/kg in 50ml 0.9% saline at 1-1.5ml/hr (10-15u/kg/hr) IV. Full dose: 75u/kg (adult 5000u) IV stat, then 500u/kg in 50ml saline at 2-4ml/hr (20-40u/kg/hr)<12mo, 2-3ml/hr (20-30 u/kg/hr) child, 1.5-2ml/hr (15-20u/kg/hr) adult; ad-just to give APTT 60-85 sec, or anti-Xa 0.3-0.7u/ml. Hep lock: 100u/ml.

**Heparin calcium.** Low dose: 75u/kg SC 12H.

**Heparin, low molecular weight.** See certoparin, dalteparin, danaparoid, enoxaparin, nadroparin.

**Hepatitis A vaccine (Havrix).** Inactivated. 0.5ml (child) or 1ml (adult) IM stat, and in 6-12mo (2doses). Boost every 5yr.

**Hepatitis A vaccine (VAQTA).** Inactivated. 0.5ml (child) or 1ml (>17yr) IM stat, > 6-18mo (2 doses)

**Hepatitis A + hepatitis B vaccine (Twinrix)**

Inactivated. 0.5ml, >15yr 1ml IM stat, after 1mo, and after 6mo (3 doses). Boost every 5yr.



**Hepatitis B vaccine (Engerix-B, HB Vax II).**

Inactivated. Engerix-B 10mcg/dose (<10yr), 20mcg (>9yr); HB Vax II 2.5mcg/dose (<10yr), 5mcg (10-19yr), 10mcg (>19yr), 40mcg (dialysis) IM stat, after 1mo, and after 6mo (3 doses). Boost every 5yr.

**Herpes zoster vaccine (Zostavax).** Live. Age  $\geq$  50yr: 0.65ml SC once. See also Immunoglobulin, zoster.

**Hetastarch.** 6% 10-20ml/kg IV.

**Hexachlorophane.** 3% emulsion. >12mo: apply 5ml, scrub for 3min.

**Hexamethylmelamine.** 150-260mg/m<sup>2</sup> daily oral for 14-21 consecutive days of 28 day cycle.

**Hexamidine.** See chlorhexidine.

**Hexamine.** 20mg/kg (adult 1g) 6H oral.

**Hexetidine.** 0.1% soln: rinse/gargle 15ml 8-12H.

**Histamine phosphate.** 1mg/ml base: prick, puncture or scratch testing. 0.1mg/ml base: intradermal testing.

**Histrelin.** Usually 10mcg/kg daily SC.

**Homatropine.** 2%, 5% soltn: 1 drop/eye 4H.

**Human chorionic gonadotrophin.** See Chorionic gonadotrophin.

**Human papillomavirus vaccine (Cervarix, Gardasil).** Inactivated. Females 10-46yr, males 9-15yr: 0.5ml IM, in 1-2mo, and 6mo later (3 doses).

**Hyaluronic acid.** Gel 20mg/ml: 0.7-1.4ml inj. in wrinkles

**Hyaluronidase.** Hypodermoclysis: add 1-1.5u/ml fluid. Local anaesthesia: add 50u/ml soltn.

**Hydralazine.** 0.1-0.2mg/kg (adult 5-10mg) stat IV or IM, then 4-6mcg/kg/min (adult 200-300mcg/min) IV. Oral: 0.4 mg/kg (adult 20mg) 12H, slow incr to 1.5mg/kg (max 50mg) 6-8H.

**Hydrochloric acid.** Use soltn of 100mmol/L (0.1M = 0.1N = 100mEq/L); give IV by central line only. Alkalosis: dose(ml) = BE x Wt x 3 (give half this); maximum rate 2ml/kg/hr. Blocked central line: 1.5ml/lumen over 2-4hr.

**Hydrochlorothiazide.** 1-1.5mg/kg (adult 25-50mg) 12-24H.

**Hydrochlorothiazide + quinapril 10/12.5, 20/12.5.** Adult (NOT/kg): 10/12.5 tab dly oral, incr if reqd to 20/12.5 tab, max two 10/12.5 tab daily.

**Hydrocodone.** 0.1-0.2mg/kg (max 10-15mg) 4-6H oral

**Hydrocortisone.** Usually 0.5-2mg/kg (adult 25-50mg) 6-8H oral, reducing as tolerated. 0.5%, 1% cream, ointment: apply 6-12H. 1% cream + clioquinol: apply 8-24H. 10% rectal foam: 125mg/dose. 2.5% eye ointment: apply 6H.

**Hydrocortisone sodium succinate.** 2-4mg/kg 3-6H IM, IV reducing as tolerated. Physiological: 5mg/m<sup>2</sup> 6-8H oral; 0.2mg/kg 8H IM, IV. Physiological, stress: 1mg/kg 6H IM, IV.

**Hydrocortisone 1% + pramocaine 1%.** Cream, foam: apply 8-12H after defaecation.

**Hydroflumethiazide.** 0.5-2mg/kg (adult 25-100mg) 12-48H.

**Hydrogen peroxide.** 10 volume (3%). Mouthwash 1:2 parts water. Skin, ear disinfectant 1:1 pt water.

**Hydromorphone.** Oral: 0.05-0.1mg/kg (adult 2-4mg) 4H. IM, SC: 0.02-0.05mg/kg (adult 1-2 mg) 4-6H. Slow IV: 0.01-0.02mg/kg (adult 0.5-1 mg) 4-6H. Palliative care: incr to 40-50mg/day (up to 500mg/day) oral in divided doses.

**Hydroquinone.** 4% cream: apply 12H.

**Hydrotalcite.** 20mg/kg (adult 1g) 6H oral.

**Hydroxocobalamin (Vit B12).** 20mcg/kg (adult 1000mcg) IM dly for 7 d then wkly (treatment), then every 2-3mo (prophylaxis); IV dangerous in megaloblastic anaemia. Homocystinuria, methylmalonic aciduria: 1mg daily IM; after response, some patients maintained on 1-10mg daily oral.

**Hydroxyapatite.** 20-40mg/kg (adult 1-2g) 8H oral.

**Hydroxycarbamide.** See hydroxyurea.

**Hydroxychloroquine sulphate.** Doses as sulphate. Malaria: 10mg/kg (max 600mg) daily for 3d; prophylaxis 5mg/kg (max 300mg) once a wk oral. Arthritis, SLE: 3-6.5mg/kg (adult 200-600mg) daily oral.

**Hydroxyethylcellulose.** 0.44% 1 drop per eye 6-8H.

**Hydroxypropyl (methyl)cellulose.** See hypromellose. Hydroxyethylrutosides. 5mg/kg (adult 250mg) 6-8H for 3-4wk, then 12-24H; or 10mg/kg (adult 500mg) 12H for 3-4wk, then daily oral.

**Hydroxyprogesterone.** Adult (NOT/kg): 250-500mg/wk IM.

**Hydroxypropylcellulose.** 5mg insert: 1 in each eye dly

**Hydroxyquinone.** 4% cream: apply 12H.

**Hydroxyurea.** 80mg/kg oral every 3rd day, or 20-30mg/kg daily. CNS tumors: 1.5-3g/m<sup>2</sup> oral stat, in 2wk, then every 4-6wk. Sick cell: 15mg/kg daily, incr by 5mg/kg every 12wk to max 35mg/kg daily.

**Hydroxyzine.** 0.5-2mg/kg (adult 25-100mg) 6-8H oral. 0.5-1mg/kg (adult 25-100mg) 4-6H if reqd IM

**Hylan.** 8mg inj into knee wkly x3; max 6 doses in 6mo.

**Hyoscine hydrobromide (scopolamine hydrobromide).** 6-8mcg/kg (adult 400-600mcg) 6-8H IV, IM, SC. Motion sickness 300mcg tab (NOT/kg): 0.25 tab (2-7yr), 0.5 tab (7-12yr), 1-2 tab (>12yr) 6-24H oral 30 min before, may repeat in 4hr. Transdermal (1.5mg patch): >10yr 1 every 72hr.

**Hyoscine hydrobromide (0.4mg/ml) + papaveretum (20mg/ml).** 0.008 mg/kg (H) + 0.4 mg/kg (P) = 0.02ml/kg/dose IM.

**Hyoscine methobromide (methscopolamine).** 0.2mg/kg (adult 2.5-5mg) 6H oral.

**Hyoscine butylbromide.** 0.5 mg/kg (adult 20-40mg) 6-8H IV, IM or oral.

**Hyoscyamine (L-atropine).** 2-5mcg/kg (adult 100-300 mcg) 4-6H oral, sublingual, IM or IV.

**Hypromellose.** 0.5% soltn: 1 drop/eye prn.

**Hypromellose 0.3% + dextran 70 0.1%.**  
1 drop/eye prn.

**Ibandronate (ibandronic acid).** Adult, NOT/kg.  
Hypercalcaemia: 2-4mg IV over 2hr once.  
Osteoporosis: 2.5mg daily, or 150mg each month oral; or 3mg IV bolus every 3mo.

**Ibuprofen.** 5-10mg/kg (adult 200-400mg) 4-8H oral. Arthritis: 10mg/kg (adult 400-800mg) 6-8H. Cystic fibrosis: 20-30mg/kg 12H. PDA: 10mg/kg stat, then 5mg/kg aftr 24 and 48 hr IV over 15min.

**Ibutilide.** 0.017mg/kg (max 1mg) IV over 10min, then wait 10min and repeat once if reqd.

**Ichthammol.** 1-10% cream, ointment. Apply 6-8H.

**Icodextrin 7.5% in electrolyte soltn.** Adults: 1.5-2.5 litres as once daily replacemnt for a 6-12hr glucose dialysis.

**Idarubicin.** 12mg/m<sup>2</sup> IV over 15min dly for 3 days.

**Idebenone.** Adult (NOT/kg): 30mg 8H oral.

**Idoxuridine.** 0.1% eye drops: 1 drop every 15min for 2hr, then hly by day, 2hly at night. 0.1% soltn or 0.5% ointment: apply hourly first 24hr, then 4H.

**Ifosfamide.** Usu. 1.2-2.0g/m<sup>2</sup> IV over 4hr dly x5, or 5-6 g/m<sup>2</sup> (max 10g) IV over 24hr x1. Rpt every 2-4wk.

**Iloprost.** Adult (NOT/kg): 2.5-5mcg x6-9/day by inhalatn

**Imatinib.** Adult (NOT/kg): 400mg daily (chronic CML), 600mg daily (blast crisis) or 400mg 12H (unresponsive blast) oral.

**Imidapril.** 0.1mg/kg (adult 5mg) daily oral, incr if reqd to 0.2-0.3mg/kg (adult 10-20mg) daily.

**Imiglucerase.** Usu. initial dose 60u/kg every 2wk IV over 2hr, adjust as per response; reduce every 3-6mo.

**Imipenem (+ cilastatin).** 15mg/kg (adult 500mg) 6H IV over 30min. Severe infn: 25mg/kg IV over 1hr (adult 1g) 12H (1st wk life), 8H (2-4 wk), 6-8H or constant infns (4+ wk).

**Imipramine.** 0.5-1.5mg/kg (adult 25-75mg) 8H oral. Enuresis: 5-6yr 25mg, 7-10yr 50mg, >10yr 50-75mg nocte.

**Imiquimod.** 5% cream: apply x2-3/wk (max 16wk) before bed; wash off after 6-10hr. Molluscum: 0.2% cream x3/wk.

**Immunoglobulin, CMV.** 100-200mg/kg IV over 2hr. Transplant: dly for first 3 days, wkly x6, mthly x6

**Immunoglobulin, diphtheria.** 250u IM once.

**Immunoglobulin, hepatitis B.** 400u IM within 5 days of needle stick, repeat in 30 days; 100u IM within 24hr birth to baby of Hep B carrier.

**Immunoglobulin, antilymphocyte (thymocyte).** Horse (Atgam): 10-15mg/kg daily for 3-5 days IV over 4hr; occasionally up to 30mg/kg daily.

**Rabbit (ATG-Fresenius).** 2.5-5mg/kg dly over 4-6hr IV

**Immunoglobulin, normal, human.** Hypogammaglobulinaemia: 10-15ml/kg of 6% soltn (600-900 mg/kg) IV over 5-8hr, then 5-7.5 ml/kg (300-450 mg/kg) over 3-4hr mthly; or 0.6ml/kg of 16% soltn (100mg/kg) every 2-4wk IM. Sepsis: 0.5g/kg IV over 4hr. Kawasaki, Guillain-Barre, ITP, myasthenia gravis, Still's disease: 35ml/kg of 6% soltn (2g/kg) IV over 16hr stat, then if required 15 ml/kg (900mg/kg) IV over 8hr each month. Prevention hepatitis A: 0.1ml/kg (16mg/kg) IM. Prevention measles: 0.2ml/kg (32mg/kg) IM (repeat next day if immunocompromised).

**Immunoglobulin, rabies (Hyperab, Imogam).**

20iu (0.133 ml)/kg IM once (half SC around wound), with rabies vaccine.

**Immunoglobulin, Rh (anti-D).** 1ml (625iu, 125mcg) IM within 72hr of exposure. Large transfusion: 0.16ml (100iu, 20mcg) per ml RH positive red cells (maternal serum should be anti-D positive 24-48hr after injection).

**Immunoglobulin, respiratory syncytial virus.**

750mg/kg every month IV (50mg/ml: 1.5ml/kg/hr for 15min, 3ml/kg/hr for 15min, then 6ml/kg/hr).

**Immunoglobulin, subcutaneous (SCIG).**

Multiply previous IV immunoglobulin dose by 1.37, and divide this into weekly doses. Usually 100-200mg/kg by SC infusion weekly.

**Immunoglobulin, tetanus (TIG).** IM preparation, prophylaxis: 250-500iu (1-2amp). IV preparation, treatmnt: 4000iu (100ml) at 0.04ml/kg/min for 30 min, then 0.075 ml/kg/min IV; intrathecal usu. 250iu

**Immunoglobulin, zoster.** 1iu = approx 1.5mg.

Within 96hr of exposure: 0-10kg 300mg, 11-30kg 600mg, >30kg 900mg IM.

**Indapamide.** 0.03-0.05mg/kg (max 1.5-2.5mg) dly oral

**Indinavir.** >28 days: 500mg/m<sup>2</sup> (adult 800mg) 8H oral

**Indocyanine green.** IV. Dye dilutn: 0.1mg/kg (adult 5mg). Pulsion monitor: 0.25-0.5mg/kg. Liver function: 0.5mg/kg.

**Indomethacin.** 0.5-1mg/kg (adult 25-50mg) 8H (max 6H) oral or PR. PDA: 0.1mg/kg (<1kg) or 0.2mg/kg (>=1kg) day 1, then 0.1mg/kg daily days 2-7 oral or IV over 1hr.

**Indoramin.** 0.5-1.5mg/kg (adult 25-75mg) 8-12H oral.

**Infliximab.** 3mg/kg (arthritis, with methotrexate) 5mg/kg (Crohn's) IV over 2hr, then (if response) after 2wk, 6wk, and then 5-10mg/kg every 8wk.

**Influenza A and B vaccine (Fluvax, Vaxigrip).**

Inactivated. 0.125ml (3mo-2yr), 0.25ml (2-6yr), 0.5ml (>6yr) SC stat and 4wk later (2 doses). Boost annually (1 dose).

**Influenza A and B live nasal vaccine (Flumist).**

>5yr: 0.25 ml/nosril; rpt after 6wk if age 5-8yr and prev unimmunised. Boost annually (1 dose).





- Inosine acedoben dimepranol.** Herpes, genital warts: 20 mg/kg (adult 1g) 6-8H oral. SSPE: 10-15mg/kg 4H oral.
- Inositol nicotinate.** 20mg/kg (adult 1g) 6-8H oral.
- Insulin.** Regular insulin IV: 0.025-0.1u/kg prn, or 0.025-0.1 u/kg/hr (2.5u/kg in 50ml 4% albumin at 0.5-2ml/hr); later 1u/10g dextrose. For hyperkalaemia: 0.1u/kg insulin and 2ml/kg 50% dextrose IV. In TPN: 5-25u/250g dextrose. SC insulin (onset/peak/duration): glulisine, lispro 10-15min/1hr/ 2-5hr; aspart 15-20min/1hr/3-5hr; inhaled 10-15min/1hr/6hr; regular ½-1hr/2hr/6-8hr; detemir 1-2hr/flat/24hr; glargine 1-2hr/flat/24hr; isophane (NPH) 2-4hr/4-12 hr/18-20hr; zinc (lente) 2-3hr/7-15hr/24hr; crystalline zinc (ultralente) 4-6hr/10-30hr/24-36hr; protamine zinc 4-8 hr/ 15-20hr/24-36hr.
- Insulin (Exubera).** Initially 30-39kg 1mg, 40-59kg 2mg, 60-79kg 3mg, 80-99kg 4mg, inhaled 10min before meal.
- Interferon alfa-2a, recombinant.** Haemangioma: 1 million u/m<sup>2</sup> daily SC or IM incr over 4wk to 2-3 million u/m<sup>2</sup> dly for 16-24wk, then x3/wk. Hep B, C: 3-6 million u/m<sup>2</sup> x3/wk SC or IM for 4-6mo; higher doses may be required in hep B.
- Interferon alfa-2b, recombinant.** Condylomata: 1 mil. unit into each lesion (max 5) x3/wk x 5wk. Haemangioma: as for interferon alfa-2a. Hep B: monotherapy as for interferon alfa-2a. Hep C (adult, NOT/kg) 3 million unit x3/wk SC, + ribavirin 1000mg (1200mg if >75kg) dly oral, x 24-48wk.
- Interferon alfa-2a / alfa-2b, pegylated.** See peginterferon.
- Interferon alfa-n3.** Warts (NOT/kg): 250,000u injected into base of wart (max 10 doses/ session) x2/wk for max 8wk.
- Interferon alfacon-1.** Hepatitis C (adult, NOT/kg): usu. 9mcg (7.5mcg if not tolerated) x3/wk SC for 24wk; if relapse 15mcg x3/wk SC for 6mo.
- Interferon beta-1a.** Mult sclerosis (NOT/kg): Avonex 30mcg (6 million IU) once a wk IM, Rebif 44mcg x3/wk SC.
- Interferon beta-1b.** Mult sclerosis (NOT/kg): 250mcg (8 million IU) SC alternate days.
- Interferon gamma-1b.** Chronic granulomatous disease: 1.5mcg/kg (body area <=0.5m<sup>2</sup>) or 50mcg/m<sup>2</sup> (area >0.5m<sup>2</sup>) x3/wk SC.
- Interleukin-2.** See aldesleukin.
- Iodoquinol.** See di-iodohydroxyquinoline.
- Ipecacuanha syrup (total alkaloids 1.4mg/ml).** 1-2ml/kg (max 30ml) stat oral, NG. May rpt 1x in 30min
- Ipratropium bromide.** Resp soltn (250mcg/ml): 0.25-1ml diluted to 4ml 4-8H; severe attack every 20min for 3 doses, then 4-6H. Aerosol 20mcg/puff: 2-4 puffs 6-8H. Nasal: 84mcg/nostril 6-12H.
- Irbesartan.** 3mg/kg (adult 150mg) daily oral, incr to 6mg/kg (adult 300mg) daily if reqd.
- Irinotecan.** 350mg/m<sup>2</sup> IV over 90min every 3wk; reduce to 250-300mg/m<sup>2</sup> every 3wk if toxicity.
- Iron.** See ferrous gluconate, ferrous sulphate.
- Iron dextran, iron polymaltose.** Fe 50mg/ml: dose (ml) = 0.05 x Wt in kg x (15 - Hb in g%) IM (often in divided doses). IV infns possible (but dangerous).
- Isoconazole.** 1% cream 12H. Vaginal: 600mg (2 tab) once.
- Isoetharine.** Inhaltn soltn (1%): 0.5ml dilt to 4ml 3-6H (mild), 1ml dilt to 4ml 1-2H (moderate), undilt constant (severe, in ICU). Aerosol 340mcg/puff: 1-2 puffs 4-6H.
- Isometheptene.** 2.5mg/kg (max 130mg) stat, then 1.5mg/kg (max 65mg) 1H to max 7mg/kg (max 325mg) in 12hr oral. See also dichloral phenazone.
- Isoniazid (INH).** 10mg/kg (max 300mg) daily oral, IM or IV. TB meningitis: 15-20mg/kg (max 500mg) daily.
- Isoniazid 50mg + pyrazinamide 300mg + rifampicin 120mg tab.** 30-39kg x3, 40-49kg x4, 50-64kg x5, ≥65kg x6tab daily.
- Isoniazid + rifampicin.** 30-49kg 150mg/100mg tabs x3 dly, ≥50kg 300mg/150mg tabs x2 dly oral
- Isoprenaline.** IV infns: <33kg 0.3mg/kg in 50ml 5%dex-hep at 0.5-10ml/hr (0.05-1mcg/kg/min); >33kg give 1/5000 (0.2 mg/ml) soltn at 0.015-0.15ml/kg/hr (0.05-0.5mcg/kg/min).
- Isoproterenol.** See isoprenaline.
- Isosorbide dinitrate.** Subling: 0.1-0.2mg/kg (max 10mg) 2H or as needed. Oral: 0.5-1mg/kg (max 40mg) 6H or as needed. Slow rel tab, adult (NOT/kg): 20-80mg 12H. IV infns 0.6-2mcg/kg/min.
- Isosorbide mononitrate.** Slow release tab, adult (NOT/kg): 60-120mg daily oral.
- Isotretinoin.** Adult: 0.5-1mg/kg daily oral for 2-4wk, reducing if possible to 0.1-0.2mg/kg dly for 15-20wk. 0.05% gel: apply sparingly at night
- Isoxsuprine.** 0.2-0.5mg/kg (adult 10-20mg) 6-12H oral
- Ispaghula husk.** Adult (NOT/kg): 1-2 x5ml tea spoonfuls 6-12H oral. Half this dose 6-12yr.
- Istradipine.** 0.05mg/kg 12H oral, may incr after 2-4wk gradually to 0.1-0.2mg/kg (max 10mg) 12H
- Itraconazole.** 2-4mg/kg (adult 100-200mg) 12-24H oral after food. Trough level >0.5 mcg/ml at 10-14 days.
- Ivabradine.** 0.1mg/kg (adult 5mg) 12H oral, range 0.05-0.15 mg/kg (adult 2.5-7.5mg) 12H.
- Ivermectin.** 0.15-0.4mg/kg (adult 12-24mg) oral every 6-12 mo. Lice: 0.2mg/kg (adult 12mg) oral, repeat after 7 days.

- Ixabepilone.** 40mg/m<sup>2</sup> IV over 3hr every 21 days for median of 4 cycles. Vary dose with CYP3A4 inhibitors or inducers.
- Japanese encephalitis vaccine (Je-Vax).** Inactivated. 0.5ml (1-3yr), 1ml (>3yr) SC stat, 7-14 days later, and (optionally) 1mo later. Boost after 1yr.
- Kanamycin.** Single daily dose IV or IM. Neonate: 15mg/kg stat, then 7.5mg/kg (<30wk) 10mg/kg (30-35wk) 15mg/kg (term <1wk) daily. 1wk-10yr: 25mg/kg day 1, then 18mg/kg daily. >10yr: 20mg/kg day 1, then 15mg/kg (max 1.5g) daily. Trough level <5.0mg/L.
- Ketamine.** Sedation, analgesia: 2-4mg/kg IM, 4mcg/kg/min IV. Premed: 5mg/kg oral. Anaesthesia: 5-10mg/kg IM, 1-2mg/kg IV, infn 30mg/kg in 50ml 5%dex-hep at 1-4ml/hr (10-40mcg/kg/min). Incompatible with aminophylline, magnesium and salbutamol.
- Ketoconazole.** Oral: 5mg/kg (adult 200mg) 12-24H. 2% cream: apply 12-24H. 2% shampoo: wash hair, apply liquid for 5min, wash off.
- Ketoprofen.** 1-2mg/kg (adult 50-100mg) 6-12H (max 4mg/kg or 200mg in 24hr) oral, IM, PR. Slow release, adults (NOT/kg): 200mg daily.
- Ketorolac.** Oral: 0.2mg/kg (adult 10mg) 4-6H (max 0.8mg/kg/day or 40mg/day). IV or IM: usually 0.2mg/kg (adult 10mg) 6H; but may use 0.6mg/kg (max 30mg) stat, then 0.2-0.4mg/kg (max 20mg) 4-6H for 5 days, then 0.2mg/kg (max 10mg) 6H. Eye drops 0.5%: 1 drop 8H.
- Ketotifen.** Child >2yr (NOT/kg): 1mg 12H oral with food. Adult (NOT/kg): 1-2mg 12H oral with food.
- Labetalol.** Oral: 1-2mg/kg (adult 50-100mg) 12H, may incr wkly to max 10mg/kg (max 600mg) 6H. IV: 0.25-0.5mg/kg (adult 20mg) over 2min rpt every 10min if reqd, then 0.25-3mg/kg/hr.
- Lacidipine.** 0.04-0.12mg/kg (adult 2-6mg) dly oral.
- Lactase.** See tilactase.
- Lactulose.** 3.3g/5ml soltn. Laxative: 0.5ml/kg 12-24H oral. Hepatic coma: 1ml/kg hrly until bowel cleared, then 6-8H.
- Lamivudine.** Neonate <30 days: 2mg/kg 12H oral. Child >30 days: 4mg/kg 12H oral. Adult <50kg: 2mg/kg 12H oral. Adult >50kg: 150mg 12H or 300mg daily oral. Hepatitis b: 3-4 mg/kg (max 100mg) daily oral. See also abacavir.
- Lamivudine + zidovudine.** 150mg/300mg tab. >12yr (NOT/kg): 1tab 12H oral.
- Lamotrigine.** 0.2mg/kg (adult 25mg) oral daily, double dose every 2wk if reqd to max 1-4mg/kg (adult 50-200mg) 12H. Double dose if taking carbamazepine, phenobarbitone, phenytoin; halve dose if taking valproate.
- Lanreotide.** 0.5-1.0mg/kg (adult 30mg) IM every 2wk (adjust dose and frequency according to resp)
- Lansoprazole.** 1.5mg/kg (max 30mg) 12-24H oral.
- Lanthanum carbonate.** Adult (NOT/kg) 0.5-1g 8H with meal.
- Lapatinib.** Adult, NOT/kg: 1.25g every day oral (plus capecitabine 2g/m<sup>2</sup>/day on days 1-14 of a repeating 21 day cycle).
- Laronidase.** 0.58mg/kg IV once a week.
- L-asparaginase.** See colaspase.
- Latanoprost.** 50mcg/ml: 1drop/eye daily.
- Latanoprost 0.005% + timolol 0.5%.** 1drop per eye daily.
- Laureth-9.** Spider veins: inject 0.1-0.2ml of 0.5% (10mg/2ml). Small varices: 0.1-0.3ml of 1% (20mg/2ml). Medium varices: 0.5-1ml of 3% (60mg/2ml). Max 2mg/kg/day.
- Leflunomide.** Adult (NOT/kg): 100mg daily x3, then 20mg daily oral.
- Lenalidomide.** Adult (NOT/kg): 10mg daily oral; or 25mg daily on days 1-21 of 28 day cycles.
- Lenograstim (rHuG-CSF, Granocyte).** 150mcg/m<sup>2</sup> daily SC or IV over 30min. Keep wbc count 5,000-10,000/mm<sup>3</sup>.
- Lepirudin.** 0.4mg/kg IV stat, then 0.15mg/kg/hr (adjusted by APTT) for 2-10 days.
- Lercanidipine.** 0.2mg/kg (adult 10mg) daily oral, incr to 0.4mg/kg (adult 20mg) daily if reqd.
- Letrozole.** Adult (NOT/kg): 2.5mg daily oral.
- Leucovorin.** See folinic acid.
- Leuporelin (GnRH or LHRH).** 7.5mg depot mthly IM; or microspheres 11.25mg SC every 3mo.
- Levamisole.** Anthelmintic: 3mg/kg (adult 150mg) oral once (ascaris), repeat in 1wk (hookworm). Adenocarcinoma colon (with 5-fluorouracil 450mg/m<sup>2</sup> IV wkly): 1mg/kg (adult 50mg) 8H oral for 3 days every 2wk.
- Levetiracetam.** 10mg/kg (adult 500mg) 12H oral, incr every 2-4wk to max 30mg/kg (adult 1500mg) 12H if reqd.
- Levobetaxolol.** 0.5% soltn: 1drop/eye 12H.
- Levobunolol.** 0.25%-0.5% soltn: 1drop/eye 12-24H.
- Levobupivacaine.** See bupivacaine.
- Levocabastine.** 0.5mg/ml: 1drop/eye 6-12H max 8wk, 2 sprays/nosril 6-12H max 8wk.
- Levocetirizine.** 2.5mg (6-11yr) 5mg (adult) dly
- Levodopa + benserazide (4:1).** Adult (NOT/kg): initially levodopa 100mg 8H oral; if not controlled, incr wkly by 100mg/day to max 250mg 6H.
- Levodopa + carbidopa.** 250mg/25mg and 100mg/10mg tabs. Adult (NOT/kg): initially one 100/10 tab 8H oral; if not controlled, use one 250/25 tab for one 100/25 tab every 2nd day; if not controlled on 250/25 8H, incr by one 250/25 tab every 2nd day to max 6-8 tab/day.







- Levofloxacin.** 5-10mg/kg (adult 250-500mg) 12-24H oral or IV over 1hr. Eye 5mg/ml: 1 drop x8/day for 2 days, then 6H.
- Levomopromazine.** See methotrimeprazine.
- Levomethadyl acetate.** Adult (NOT/kg): usual starting dose 20-40mg every 2-3 days oral.
- Levonorgestrel.** Contraception: 30mcg daily oral, starting 1st day menstruatn. Intrauterine T-system 52mg: insert within 7 days of start of menstruatn, replace after 3yr.
- Levonorgestrel + oestradiol (7mcg/50mcg, 15mcg/45mcg per day) patch.** Post-menopausal (NOT/kg): 1 patch per wk.
- Levorphanol.** 0.03-0.1mg/kg 12-24H oral or SC.
- Levosimendan.** 0.3mg/kg (adult 0.15-0.3mg/kg) in 6ml/kg 5%dex (no heparin) and give 1.5ml/kg/hr for 10min (12.5mcg/kg), then 0.24ml/kg/hr (0.2mcg/kg/min; adult 0.1-0.2mcg/kg/min) for 24hr IV. Via CVC or peripheral IV; compatible only with frusemide or GTN.
- Levothyroxine sodium.** See thyroxine.
- Lignocaine.** IV: 1% soltn 0.1ml/kg (1mg/kg) over 2min, then 0.09-0.3ml/kg/hr (15-50mcg/kg/min); or 30mg/kg in 50ml 5%dex-hep at 50ml/hr for 2min, then 1.5-15ml/hr (15-50mcg/kg/min). Nerve block: without adrenaline max 4mg/kg (0.4ml/kg of 1%), with adrenaline 7mg/kg (0.7ml/kg of 1%). Topical spray: max 3-4mg/kg (Xylocaine 10% spray pack: about 10mg/puff). Topical 2% gel, 2.5% compound mouth paint/gel (SM-33), 2% and 4% soltn, 5% ointment, 10% dental ointment: apply 3H prn.
- Lignocaine 2.5% + prilocaine 2.5%.** Cream (EMLA): 1.5g/10cm<sup>2</sup> under occlusive dressing for 1-3hr
- Lincomycin.** 10mg/kg (adult 600mg) 8H oral, IM or IV over 1hr. Severe infn: 15-20mg/kg (adult 1.2g) IV over 2hr 6H.
- Lindane.** 1% cream, lotion. Scabies: apply neck down, wash off after 8-12hr. Lice: rub into hair for 4min, then wash off; rpt after 24hr (max x2/wk).
- Linezolid.** 10mg/kg 8-12H (child) or 400-600mg 12H (adult), IV over 1-2hr or oral.
- Linoleic acid.** See fatty acids.
- Liothyronine sodium (T3).** Oral: 0.2mcg/kg (adult 10mcg) 8H, may incr to 0.4mcg/kg (adult 20mcg) 8H. IV: 0.1-0.4mcg/kg (adult 5-20mcg) 8-12H. Septic shock: 0.1-0.2mcg/kg/hr (adult 100-200mcg/day) IV infnsn.
- Liotrix.** Liothyronine (T3) + thyroxine (T4) mixture.
- Lipase, lipolytic enzymes.** See pancreatic enzymes.
- Lipid.** 20%: 1-3g/kg/day IV (ml/hr = g/kg/day x Wt x 0.21).
- Lisdexamphetamine dimesylate.** NOT/kg. 6-12yr: 30mg daily oral, incr over 2-3wk to max 70mg daily.
- Lisinopril.** 0.1mg/kg (adult 5mg) daily oral, may incr over 4-6wk to 0.2-1mg/kg (adult 10-20mg) daily.
- Lithium (salts).** 5-20mg/kg 8-24H oral. Slow rel tab 450mg (adult, NOT/kg): 1-2 tab 12H. Maintain trough 0.8-1.6mmol/L (>2mmol/L toxic).
- Lodoxamide.** 0.1% soltn: 1 drop/eye 6H.
- Lofeparamide.** Adult: 70mg morning 70-140mg nocte oral.
- Lofexidine.** 2-8mcg/kg (max 100-400mcg) 6-12H oral
- Lomefloxacin.** 8mg/kg (adult 400mg) daily oral.
- Lomustine (CCNU).** 100-130mg/m<sup>2</sup> oral every 6 wk
- Loperamide.** 0.05-0.1mg/kg (adult 2-4mg) 8-12H oral, incr if reqd to max 0.4mg/kg (max 4mg) 8H
- Lopinavir + ritonavir.** >2yr: 230/57.5 mg/m<sup>2</sup> (max 400/100mg) 12H oral; with nevirapine or efavirenz 300/75mg/m<sup>2</sup> (max 533/133mg) 12H
- Loprazolam.** (NOT/kg): 1mg (max 2mg) nocte oral
- Loracarbef.** 4-8mg/kg (max 200-400mg) 12H oral
- Loratadine.** 5mg (2-5yr), 10mg (>5yr) dly oral
- Lorazepam.** 0.02-0.06mg/kg (adult 1-3mg) 8-24H oral. IV: 0.05-0.2mg/kg IV over 2min, then 0.01-0.1mg/kg/hr.
- Lormetazepam.** Adult (NOT/kg): 0.5mg (max 1.5mg) nocte oral.
- Losartan.** 0.5-2mg/kg (adult 25-100mg) dly oral.
- Lovastatin.** 0.4-0.8mg/kg (adult 20-40mg) 12-24H oral. Slow rel (adult, NOT/kg): 10-60mg nocte
- Lovastatin + slow-release niacin (20/500mg, 20/750mg, 20/1000mg).** 20mg/500mg at bed time oral, incr if reqd every 4wk by 500mg niacin to max 40mg/2000mg.
- Loxapine.** 0.2-1mg/kg (max 10-60mg) 6-12H oral, IM
- Lubiprostone.** Adult (NOT/kg): 24mcg 12-24H oral with food.
- Lumefantrine (benflumetol).** See artemether.
- Lumiracoxib.** Adult, NOT/kg: 100mg daily oral.
- Lutropin alfa (luteinising hormone).** Adult (NOT/kg): 75iu daily SC, with 75-150iu FSH
- Lymecycline.** 408mg = 300mg tetracycline base. Adult (NOT/kg): 408mg 12H oral.
- Lymphocyte immune globulin.** See immunoglobulin, lymphocyte immune.
- Lypressin (lysine-8-vasopressin).** 1 spray (2.5iu) into 1 nostril 4-8H, may incr to 1 spray both nostrils 4-8H.
- Lysuride.** Migraine: 0.5mcg/kg (adult 25mcg) 8H oral. Parkinson's, adults (NOT/kg): 0.2mg dly, incr by 0.2mg daily each wk to max 1.6mg 8H oral.
- Macrogol 3350,** 105g/L. 2-11yr 6.563g in 60ml water, >11yr 13.125g in 125ml water: 1 sachet dly oral, incr to 2-3/day if reqd. Faecal impactn >2yr: one 13.125g sachet in 125ml water per 5kg body wt (adult 8 sachet) consumed in <6hr (max 3 days therapy). See also colonic lavage.

**Macrogol 400 (polyethylene glycol) 1% + tetrahydrozoline 0.05%.** 1 drop/eye 8-12H.

**Mafenide acetate.** 8.5% cream: apply 2mm layer 12-24H. 5% soltn: apply 4-8H to keep dressings wet.

**Maggots of *Lucilia sericata*, sterile.** Packs: standard (for std wound), boot (toe, amputated stump), boot (foot), sleeve (limb wound). Change maggots after 3 days; sooner if reqd. See [www.ZooBiotic.co.uk/products-LarvE.htm](http://www.ZooBiotic.co.uk/products-LarvE.htm)

**Magnesium chloride 10%.** 0.48g/5ml = Mg 1mmol/ml. 0.4ml/kg 12H slow IV. Myocardial infarct (NOT/kg): 5ml/hr IV for 6hr, then 1ml/hr for 24-48hr. VF: 0.1-0.2ml/kg IV.

**Magnesium hydroxide.** Antacid: 10-40mg/kg (max 2g) 6H oral. Laxative: 50-100mg/kg (max 5g) oral. See also aluminium hydroxide + magnesium hydroxide + simethicone.

**Magnesium sulphate 50% (2mmol/ml).**

Deficiency: 0.2ml/kg (max 10ml) 12H IM, slow IV. Asthma, digoxin tachycardia, eclampsia, prem labour, pul ht: 0.1ml/kg (50mg/kg) IV over 20min, then 0.06 ml/kg/hr (30 mg/kg/hr); keep serum Mg 1.5-2.5mmol/l (pul ht 3-4mmol/l). Myocardial infarct (NOT/kg): 2.5 ml/hr (5mmol/hr) IV for 6hr, then 0.5ml/hr (1mmol/hr) for 24-48hr. VF: 0.05-0.1ml/kg (0.1-0.2mmol/kg) IV. Incompatible with aminophylline, ketamine, salbutamol. Laxative: 1ml/kg = 0.5g/kg (max 15g) as 10% soltn 8H for 2 days oral.

**Malathion.** See maldison.

**Maldison.** 0.5% liq: 20ml to hair, wash off aftr 12hr.

**Mannitol.** 0.25-0.5g/kg IV (2-4ml/kg of 12.5%, 1.25-2.5ml/kg of 20%, 1-2ml/kg of 25%) 2H prn, if serum osmolality <320-330mmol/L.

**Maroprostine.** 0.15-1mg/kg (max 10-50mg) 8-24H oral.

**Maraviroc.** Adult (NOT/kg): 150mg (with strong CYP3A inhibitors, incl protease inhibitors), 300mg (with tipranavir or ritonavir), 600mg (with CYP3A inducers, incl efavirenz) 12H oral.

**Marimastat.** (NOT/kg): 5-25mg (usu. 10mg) 12H oral

**Mazindol.** (NOT/kg): 0.5mg dly oral, up to 3mg dly

**Measles vaccine (Attenuvax).** Live. >12mo: 0.5ml SC x1

**Measles + mumps vaccine (Rimparix).** Live. >12mo: 0.5ml SC once.

**Measles + mumps + rubella vaccine (MMR1, Priorix).** Live. >12mo: 0.5ml SC.

**Mebendazole.** NOT/kg: 100mg 12H x3 days.

Enterobiasis: 100mg once, may rpt aftr 2-4wks.

**Mebexverine.** 135mg tab: (NOT/kg) 1-3 tab dly oral

**Mebhydrolin.** 1-2mg/kg (max 50-100mg) 8-12H oral

**Mecamylamine.** 0.05mg/kg (adult 2.5mg) 12H oral; may incr to max 0.5mg/kg (25mg) 6H oral.

**Mecasermin.** 40-80mcg/kg (max 120mcg/kg) 12H SC.

**Mechlorethamine.** See mustine HCl.

**Medizine.** See meclozine.

**Meclofenamate.** 1-2mg/kg (adult 50-100mg) 6-8H oral.

**Medozine.** 0.5-1mg/kg (adult 25-50mg) 12-24H oral.

**Mecysteine.** Adult (NOT/kg): 200mg 8-12H oral.

**Medroxyprogesterone.** Adult (NOT/kg): 5mg dly for 5-10 days per mth oral; precoc. puberty 5-10mg dly; to achieve amenorrhoea 10-20mg dly; uterine hge 60mg dly reducing over 10 d to 10mg; malignancy 0.5g dly IM or oral for 4wk, then 1g wkly. Depot contraceptive: 150 mg deep IM during 1st 5 days of cycle, then repeat every 12wk. See also conjugated oestrogens.

**Medroxyprogesterone + oestradiol (2.5mg/1mg, 5/0.625, 5/1, 5/2) tabs.** 1 tab daily oral.

**Medroxyprogesterone 10mg tab + oestradiol 4mg patch.** NOT/kg: 10mg tab daily oral for first 10-14 days of each 28 day cycle, and 4mg patch x2/wk continuously.

**Medrysone.** 1% soltn: 1 drop/eye 6-12H.

**Mefenamic acid.** 10mg/kg (adult 500mg) 8H oral.

**Mefloquine.** 15mg/kg (adult 750mg) stat, then 10mg/kg (adult 500mg) after 6-8hr. Prophylaxis: 5mg/kg (adult 250mg) wkly.

**Mefruside.** 0.5-1mg/kg (up to 2mg/kg for 3 d) dly 10-14 d, then 0.5-1mg/kg (25-50mg) every 2-3 d.

**Megestrol acetate.** NOT/kg: 80mg/dose 12H oral.

**Meglumine antimonate.** Soltn 85mg/ml of pentavalent antimony. Same dose as sodium stibogluconate, deep IM.

**Melatonin.** Usu. 0.1mg/kg (adult 6mg) nocte oral.

**Meloxicam.** 0.15-0.3mg/kg (max 7.5-15mg) dly oral, PR

**Melphalan.** Usu. 6mg/m<sup>2</sup> dly x5, rpt every 6wk.

**Mementine.** Adult (NOT/kg): 5mg daily oral, incr by 5mg wkly to max 10mg 12H.

**Menaphthone sodium bisulphite (vitamin K3).**

**(Menadione, menadiol).** NOT/kg: 5-10mg x1-2/wk (infant) 10mg daily (child) 10mg 8H (adult) oral. Mitochondrial dis (all ages, not/kg): 10mg 6H oral.

**Meningococcus gp A, C, W135, Y vaccine**

**(Mence-vax ACWY, Menomune).** Inactive. >2yr: ½ml SC. Boost 1-3yrlly.

**Meningococcus gp A, C, W135 and Y conjugated vaccine (Menactra).** Inactivated. >10yr: 0.5ml IM.

**Meningococcus gp C, conjugate vaccine (Meningitec, Menjugate, NeisVac-C).** Inactivated. 0.5ml IM: 3 doses 1-2mo apart (6wk-6mo), 2 doses (6-12mo), 1 dose (>12mo).

**Mepivacaine.** Max dose 5-7mg/kg.

**Meprobamate.** 5-10mg/kg (max 800mg) 8-12H oral.

**Meptazinol.** 4mg/kg (adult 200mg) 3-6H oral.

**Mepyramine.** 2-4mg/kg (adult 100-200mg) 8H oral.

**Mequitazine.** 0.1mg/kg (adult 5mg) 12H oral.

**Mercaptamine.** See cysteamine.





**Mercaptopurine (6MP).** 75-100mg/m<sup>2</sup> daily oral.

**Meropenem.** 10-20mg/kg (adult 0.5-1g) 8H IV over 5-30min. Severe infxn: 20-40mg/kg (adult 1-2g) 12H (1st wk life) 8H (>1wk) or constant infsn.

**Mesalazine (Mesalamine).** Usual high initial dose, lower maintenance. Mesasal, Salofalk: 15-20mg/kg (adult 500mg) 8H, decr to 10mg/kg (adult 250mg) 8H oral, NOT/kg: 0.4-1.6g 8H (Asacol, Coltec); 0.5-1g 6H (Pentasa, ethyl-cellulose coat) 6H oral; 2-4 tab daily (Lialda, delayed-release 1.2g tab) oral. or 6mo. Suppos: 0.5-1g 8H. Enema: 1-4g nocte.

**Mesna.** IV over 30min: 20% of cyclophosphamide or ifosfamide dose at 0, 4 and 6 hr. Oral: 40% of dose of cytotoxic at -2, 2 and 6hr. Nebuliser: 0.6-1.2g (NOT/kg) 4-6H.

**Mesoridazine.** Oral: 0.25-3mg/kg (adult 25-150mg) 8H. IM: 0.5mg/kg (adult 25mg, max 200mg/day).

**Mesterolone.** 0.5mg/kg (adult 25mg) 6-12H oral.

**Mestranol 50mcg + norethisterone 1mg.**

Contraception: 1 tab daily from 5th to 25th day of menstrual cycle.

**Metaproterenol.** See orciprenaline.

**Metaraminol.** IV: 0.01mg/kg stat (repeat prn), then 0.15 mg/kg in 50ml 5% dextrose (no heparin) at 1-10ml/hr (0.05-0.5 mcg/kg/min) and titrate dose against BP. SC: 0.1mg/kg.

**Metaxalone.** 15mg/kg (max 800mg) 6-8H oral.

**Metformin.** Adult (NOT/kg): initially 500mg 8-24H oral, max 1g per dose 8H. See also glibenclamide.

**Methacycline.** NOT/kg: 150mg (>8y) 300mg (>12y) 12H oral.

**Methadone.** 0.1-0.2mg/kg (adult 5-10mg) 6-12H oral, SC, IM.

**Methamphetamine.** See methylamphetamine.

**Methazolamide.** 1-2mg/kg (adult 50-100mg) 8-12H oral

**Methdilazine.** 0.1-0.3mg/kg (adult 4-16mg) 12-24H oral

**Methenamine hippurate / mandelate.** See hexamine.

**Methenolone.** (NOT/kg). Oral: 5-10mg 12H IM: 100mg every 1-2wk or 200mg every 2-3wk (carcinoma); 50-100mg every 2wk, then every 3-4wk (osteopor).

**Methimazole.** 0.3-1mg/kg (adult 20-60mg) dly oral, reducing to 0.1-0.5mg/kg (adult 5-30mg) dly.

**Methionine.** 50mg/kg (max 2.5g) oral 4H for 4 doses. Prophylaxis: 1mg to paracetamol 5mg.

**Methocarbamol.** Oral: 30mg/kg (adult 1.5g) 6H for 3 d, then 15-20mg/kg (adult 0.75-1g) 6-8H. IV over 5-10 min or IM: 15mg/kg (adult 750mg) 6H.

**Methohexital.** See methohexitone.

**Methohexitone.** 1-2mg/kg (adult 50-120mg) slow IV

**Methoin.** 1mg/kg (adult 50mg) dly oral, may incr by 1mg/kg each wk to max 10mg/kg (adult 600mg) dly

**Methotrexate.** Leukaemia: typically 3.3mg/m<sup>2</sup> IV dly for 4-6wk; then 2.5mg/kg IV every 2wk, or 30mg/m<sup>2</sup> oral or IM x2/wk; higher doses with folinic acid rescue. Intrathecal: 12mg/m<sup>2</sup> wkly oral, IV, IM or SC. Adult psoriasis: 0.2-0.5mg/kg wkly oral, IV or IM until response, then reduce.

**Methotrimeprazine.** 0.25-1mg/kg (adult 12.5-50 mg) 6-8H oral, IM, IV. Up to 1g/d severe psychosis

**Methoxamine.** 0.1-0.4mg/kg (adult 5-20mg) IM, or 0.1-0.2 mg/kg (adult 5-10mg) IV over 5-10min (at least 15min between doses).

Nose drop 0.25%: 1-3drop/nostril 6-12H.

**Methoxsalen.** Adult (NOT/kg): 20mg 2hr bef UV exposure. 1% lotion: wkly bef 1min of UV light.

**Methscopolamine.** See hyoscine methobromide.

**Methsuximide.** 5mg/kg (adult 300mg) dly, may incr to max 10mg/kg (adult 400mg) 8-12H oral.

**Methyl aminolevulinate.** See Aminolevulinic acid.

**Methylclothiazide.** 0.05-0.2mg/kg (adult 2.5-10mg) daily oral.

**Methylcellulose.** Constipation: 30-60mg/kg (adult 1.5-3g) with at least 10ml/kg (adult 300ml) fluid 12H oral. Obesity: 30mg/kg (adult 1.5g) with 5ml/kg water ½hr before a meal.

**Methylcysteine.** 4mg/kg (adult 200mg) 6-12H oral.

**Methyldopa.** 3mg/kg (adult 150mg) 8H oral, may incr to max 15mg/kg/dose (adult 750mg).

**Methyldopate.** 5-20mg/kg (adult 0.25-1g) 6H IV over 1hr.

**Methylene blue.** 1-2mg/kg (G6PD deficiency 0.4mg/kg) IV prn. Septic shock: 2mg/kg stat IV, then 0.25-2mg/kg/hr.

**Methylergometrine.** Adult (NOT/kg): 200mcg IM, IV over 5min, or oral; may rpt in 2hr, then 4-6H.

**Methylergonovine.** See methylergometrine.

**Methylphenidate.** 0.1mg/kg oral 8am, noon and (occasionally) 4pm; incr if reqd to max 0.5mg/kg/dose (adult 20mg). Long acting: 20-60mg (18-54mg in US) in morning. Transdermal patch: apply for up to 9hr; start with 12.5cm<sup>2</sup>, and incr to 18.75cm<sup>2</sup>, 25cm<sup>2</sup>, 37.5cm<sup>2</sup> if reqd.

**Methylprednisolone.** Asthma: 0.5-1mg/kg 6H oral, IV or IM day 1, 12H day 2, then 1mg/kg daily, reducing to minimum effective dose. Severe croup: 4mg/kg IV stat, then 1mg/kg 8H. Severe sepsis before antibiotics (or within 4hr of 1st dose): 30mg/kg IV once. Spinal cord injury (within 8hr): 30mg/kg stat, then 5mg/kg/hr 2 days. Lotion 0.25%: apply sparingly 12-24H. Methylpred 1mg = hydrocortisone 5mg in glucocorticoid activity, 0.5mg in mineralocorticoid.

**Methylprednisolone aceponate.** 0.1% cream, ointment: apply 12-24H.

**Methyltestosterone.** 2.5-12.5mg/day buccal.

- Methysergide maleate.** 0.02mg/kg (adult 1mg) 12H oral, incr to max 0.04mg/kg (adult 2mg) 8H for 3-6mo
- Metipranolol.** 0.1%, 0.3%, adult: 1 drop/eye 12H.
- Metirosine.** 5-20mg/kg (adult 0.25-1g) 6H oral.
- Metoclopramide.** 0.15-0.3mg/kg (adult 10-15mg) 6H IV, IM, oral; 0.2-0.4mg/kg (adult 10-20mg) 8H PR. Periop: 0.5 mg/kg (adult 15-20mg) IV stat, then 0.2mg/kg (adult 10mg) 4-6H if reqd. With chemotherapy: up to 1-2mg/kg 4H IV.
- Metocurine iodide.** ICU: 0.4mg/kg IV prn. Theatre: 0.1-0.4 mg/kg stat, then 0.01-0.02mg/kg/dose.
- Metolazone.** 0.1-0.2mg/kg (adult 5-10mg) dly oral. Up to 0.5mg/kg (adult 30mg) dly short term.
- Metoprolol.** IV: 0.1mg/kg (adult 5mg) over 5 min, rpt every 5 min to max 3 doses, then 1-5mcg/kg/min. Oral: 1-2mg/kg (adult 50-100mg) 6-12H.
- Metronidazole.** 15mg/kg (max 1g) stat, then 7.5mg/kg (max 1g) 12H in neonate (1st maint. dose 48hr after load if <2kg, 24hr in term baby), 8H (4+ wk) IV, PR or oral. Giardiasis: 30mg/kg (adult 2g) dly x3 oral. Amoebiasis: 15mg/kg (adult 750-800mg) 8H oral x 10 d, then diloxanide furoate 10mg/kg (adult 500mg) 8H oral x 10 d. C.difficile: 10mg/kg (adult 500mg) 8H oral. Topical gel 0.5%: apply dly. Level 60-300umol/ml (x0.17mcg/ml).
- Metyrapone.** Diagnosis: 15mg/kg (min 250mg) 4H x6 dose oral. Cushing: 1-20mg/kg (max 1g) 4H.
- Mexiletine.** IV infsn: 2-5mg/kg (max 250mg) over 15 min, then 5-20mcg/kg/min (max 250mg/hr). Oral: 8mg/kg (max 400mg) stat, then 4-8mg/kg (max 400mg) 8H starting 2hr after loading dose.
- Mezlocillin.** 50mg/kg 6-8H (1st wk life), 4-6H (2+ wk) IM or IV. Serious infsn: 60mg/kg (max 3g) 4H.
- Mianserin.** 0.2-0.5mg/kg (adult 10-40mg) 8H oral.
- Micafungin.** 3mg/kg (adult 50-150mg) dly IV over 1hr. Prophylaxis: 1mg/kg (adult 50mg) dly IV over 1hr.
- Miconazole.** 7.5-15mg/kg (adult 0.6-1.2g) 8H IV over 1hr. Topical: 2% cream, powder, lotion, tincture, gel 12-24H. Vaginal: 2% cream or 100mg ovule dly x7.
- Microlax enema.** <12mo 1.25ml, 1-2yr 2.5ml, >2yr 5ml.
- Midazolam.** Sedation: usually 0.1-0.2mg/kg (adult 5mg) IV or IM, up to 0.5mg/kg used in children; 0.2mg/kg (repeated in 10min if reqd) nasal; 0.5 mg/kg (max 20mg) oral. Infusion (ventilt): 3mg/kg in 50ml 5%dex-hep at 1-4ml/hr (1-4mcg/kg/min); fitting usually 2-4 ml/hr (range 1-24ml/hr); 1mg = 2-3mg diazepam.
- Midodrine.** 0.06mg/kg (adult 3mg) morning and 4-6pm oral, incr gradually if required to max 0.2-0.4mg/kg (adult 10-20mg) morning, noon, and late afternoon (not after 6pm).
- Mifepristone.** Termination (NOT/kg): 200-600mg oral once, then if abortion incomplete gemeprost 1mg PV or miso-prostol 400mcg oral or misoprostol 800mcg PV in 48hr.
- Miglitol.** (NOT/kg): 25mg 8-24H incr over 3-6mo to usu. maintenance dose 50mg (max 100mg) 8H oral
- Milrinone.** <30kg: 1.5mg/kg in 50ml 5%dex-hep, 2.5ml over 1hr (75mcg/kg), then 1-1.5 ml/hr (0.5-0.75mcg/kg/min). >30kg: 1.5mg/kg made up to 100ml in 5%dex-hep, 5ml over 1hr (75mcg/kg), then 2-3ml/hr (0.5-0.75mcg/kg/min).
- Mineral mixture (Aminogram).** <5.5kg: 1.5g/kg daily oral, mixed with feed. >5.5kg: 8g dly
- Mineral oil.** See paraffin liquid.
- Minocycline.** Over 8yr: 4mg/kg (max 200mg) stat, then 2mg/kg (max 100mg) 12H oral or IV over 1hr. Sustained rel tabs (NOT/kg): 45mg (45-59kg), 90mg (60-89kg), 135mg (90kg or more) dly oral.
- Minoxidil.** 0.1mg/kg (max 5mg) daily, incr to max 0.5mg/kg (max 25mg) 12-24H oral.
- Mirtazapine.** 0.3-1mg/kg (adult 15-60mg) dly oral.
- Misoprostol (PGE1 analogue).** 5mcg/kg (max 200mcg) 4-6H oral. See also mifepristone.
- Mitomycin-C.** 2mg/m<sup>2</sup> IV daily x10 days, repeat only if wbc >3000/mm<sup>3</sup> + platelets >75,000.
- Mitotane.** 10-80mg/kg (adult 0.5-4g) 6H oral.
- Mitozantrone (Mitoxantrone).** Breast cancer, lymphoma: 10-14mg/m<sup>2</sup> IV over 10min every 3wk. Leukaemia: 10-12mg/m<sup>2</sup> IV over 10min dly x 3-5 d
- Mivacurium.** 0.15mg/kg stat, then 0.1mg/kg/dose IV. Infsn: 5-15mcg/kg/min.
- Mizolastine.** (NOT/kg): slow rel tab, 10mg dly oral
- Moclobemide.** 2-3mg/kg (adult 50-150mg) 6-12H oral
- Modafinil.** 2-4mg/kg (adult 100-200mg) 12H oral. Adult (NOT/kg): 200mg morn (obs sleep apnoea), 1hr before shift (night work sleep disorder) oral.
- Moexipril.** 0.15-0.2mg/kg (adult 7.5-10mg) 8-24H oral
- Molindone.** 0.1-1.5mg/kg (adult 50-75mg) 8H oral.
- Molgramostim.** 5-10mcg/kg dly SC or IV over 6hr.
- Mometasone.** 0.1% cream or oint: apply daily. 50mcg spray: adult 2 sprays/nostril daily.
- Montelukast.** NOT/kg: 4mg (2-5yr) 5mg (6-14yr) 10mg (>14yr) daily at bedtime, oral.
- Moracizine.** 4-6mg/kg (adult 200-300mg) 8H oral.
- Moroctogog alfa.** Recombinant human factor 8; see Factor 8.
- Morphine.** ½ life 2-4 hr. IM: neonat 0.1mg/kg, child 0.1-0.2 mg/kg, adult 10-20mg; ½ this IV over 10 min. IV (ventilt): 0.1-0.2mg/kg/dose (adult 5-10mg). Infsn of 1mg/kg in 50ml 5%dex-hep: ventilated neonat 0.5-1.5 ml/hr (10-30mcg/kg/hr), child/adult 1-4ml/hr (20-80mcg/kg/hr). Patient controlled: 20mcg/kg boluses (1ml of 1mg/kg in 50ml) with 5min lockout time + (in child) 5mcg/kg/hr. Oral double IM dose; slow release: start with 0.6mg/kg 12H and incr every 48hr if reqd.
- Morrhuate sodium.** (NOT/kg): 50-250mg per injtn.







- Moxifloxacin.** 10mg/kg (adult 400mg) daily oral.  
0.5% ophthalmic: 1 drop/eye 8H for 7 days.
- Moxisylyte.** Adult (NOT/kg): 40-80mg 6H oral.
- Moxonidine.** 4mg/kg (adult 200mg) 8-24H oral.
- Mumps vaccine (Mumpsvax).** Live. >12mo: 0.5ml SC once. See also measles, mumps, rubella vacc.
- Mupirocin.** 2% ointment: apply 8-12H.
- Muromonab-CD3 (Orthoclone OKT3).** 0.1mg/kg (adult 5mg) daily for 10-14 days IV over 1min.
- Mustine HCl (nitrogen mustard).** 0.1mg/kg IV daily for 3-4 days. Hodgkins: 6mg/m<sup>2</sup> IV.
- Mycophenolate mofetil.** 600mg/m<sup>2</sup> 12H oral.
- Nabilone.** Adult: 1mg 12H, up to 2mg 8H oral.
- Nabumetone.** 10-20mg/kg (adult 0.5-1g) 12-24H oral
- Nadolol.** 1-5mg/kg (adult 40-240mg) daily oral.
- Nadroparin.** Venous thrombosis: 90anti-XaU/kg 12H SC. Prophylaxis: genrl surgery 2850anti-XaU (adult, NOT/kg) daily SC; orthopaedics 40anti-XaU/kg 24H (start 12hr pre-surgery) SC, then 55 anti-XaU/kg daily. Haemodialysis: 65anti-XaU/kg into arterial line at start 4hr session.
- Nafarelin.** Adult: 200mcg spray to 1 nostril 12H.
- Nafillin.** Oral: 15-30mg/kg 6H. Severe infn (slow IV, IM): 40mg/kg (max 2g) 12H (1st wk life), 8H (2nd wk), 6H or constant infsn (>2wk).
- Naftifine.** 1% cream, gel: apply daily.
- Naftidrofuryl.** 2-4mg/kg (adult 100-200mg) 8H (oral) or 12H (IM, or IV or IA infsn over 2hr).
- Nalbuphine.** 0.2-0.5mg/kg (adult 20-30mg) 3-6H SC, IM or IV. Anaesthesia: 0.3-1mg/kg IV over 15min, then 0.2-0.5mg/kg every 30min.
- Nalidixic acid.** 15mg/kg (adult 1g) 6H oral, reducing to 7.5mg/kg (adult 500mg) 6H after 2wk.
- Nalmefene.** Opiate intoxication: 0.007mg/kg IV, and 0.0014 mg/kg after 2-5min (15min if IM, SC) if reqd. Postop sedtn: 0.25mcg/kg every 2-5min (max 4 doses). Half life 10hr.
- Naloxone.** Postop sedatn: 0.002mg/kg/dose (0.4mg dilutd to 20ml, give 0.1ml/kg/dose) rpt every 2min x4 if reqd, then 0.3mg/kg in 30ml 5%dex-hep at 1ml/hr (0.01 mg/kg/hr) IV. Opiate overdose (including newborn): 0.01 mg/kg (max 0.4mg) (0.4mg dilutd to 10ml, give 0.25ml/kg /dose), rpt every 2min (15min if IM or SC) x4 if reqd, then 0.3mg/kg in 30ml 5%dex-hep at 1ml/hr (0.01mg/kg/hr) IV.
- Naltrexone.** 0.5mg/kg (adult 25mg) stat, then 1mg/kg (adult 50mg) daily oral. Adult (NOT/kg): 380mg every 4wk IM.
- Nandrolone decanoate.** Anaemia: 1-4mg/kg (adult 50-200mg) wkly deep IM. Osteoporosis: adult (NOT/kg) 50mg deep IM every 3wk.
- Naphazoline.** 0.012-0.1%: 1-2drop/nostril, 1 drop/eye 3-4H.
- Naproxen.** 1mg = 1.1mg naproxen sodium. >2yr: 5-10mg/kg (adult 250-500mg) 8-12H oral. Adult: 500mg 12H PR.
- Naratriptan.** 0.05mg/kg (adult 2.5mg), may rpt aftr 4hr
- Natalizumab.** Adult (NOT/kg): 300mg IV over 1hr every 4wk.
- Nateglinide.** Adult (NOT/kg): 60-120mg 8H oral.
- Nebivolol.** 0.1mg/kg (adult 5mg) daily oral, incr to max 1mg/kg (adult 40mg) daily.
- Nedocromil.** Inhaltn: 4mg (2 puffs) 6H, reducing to 12H when improved. 2% eye drops: 1 drop/eye 6-24H.
- Nefazodone.** 1mg/kg (adult 50 mg) 12H oral, incr by 1mg/kg/dose (adult 50mg) each wk to 4-6mg/kg (adult 200-300mg) 12H. Slow rel: dly dose.
- Nefopam hydrochloride.** Oral: 0.5-2mg/kg (adult 30-90mg) 8H. IM: 0.4mg/kg (adult 20mg), may rpt in 6hr.
- Neisseria meningitidis vaccine.**  
See meningococcal vaccine
- Nelarabine.** Child: 650mg/m<sup>2</sup> IV over 1hr dly x 5 d; rpt every 21 days. Adult: 1500mg/m<sup>2</sup> IV over 2hr on days 1, 3 and 5; rpt every 21 days.
- Nelfinavir.** Infant 40-75mg/kg 12H oral, child 50-60mg/kg 12H, adult 750mg 8H or 1250-1500mg 12H.
- Neomycin.** 1g/m<sup>2</sup> 4-6H oral (max 12g/day). Bladder washout: 40-2000mg/L. See also colistin; dexamethasone; gramicidin.
- Neomycin 0.5% + prednisolone sodium phosphate 0.5%.** 1 drop/eye 4-6H.
- Neostigmine.** Reverse relaxants: 0.05-0.07 mg/kg (adult 0.5-2.5mg) IV; suggested dilutn: neostigmine (2.5mg/ml) 0.5ml + atropine (0.6mg/ml) 0.5ml + saline 0.5ml, give 0.1ml/kg IV. Myasthenia gravis: 0.2-0.5mg/kg (adult 1-2.5mg) 2-4H IM, SC.
- Nesiritide.** 2mcg/kg IV, then 0.01mcg/kg/min (range 0.005-0.03mcg/kg/min).
- Netilmicin. IV or IM.** 1wk-10yr: 8mg/kg day1, then 6mg/kg dly. >10yr: 7mg/kg day 1, then 5mg/kg (max 240-360mg) dly. Neonate: 5mg/kg dose: <1200g 48H (0-7 days of life), 36H (8-30 days), 24H (>30 days); 1200-2500g 36H (0-7 days of life), 24H (>7 days); term 24H (0-7 days of life), then as for 1wk-10yr. Trough level <1.0mg/L.
- Nevirapine.** Child: 120mg/m<sup>2</sup> daily for 2wk oral, then 150-200mg/m<sup>2</sup> daily for 2wk, then 12H if no rash. Adult (NOT/kg): 200mg daily for 2wk, then 12H oral if no rash.
- Niacin + lovastatin.** See lovastatin + niacin.
- Niacin + simvastatin** (500mg/20mg, 750/20, 1000/20). Adult (NOT/kg): 500mg/20mg nocte oral, incr by 500mg every 4wk to max 2000/40mg.

- Nicardipine.** 0.4-0.8mg/kg (adult 20-40mg) 8H oral. 1-3mcg/kg/min (max 20mg/hr) IV.
- Niclosamide.** 50mg/kg (adult 2g) oral.
- Nicotinamide.** 4% gel: apply sparingly 12-24H
- Nicorandil.** 0.1-0.6mg/kg (adult 5-30mg) 12H oral.
- Nicotine inhaler.** 10mg cartridges. Adult: inhale 6-12 cartridges/day x 3mo, then reduce over 6-8wk.
- Nicotine resin chewing gum.** NOT/kg: 2-4mg chewed over 30min when inclined to smoke; usually need 16-24mg/day, max 60mg/day.
- Nicotine transdermal patches.** Usu. 21mg, 14mg, and 7mg per 24hr. Adult: if smoked >20cig/day apply strongest patch dly 3-4wk, medium patch dly 3-4wk (initial dose if smoked <=20cig/day), then weakest patch dly 3-4wk.
- Nicotinic acid.** Hypercholesterolaemia and hypertriglyceridaemia: 5mg/kg (adult 200mg) 8H, gradually incr to 20-30mg/kg (adult 1-2g) 8H oral.
- Nicotinyl alcohol tartrate.** Adult (NOT/kg): 25-50 mg 6H, slow release tab 150-300mg 12H oral.
- Nicomalone.** 0.2mg/kg (adult 10mg) day 1, 0.12mg/kg (adult 6mg) day 2, then 0.02-0.25mg/kg (adult 1-12mg) dly oral. INR 2-2.5 for prophylaxis, 2-3 for treatment.
- Nifedipine.** Caps 0.25-0.5mg/kg (adult 10-20mg) 6-8H, tabs 0.5-1mg/kg (adult 20-40mg) 12H oral or sublingual.
- Nilotinib.** Adult (NOT/kg): 400mg 12H oral.
- Nilutamide.** Adult (NOT/kg): 300mg daily oral for 4wk, then 150mg daily.
- Nimodipine.** 10-15mcg/kg/hr (adult 1mg/hr) IV for 2hr, then 10-45mcg/kg/hr (adult 2 mg/hr). Adult: 60mg 4H oral.
- Nisoldipine.** Slow rel: 0.2 mg/kg (adult 10mg) dly oral, incr to 0.4-0.8mg/kg (adult 20-40mg) dly.
- Nitazoxanide.** 100mg (12-47mo) 200mg (4-11yr) 500mg (>11yr) 12H for 3 days oral.
- Nitrazepam.** Child epilepsy: 0.125-0.5mg/kg 12H oral. Hypnotic (NOT/kg): 2.5-5mg (child) 5-10mg (adult) nocte.
- Nitric oxide.** 1-40ppm (up to 80ppm used occasionally). 0.1 L/min of 1000ppm added to 10 L/min gas gives 10ppm. [NO] = Cylinder [NO] x (1 - (Patient FIO<sub>2</sub> / Supply FIO<sub>2</sub>)). [NO] = Cylinder [NO] x NO flow / Total flow.
- Nitrofurantoin.** 1.5mg/kg (adult 50-100mg) 6H oral. Prophylaxis: 1-2mg/kg (adult 50-100mg) nocte
- Nitrofurazone.** 0.2% cream, soltn: apply every 1-3d
- Nitrogen mustard.** See mustine HCl.
- Nitroglycerine.** See glyceryl trinitrate.
- Nitroprusside.** See sodium nitroprusside.
- Nizatidine.** 3-5mg/kg (adult 150mg) 12H oral for max 8wk, then dly. H pylori (adult): 300mg 12-24H.
- Nonacog alfa (Recombinant human factor 9).** See factor 9.
- Noradrenaline.** 0.15mg/kg in 50ml 5%dex-hep at 1-10ml/hr (0.05-0.5mcg/kg/min). Flow <2ml/h may cause swings in BP.
- Norepinephrine.** See noradrenaline.
- Norethisterone (Norethindrone).** Contraceptn: 350mcg dly, start 1st day menstruatn; or 200mg oily soltn IM in 1st 5d of cycle, rpt once after 8wk. Menorrhagia: 10mg 3H until hge stops, then 5mg 6H x 1wk, then 5mg 8H x 2wk; or 5mg 8-12H on day 19-26 cycle.
- Norfloxacin.** 10mg/kg (adult 400mg) 12H oral.
- Normacol granules.** 6mo-5yr half teasp 12H, 6-10yr 1 teasp 12H, >10yr 1 teasp 8H.
- Nortriptyline.** 0.5-1.5mg/kg (adult 25-75mg) 8H oral
- Noxythiolin.** 1-2.5% soltn into body cavity 12-24H, left at least 30min. Max dly dose 200mg/kg (max 10g)
- NTBC (nitro-trifluoromethylbenzoyl cyclohexanediol).** 0.5mg/kg 12H oral.
- Nystatin.** 100,000u <12mo, 500,000u (1 tab) >12mo 6H NG or oral. Prophylaxis 50,000u <12mo, 250,000u >12mo 8H. Topical: 100,000u/g gel, cream, ointment 12H. Vaginal: 100,000u 12-24H. See also gramicidin + neomycin + nystatin + triamcinolone cream and ointment.
- Octocog alfa (Recombinant factor 8).** See Factor 8.
- Octreotide.** Diarrhoea: 1mcg/kg (adult 50mcg) 12-24H SC, may incr to 10mcg/kg (adult 250mcg) 8H. IV: 1mcg/kg stat, then 1-5mcg/kg/hr. Chyle: 5mcg/kg/hr IV. Acromegaly (NOT /kg): 0.05-0.1mg 8-12H SC incr if reqd to max 0.5mg 8H for 4wk, then slow 20mg (10-30mg) every 4wk deep IM.
- Oestradiol.** NOT/kg. Osteoporosis: every wk apply a patch releasing 12.5mcg/day. Induction puberty: 0.5mg alternate days oral, incr over 2-3yr to 2mg/day (add progestogen for 14 days/mo when dose 1.5mg/day or when bleeding occurs). Tall stature: 12mg/day oral until bone age >16yr (add progestogen for 14 days/ cycle). Gonadal failure: 2mg/day oral (add progestogen for 14 days/cycle).
- Oestriol.** Induction puberty: 0.25 mg/day incr to 2mg/day (+ progestogen 12d/cycle) oral. Epiphyseal maturatn: 10mg/d (+ progestogen 12d/cycle). Vaginal: 0.5mg dly, reducing to x2/wk.
- Oestrone.** Hypogonadism: 1.25-7.5mg dly oral.
- Oestropiate.** Adult (NOT/kg): 0.625-7.5mg dly start 1st day menstruation, for 3 of every 4wk oral
- Ofloxacin.** 5mg/kg (adult 200mg) 8-12H, or 10mg/kg (adult 400mg) 12H oral or IV over 1hr. 0.3%: 1 drop/eye hrly x 2 days (4H overnight), reducing to 3-6H.

**OKT3.** See muromonab-CD3.

**Olanzapine.** 0.1-0.2mg/kg (adult 5-10mg) daily oral; slow incr to 0.4mg/kg (adult 20mg) daily if reqd. See also fluoxetine.

**Olmesartan.** 0.4-0.8mg/kg (adult 20-40mg) daily oral. See also amlodipine + olmesartan.

**Olopatadine.** 0.1% soltn: 1 drop/eye twice a day.

**Olpadronate.** 0.5mg/kg daily oral.

**Olalazine.** NOT/kg: 250mg 12H, incr to max 500mg 6H oral. Maintenance: 500mg 12H.

**Omalizumab.** NOT/kg: 150-375mg SC every 2-4wk depending on body weight and serum IgE level.

**Omeprazole.** Usually 0.4-0.8mg/kg (adult 20-40mg) 12-24H oral. ZE synd: 1mg/kg (adult 60mg) 12-24H oral, incr up to 3mg/kg (adult 120mg) 8H if reqd. IV: 2mg/kg (adult 80mg) stat, then 1mg/kg (adult 40mg) 8-12H. H.pylori: 0.8mg/kg (adult 40mg) daily oral + metronidazole 8mg/kg (adult 400mg) 8H + amoxicillin 10mg/kg (adult 500mg) 8H for 2wk

**Ondansetron.** IV: prophylaxis 0.15mg/kg (adult 4mg); treatment 0.2mg/kg (adult 8mg) over 5 min, or 0.2-0.5mcg/kg/min. Oral: 0.1-0.2 mg/kg (usual max 8mg) 6-12H.

**Oprelvekin (IL-11).** 2mg/m<sup>2</sup> (adult 50mcg/kg) SC dly  
**Oral rehydratn soltn (ORS).** See glucose electrolyte soltn.

**Orciprenaline.** Oral: 0.25-0.5mg/kg (adult 20mg) 6H. Resp soltn (2%): 0.5ml dilt to 4ml 3-6H (mild), 1ml dilt to 4ml (moderate), undiluted continuously (severe, in ICU). Aerosol 750mcg/dose: 2 puffs 4-6H.

**Orlistat.** 1.5-3mg/kg (adult 60-120mg) with each main meal containing fat (max 3 doses/day).

**Ornipressin (POR 8).** IV: 0.1u/kg/hr (max 6u/hr) for max 4hr, then 0.03u/kg/hr (max 1.5u/hr). SC: 5u in 30ml saline, max total dose 0.1u/kg.

**Orphenadrine.** 1-2mg/kg (adult 50-100mg) 8H oral.

**Osallazine.** Adult (NOT/kg): 500mg 6H oral.

**Oseltamivir.** 2mg/kg (adult 75mg) 12H for 5 days oral. Prophylaxis: 2mg/kg (adult 75mg) daily.

**Oxacillin.** 15-30mg/kg 6H oral, IV, IM. Severe infn: 40 mg/kg (max 2g) 12H (1st wk life), 8H (2nd wk), 6H or infsn (>2wk).

**Oxaliplatin.** 85mg/m<sup>2</sup> every 2wk over 2-6hr IV before 5-FU.

**Oxandrolone.** 0.1-0.2mg/kg (adult 2.5-20mg) daily oral. Turner's synd: 0.05-0.1mg/kg daily.

**Oxaprosin.** Usually 20mg/kg (max 1200mg), range 10-26mg/kg (max 1800mg), daily oral.

**Oxazepam.** 0.2-0.5mg/kg (adult 10-30mg) 6-8H oral

**Oxcarbazepine.** 4-5mg/kg (adult 300mg) 12H oral; incr wkly by max 5mg/kg/dose (adult 300mg) to usually 15mg/kg/dose (adult 750mg), max 25mg/kg/dose (adult 1200mg).

**Oxerutin.** 10mg/kg (adult 500mg) 12H oral.

**Oxethazaine.** 10mg/5ml (with Al hydrox + Mg hydrox): adult (NOT/kg) 5-10ml 6-8H oral.

**Oxiconazole.** 1% cream, lotion: apply 12-24H.

**Oxitropium.** Inhaltn: 200mcg (NOT/kg) 8-12H.

**Oxpentifylline (Pentoxifylline).** Adult (NOT/kg): slow release tab 400mg 8-12H oral.

**Oxprenolol.** 0.5-2mg/kg (adult 30-120mg) 8-12H oral

**Oxybuprocaine.** 4mg/ml (0.4%): 1 drop/eye 8-12H. Deep anaes: 1 drop/eye every 90sec x3 doses. See also fluorescein + oxybuprocaine.

**Oxybutynin.** <5yr: 0.2mg/kg 8-12H oral. >5yr (NOT/kg): 2.5-5mg 8-12H oral. Slow rel: adult 5-30mg daily oral. Adult: apply 39cm<sup>2</sup> patch (3.9mg/day) x2/wk.

**Oxycodone.** 0.1-0.2mg/kg (adult 5-10mg) 4-6H oral, SC or IV (beware hypoventiltn); incr if reqd. IV infsn: 0.05mg/kg/hr (adult 2mg/hr) adjusted. Slow rel: 0.6-0.9mg/kg (adult 10mg) 12H oral, incr if reqd. Suppos: adult 30mg 6-8H PR.

**Oxymetazoline.** 0.25mg/ml = 0.025% (<6yr), 0.5mg/ml = 0.05% (>6yr): 2-3 drops or sprays in each nostril 8-12H.

**Oxymetholone.** 1-2mg/kg (up to 5mg/kg) dly oral

**Oxymorphone.** Usu. 0.02-0.03mg/kg (adult 1-1.5mg) 4-6H IM or SC. Slow IV: 0.01mg/kg (adult 0.5mg) 4-6H. Oral: 0.1-0.4mg/kg (adult 5-20mg) 4-6H; slow-rel adult 5mg 12H. PR: 0.1mg/kg (adult 5mg) 4-6H.

**Oxytetracycline.** >8yr (NOT/kg): 250-500mg 6H oral, or 250-500mg 6-12H slow IV.

**Oxytocin.** Labour (NOT/kg): 1-4mU/min IV, may incr to 20 mU/min max. Lactation: 1 spray (4iu) into each nostril 5min before infant feeds.

**Paclitaxel.** 175mg/m<sup>2</sup> IV every 3wk, x3-6 doses. Albumin-bound: 260mg/m<sup>2</sup> IV every 3wk.

**Palifermin.** 60mcg/kg IV daily for 3 days before chemo, and for 3 days after.

**Palivizumab.** 15mg/kg IM once a month.

**Paliperidone (3mg, 6mg, 9mg slow release).** Adult (NOT/kg): usually 6mg daily oral; may incr by 3mg every 5-7 days.

**Palonosetron.** Adult: 0.25mg IV 30min bef. chemo

**Pamidronate.** Osteoporosis, OI: 3-7mg/kg dly oral, 1mg/kg (adult 15-90mg) IV over 4hr dly x3 every 4mo, or x1 every 3-4wk. Hypercalcaemia 20-50mg/m<sup>2</sup> (depending on Ca level) IV over 4hr every 4wk.

**Pancreatic enzymes.** Cotazyme, Creon, Nutrizym, Pancrease, Pancrex, Ultrase, Viokase. NOT/kg: usu. 1-5 caps with meals. Max lipase 10,000u/kg/d.

**Pancuronium.** ICU: 0.1-0.15mg/kg IV prn.

Theatre: 0.1mg/kg IV, then 0.02mg/kg prn. Infusion: 0.25-0.75mcg/kg/min.

**Panitumumab.** 6mg/kg IV over 1-2hr every 14 days.

- Pantoprazole.** 1.0mg/kg (adult 40mg) 12-24H oral, IV. GI hge, adult: 80mg stat, then 8mg/hr. ZE: 80mg 8-12H adjusted to achieve acid <10mmol/l.
- Papaveretum (Omnopon).** 0.2mg/kg IV, 0.4mg/kg IM (t½ 2-4hr). ICU: 0.3mg/kg IV, 0.6mg/kg IM. See also hyoscine + papaveretum.
- Papaverine.** (NOT/kg): 150-300mg 12H oral, 12-40 mg x1-2/wk intracavernosal. IA lines: 0.12mg/ml.
- Para-aminobenzoic acid.** See aminobenzoate.
- Para-aminohippuric acid.** See aminohippuric acid.
- Paracetamol.** Oral or IV: 20mg/kg stat, then 15mg/kg 4H (max 4g/day); child usual daily max 90mg/kg for 48hr, then max 60mg/kg. Rectal: 40mg/kg stat, then 30mg/kg 6H (max 5g/day). Overdose: acetylcysteine.
- Paraffin.** Liquid: 1ml/kg (adult 30-45ml) dly oral. Lqd 50% + white soft 50%, ointmnt: apply 6-12H
- Paraldehyde.** IM: 0.2ml/kg (adult 10ml) stat, then 0.1 ml/kg 4-6H. IV: 0.2ml/kg (adult 10ml) over 15 min, then 0.02ml/kg/hr (max 1.5ml/hr). Rectal, NG: 0.3ml/kg (adult 10ml) dilute1:10.
- Parathyroid hormone.** Adult (NOT/kg): 100mcg daily SC. See also teriparatide.
- Parecoxib.** Adult (NOT/kg): 40mg stat IM or IV, then 20-40mg 6-12H; max 80mg/day.
- Paricalcitol.** 0.04-0.1mcg/kg x2-3/wk IV during dialysis, may incr every 2-4wk to max 0.24 mcg/kg. Or dose in mcg = [IPTH picomol/L] / 7.
- Paroxetine.** 0.4mg/kg (adult 10mg) dly oral, may incr over 4wk to 1mg/kg (adult 20-60mg) daily.
- Pegademase.** 10u/kg IM wkly, incr to 20u/kg wkly.
- Pegaptanib sodium.** Adult: 1.65mg (0.3mg of free acid form) by intravitreal inj every 6wk.
- Pegaspargase.** 82.5iu/kg (<0.6m²) or 2500iu/m² (>0.6m²) IM, or IV over 2hr, every 14 days.
- Pegfilgrastim.** >44kg: 6mg SC 24hr after chemo.
- Peginterferon alfa-2a.** Hep C (NOT/kg): 180mcg wkly SC, + ribavirin 1g (1.2g if >75kg) dly oral, x 48wk
- Peginterferon alfa-2b.** Hep C: 1.5mcg/kg wkly, + ribavirin 15mg/kg (adult 800mg) dly oral, x48wk.
- Pegvisomant.** 40mg SC stat, then 10mg dly adjustd up/down by 5mg (max 30mg/d) every 4-6wk based on serum IGF-1 concentration.
- Pemetrexed.** 500mg/m² IV over 10min every 3wk.
- Pemoline.** >6yr (NOT/kg): 20-120mg daily oral.
- Penbutolol.** 0.4-1.5mg/kg (adult 20-80mg) dly oral
- Penciclovir.** 1% cream (10mg/g): apply x6/d x 4d
- Penicillamine (d-penicillamine).** Arthritis: 1.5mg/kg (adult 125mg) 12H oral, incr over 3mo to max 3mg/kg (adult 375 mg) 6-8H. Wilson's disease, lead poisoning: 5-7.5 mg/kg (adult 250-500mg) 6H oral. Cystinuria: 7.5mg/kg (adult 250-1000 mg) 6H oral, titrated to urine cystine <100-200mg/day.
- Penicillin, benzathine.** 1mg = 1250u. Usu. 25mg/kg (max 900mg) IM once. Venereal disease: 40mg/kg (max 1.8g) IM x 1. Strep prophylaxis: 25mg/kg (max 900mg) IM 3-4wkly, or 10mg/kg IM 2wkly.
- Penicillin, benzathine + procaine.** 900mg/300mg in 2ml: 0-2yr ½ vial, ≥ 3yr 1 vial IM x 1.
- Penicillin, benzyl (penicillin G, crystalline).** 1mg = 1667u. 30mg/kg 6H. Severe infn: 50mg/kg (max 2g) IV 12H (1st wk life), 6H (2-4 wk), 4H or constnt infsn (>4 wk).
- Penicillin, procaine.** 1mg = 1000u. 25-50mg/kg (max 1.2-2.4g) 12-24H IM. Single dose: 100mg/kg (max 4.8g).
- Penicillin V.** See phenoxymethylpenicillin.
- Penicilloyl polylysine (Prepen).** 0.00006 molar. Scratch: 1 drop. Intradermal: 0.01-0.02ml
- Pentaerythritol tetranitrate.** 0.2-1mg/kg (adult 10-60mg) 6-8H oral.
- Pentagastrin.** 6mcg/kg SC, or 0.6mcg/kg/hr IV.
- Pentamidine isethionate.** 3-4mg/kg (1.7-2.3mg/kg base) IV over 2hr or IM daily for 10-14 days (1mg base = 1.5mg mesylate = 1.74mg isethionate). Neb: 600mg/6ml daily for 3wk (treatment), 300mg/3ml every 4wk (prophylaxis).
- Pentastarch.** 10% soltn: 10-40mg/kg IV.
- Pentazocine.** Oral: 0.5-2.0mg/kg (adult 25-100mg) 3-4H. SC, IM or slow IV: 0.5-1mg/kg (adult 30-60mg) 3-4H. PR: 1mg/kg (adult 50mg) 6-12H.
- Pentobarbitone.** 0.5-1mg/kg (adult 30-60mg) 6-8H oral, IM, slow IV. Hypnotic: 2-4mg/kg (adult 100-200mg).
- Pentosan.** 2mg/kg (adult 100mg) 8H oral.
- Pentostatin.** 4mg/m² IV wkly.
- Pentoxifylline.** See oxpentifylline.
- Pentoxyverine.** 0.3mg/kg (adult 15mg) 3-6H oral.
- Peppermint oil.** (NOT/kg). 0.2ml cap: 1-2 8H oral
- Pergolide.** Parkinson's: 1mcg/kg (max 50mcg) daily, incr to max 25mcg/kg (max 2mg) 8H oral. Hyperprolactinaemia: 0.5-3mcg/kg daily.
- Perhexiline.** 2mg/kg (adult 100mg) dly oral; adjust every 2-4wk to max 6-8mg/kg (adult 300-400mg) dly. Maintain plasma level 150-600mcg/l.
- Percyazine.** 0.5mg/yr of age (1-10yr) 10mg (>10yr) daily oral, incr if reqd to max 1mg/yr (1-10yr) 25mg (>10yr) 8H.
- Perindopril.** 0.05-0.15mg/kg (adult 2-8mg) daily oral.
- Permethrin.** 1% creme rinse (head lice): wash hair, apply creme for 10min, wash off; may repeat in 2wk. 5% cream (scabies): wash body, apply to whole body except face, wash off after 12-24hr.
- Perphenazine.** 0.1-0.3mg/kg (max 5-20mg) 8-12H oral

- Pertussis.** See diphtheria + tetanus + pertussis vacc.
- Pethidine.** 0.5-1mg/kg (adult 25-50mg) IV, 0.5-2mg/kg (adult 25-100mg) IM (half life 2-4hr). Infsn: 5mg/kg in 50ml at 1-4ml/hr (0.1-0.4mg/kg/hr). PCA 5mg/kg in 50ml: usu. bolus 2ml with lockout 5min, optionl backgrnd 0.5ml/hr.
- Phenacemide.** 10-20mg/kg (adult 0.5-1g) 8H oral.
- Phenazone.** See benzocaine + phenazone.
- Phenazocine.** 0.1-0.4mg/kg (adult 5-20mg) 4-6H oral or sublingual.
- Phenazopyridine.** 4mg/kg (adult 200mg) 6H oral x 2d
- Phendimetrazine.** 0.4-1.4mg/kg (adult 20-70mg) 8H oral.
- Phenelzine.** 0.3-2mg/kg (adult 15-90mg) 8H oral.
- Phenindamine.** 0.5-1mg/kg (adult 25-50mg) 8-12H oral.
- Phenindione.** 2mg/kg (adult 100mg) 12H day 1, 1mg/kg (adult 50mg) 12H day 2, then 0.25-1mg/kg (adult 12.5-50mg) 12H oral. INR for prophylaxis 2-2.5, treatment 2-3.
- Pheniramine.** 0.5-1mg/kg (adult 25-50mg) 6-8H oral. Slow release tab 75mg at night.
- Phenobarbitone.** Loading dose in emergency: 20-30mg/kg IM or IV over 30min stat. Ventilated: repeat doses of 10-15mg/kg up to 100mg/kg per day (beware hypotension). Usual maintenance: 5mg/kg (adult 300mg) daily IV, IM or oral. Infant colic: 1mg/kg 4-8H oral. Level 80-120 umol/L (x0.23=mcg/ml).
- Phenolphthalein.** 0.5-5mg/kg (adult 30-270mg) nocte oral. See also agar + paraffin + phenolphthalein.
- Phenoperidine.** 0.03-0.05mg/kg (adult 1mg) every 40-60min. Ventilated: 0.1-0.15mg/kg (adult 2-5mg) every 40-60min.
- Phenothrin.** Apply; shampoo after 30min (0.5% mousse) 2hr (0.2% lotion), 12hr (0.5% emulsion); comb hair when wet.
- Phenoxybenzamine.** 0.2-0.5mg/kg (adult 10-40mg) 8-12H oral. Cardiac surgery: 1mg/kg IV over 1-4hr stat, then 0.5 mg/kg 8-12H IV over 1hr or oral.
- Phenoxymethylpenicillin (penicillin V).** 7.5-15mg/kg (adult 250-500mg) 6H oral. Prophylaxis: 12.5mg/kg (adult 250mg) 12H.
- Phentermine.** Adult (NOT/kg): 30-40mg daily oral, reducing to 15-40mg daily.
- Phentermine resin.** (NOT/kg): 15-30mg dly oral.
- Phentolamine.** 15mg/kg in 50ml 5% dex-hep at 1-10ml/hr (5-50mcg/kg/min) IV. May accumulate (t ½ 19min, longer if renal impairment).
- Phenylbutazone.** Initially 2mg/kg (adult 100mg) 4H, reducing to 1-2mg/kg (adult 50-100mg) 6-8H oral.
- Phenyltoloxamine.** 1mg/kg (adult 50mg) 8H oral.
- Phenylephrine.** IV: 2-10mcg/kg stat (adult 500mcg), then 1-5mcg/kg/min. SC or IM: 0.1-0.2mg/kg (max 10mg). Oral: 0.2mg/kg (max 10mg) 6-8H. 0.15%, 10% eye drops: 1 drop/eye 6-8H. 0.25%, 0.5% nose drops: 1-3 drops/sprays per nostril 6-8H.
- Phenylephrine 0.12% + prednisolone acetate 1%.** 1 drop per eye 6-12H.
- Phenytoin.** Loading dose in emergency: 15-20mg/kg (max 1.5g) IV over 1 hr. Initial maintenance, oral or IV: 2mg/kg 12H (prem); 3mg/kg 12H (1st wk life), 8H (2wk-4yr), 12H (5-12yr); 2mg/kg (usual max 100mg) 8H >12 yr. Level 40-80 umol/L (x0.25 = mcg/ml).
- Pholcodine.** 0.1-0.2mg/kg (adult 5-15mg) 6-12H oral
- Phosphate, potassium (1mmol/ml).** 0.1-1.5mmol/kg/day (max 70mmol/day) IV infsn.
- Phosphate, sodium.** Laxative, diluted, NOT/kg: 250mg (2-4yr) 250-500mg (>4yr) 6H oral.
- Phosphate, sodium (Fleet enema).** Na 1.61m Eq/L + PO<sub>4</sub> 4.15 mEq/L + K<sup>+</sup> 1.38m Eq/L: 33ml (2-5yr), 66ml (5-11yr), 133ml (adult) rectal.
- Phosphatidylcholine.** 60mg/kg (max 3g) dly oral
- Phosphocysteamine.** 10mg/kg 6H oral, incr by 2.5mg/kg/dose every 2wk to 10-20mg/kg 6H so leukocyte half-cysteine <2nmol / mg protein 6hr after dose.
- Physostigmine.** 0.02mg/kg (max 1mg) IV every 5 min until response (max 0.1mg/kg), then 0.5-2.0mcg/kg/min.
- Phytomenadione (vitamin K1).** Deficiency with hge: FFP 10ml/kg, then 0.3mg/kg (max 10mg), IM or IV over 1hr. Prophylaxis in neonates (NOT/kg): 1mg (0.1ml) IM at birth. Warfarin reversal: 0.1mg/kg (max 5mg) SC or oral (repeat if reqd); if severe hge 0.3mg/kg (max 10mg) with FFP 10ml/kg. Mitochondrial disease (NOT/kg): 10mg 6H oral.
- Picibanil (OK-432).** 1 Klinische Einheit = 0.1mg. 1 mg into tumour 1-2wk preop, then 0.5mg/2wk ID for 1yr postop.
- Pilocarpine.** 0.1mg/kg (adult 5mg) 4-8H oral. 0.5%, 1%, 2%, 3%, 4% eye drops: 1 drop/eye 6-12H.
- Pimecrolimus.** 1% cream: apply 12H.
- Pimozide.** 0.04mg/kg (adult 20mg) daily oral, incr if reqd to max 0.4mg/kg (adult 20mg) dly.
- Pindolol.** 0.3mg/kg (adult 15mg) 8-24H oral.
- Pine tar.** Gel, solution: 5ml to baby bath, 15-30ml to adult bath; soak for 10min.
- Pioglitazone.** Adult (NOT/kg): 15-45mg dly oral.
- Pipecuronium.** 20-85mcg/kg IV stat, then 5-25mcg/kg prn.
- Piperacillin.** 50mg/kg (adult 2-3g) 6-8H IV. Severe inftn: 75mg/kg (adult 4g) 8H (1st wk life) 6H (2-4 wk) 4-6H (>4wk) or constant infsn.

- Piperacillin 1g + tazobactam 125mg.** As for piperacillin.
- Piperazine.** 75mg/kg (max 4g) oral daily for 2 days (ascaris), 7 days (pinworm).
- Piperazine oestrone sulphate.** Induction puberty (NOT/kg): 0.156mg daily, incr over 2-3yr to 1.25mg (add progestogen for 12 days per cycle).
- Piperonyl butoxide bioallethrin.** Apply enough to wet scalp or body, leave 30min, wash off.
- Pipotiazine.** Oily injtn: initially 0.5mg/kg (adult 25mg), then gradual incr to 1-4mg/kg (adult 50-200mg) every 4wk IM.
- Piracetam.** 15mg/kg (max 800mg) 8H oral, IM or IV
- Pirbuterol.** Oral: 0.2-0.3mg/kg (adult 10-15mg) 6-8H. In-haltn (NOT/kg): 0.2-0.4mg 4-6H.
- Piroxicam.** 0.2-0.4mg/kg (adult 10-20mg) dly oral. Gel 5mg/g: apply 1g (3cm) 6-8H for up to 2wk.
- Pivampicillin.** 15mg/kg (adult 500mg) 8-12H oral.
- Pivampicillin 1.25mg + pivmecillinam 1mg.** 10mg /kg/dose (adult 250mg) of pivampicillin 12H oral.
- Pivmecillinam.** 5-10mg/kg (adult 200-400mg) 6-8H oral.
- Pizotifen.** NOT/kg: 0.5mg daily oral, incr if reqd to max 0.5mg morning and 1mg at night.
- Plicamycin.** Testicular tumours: 25-30mcg/kg dly for 8-10 days IV over 6hr, rpt mthly if resp. Hypercalcaemia: 25mcg/kg daily for 3-4 days, then x1-3/wk.
- Pneumococcal vaccine, polysaccharide (Pneumovax 23).** Inactivated. >2yr: 0.5ml SC or IM once. Boost every 5yr.
- Pneumococcal vaccine, CRM conjugate (Prevenar).** Inactivated. 0.5ml IM. <6mo: 2mo, 3mo, 4mo, 12-15mo (4 doses). 6-11mo: 6mo, 7mo, 12-15mo (3 doses). 12-23mo: 2 doses 2mo apart. >23mo: 1 dose.
- Podophyllotoxin.** 0.5% paint: apply 12H for 3 days, then none for 4 days; 4wk course.
- Podophyllum.** 15%-25% soltn, oint: apply to wart x2/day.
- Poliomyelitis vaccine, oral (Sabin).** Live. 2 drops oral at 2mo, 4mo and 6mo (3 doses). Boost at 5yr, and if going to epidemic area.
- Poliomyelitis vaccine, SC (IPOL).** Inactivated. 0.5ml SC stat, 8wk later, and 8wk later (3 doses). Boost 12mo later, and at school entry.
- Poloxamer (Poloxalkol).** 10% soltn: <6mo 10drops, 6-18mo 15drops, 18mo-3yr 25drops 8H oral.
- Polyethylene glycol.** See colonic lavage, macrogol.
- Polymyxin B.** See bacitracin; dexamethasone.
- Polynoxylin.** 10% gel: apply 12H.
- Polygeline.** 10-20ml/kg (may rpt). Half life 2hr.
- Polystyrene sulphonate.** See sodium polystyrene sulphonate
- Polythiazide.** 0.02-0.1mg/kg (adult 1-4mg) dly oral.
- Polyvinyl alcohol.** 1.4%, 3% soltn: 1 drop/eye pm.
- POR 8.** See ornipressin.
- Porfimer.** 2mg/kg IV, then 630nm laser light after 40-50hr and 96-120hr; max 3 courses at least 30 days apart.
- Posaconazole.** Invasive infn: 4mg/kg (adult 200mg) 6H oral. Oral candida: 4mg/kg (adult 200mg) stat, then 2mg/kg (adult 100mg) daily. Prophylaxis: 4mg/kg (adult 200mg) daily.
- Potassium.** Deficiency: usually 0.3mmol/kg/hr (max 0.4 mmol/kg/hr) for 4-6 hr IV, then 4 mmol/kg/day. Max oral dose 1 mmol/kg (<5yr), 0.5 mmol/kg (>5yr). Maintenance 2-4 mmol/kg/day. If peripheral IV, max 0.05 mmol/ml. 1g KCl = 13.3mmol K, 7.5% KCl = 1 mmol/ml.
- Potassium citrate.** See citric acid + potassium citrate.
- Potassium guaiacolsulfonate.** 1-3mg/kg (adult 50-160 mg) 4-6H oral.
- Pralidoxime.** 50mg/kg (adult 2g) over 30min, then 20 mg/kg/hr (adult 1g/hr) for 48hr, then 20mg/kg (adult 1g) 4H.
- Pramipexole.** Adult (NOT/kg): 0.125mg 8H incr by 0.125-0.25mg every 5-7 days to 0.5-1.5mg 8H oral. Restless legs: 0.125mg (max 0.5mg) 2-3 hours before bed.
- Pramlintide.** Reduce insulin dose by 50% initially. (NOT/kg) Type 1 diabetes: 15mcg SC before meals (x4/day), incr if tolerated to 30-60mcg/dose. Type 2: 60mcg SC before meals (x4/day), incr if toleratd to 90-120mcg/dose.
- Pramocaine.** See hydrocortisone + pramocaine cream.
- Pramoxine.** 1% cream, lotion: apply 6-8H.
- Pravastatin.** Adult (NOT/kg): 20-80mg nocte oral
- Praziquantel.** 20mg/kg oral once (tapeworm), 4H x3 doses (schistosomiasis), 8H x6 doses (other flukes), 8H 14 days (cysticercosis).
- Prazosin.** 5mcg/kg (max 0.25mg) test dose, then 0.025-0.1 mg/kg (adult 1-5mg) 6-12H oral.
- Prednisolone.** Oral.  
Alopecia, autoimmune liver, epilepsy, SLE, ulcerative col: 2mg/kg dly, gradually reducing.  
Asthma: 0.5-1mg/kg 6H for 24hr, 12H x2, then 1mg/kg daily.  
Croup: 1mg/kg stat and in 12hr; severe 4 mg/kg stat, then 1mg/kg 8H.  
ITP: 4mg/kg daily.  
Nephrotic syndr: 60mg/m<sup>2</sup> (max 80mg) daily, reducing over several months.  
Physiological: 4-5mg/m<sup>2</sup> daily.  
Eye 0.5%: initially 1drop/eye 2H, then 6-12H.  
1 mg = hydrocortisone 4mg in glucocorticoid activity, 0.8mg in mineralocorticoid.



- Prednisolone sodium phosphate.** 0.5%: ear 2-3 drops/ear, eye 1 drop/eye 2-6H.
- Pregabalin.** Adult (NOT/kg): 50mg 8H oral, incr gradually if reqd to max 200mg 8H.
- Prilocaine.** Max dose 6mg/kg (0.6ml/kg of 1%). With adrenaline max dose 9mg/kg (0.9ml/kg of 1%).
- Primaquine.** Usually 0.3mg/kg (adult 15mg) daily for 14-21 days oral. Gameteocyte: 0.7mg/kg (adult 45mg) once.
- Primidone.** Initially 2.5mg/kg (adult 125mg) nocte, may incr to max 15mg/kg (adult 750mg) 12H oral. Trough level (phenobarbitone) 60-120umol/L.
- Probenicid.** 25mg/kg (adult 1g) stat, then 10mg/kg (adult 500mg) 6H oral.
- Probutol.** 10mg/kg (adult 500mg) 12H oral.
- Procainamide.** IV: 0.4mg/kg/min (adult 20mg/min) for max 25min, then 20-80mcg/kg/min (max 2g/day). Oral: 5-8mg/kg 4H. Level 3-10mcg/ml.
- Procaine.** Max dose 20mg/kg (1ml/kg of 2%).
- Procarbazine.** 1mg/kg (adult 50mg) daily oral, incr over 4-6 days to 4-6mg/kg (adult 200-300mg) daily until remission, then 1-2mg/kg (adult 50-100mg) daily. Suspend if wbc <3000/mm<sup>3</sup> or platelets <80,000/mm<sup>3</sup>.
- Prochlorperazine.** 1mg base = approx 1.5mg edisylate, maleate or mesylate. Only use if >10kg. Oral (salt): 0.2mg/kg (adult 5-10mg) 6-8H, may incr slowly to max 0.6mg/kg (max 35mg) 6H in psychosis. IM, slow IV (salt): 0.2mg/kg (adult 12.5mg) 8-12H. Buccal (salt): 0.05-0.1mg/kg (max 6mg) 12-24H. PR (base): 0.2mg/kg (adult 25mg) 8-12H.
- Procydiline.** 0.05-0.2mg/kg (adult 2.5-10mg) 6-8H oral.
- Progesterone.** Adult (NOT/kg). Premenst syndr: 200-400mg PV or PR 12-24H (last half of cycle). Dysfunctional uterine hge: 5-10mg/day IM for 5-10 days before menses. Prevent abortion: 25-100mg IM every 2-4 days.
- Proguanil.** 3.5mg/kg (adult 200mg) daily oral after food. See also atovaquone + proguanil.
- Promazine.** Oral: 2-4mg/kg (adult 100-200mg) 6H. IM 0.7mg/kg (max 50mg) 6-8H.
- Promethazine.** Antihistamine, antiemetic: 0.2-0.5mg/kg (adult 10-25mg) 6-8H IV, IM or oral. Sedative, hypnotic: 0.5-1.5mg/kg (adult 25-100mg).
- Proxymetacaine.** 0.5%: 1 drop/eye before procedure
- Propacetamol.** IV preparation: 1g = 0.5g paracetamol.
- Propafenone.** Oral: 70mg/m<sup>2</sup> (adult 150mg) 8H, incr if reqd to max 165mg/m<sup>2</sup> (adult 300mg) 8H. IV: 2mg/kg over 2hr, then 4mcg/kg/min incr if reqd to max 8mcg/kg/min.
- Propamidine.** 0.1%: 1 drop/eye 6H for up to 2d
- Propantheline.** 0.3-0.6mg/kg (adult 15-30mg) 6H oral
- Propiverine.** 0.3mg/kg (adult 15mg) 6-12H oral.
- Propofol.** Sedation in ICU: 1-3mg/kg/hr (max 4mg/kg/hr) IV, for no longer than 48 hr. Short-term anaesthesia: child 2.5-3.5mg/kg stat, then 7.5-15mg/kg/hr IV; adult 1-2.5mg/kg stat, then 3-12 mg/kg/hr IV.
- Propoxyphene.** See dextropropoxyphene.
- Propranolol.** 0.2-0.5mg/kg (adult 10-25mg) 6-12H oral, slow incr to max 1.5mg/kg (max 80mg) 6-12H if required.
- Propylthiouracil.** 50mg/m<sup>2</sup> 8H oral, reduce with response.
- Proscillaridin.** 10-15mcg/kg (adult 500-750mcg) 8-12H oral.
- Prostacyclin.** See epoprostenol.
- Prostaglandin.** See alprostadil (PGE1), carboprost (15-Me-PGF2-alpha), dinoprost (PGF2-alpha), dinoprostone (PGE2), epoprostenol (PGI2), prostacyclin, gemeprost (PGE1 analogue), and misoprostol (PGE1 analogue).
- Protamine.** IV 1mg/100u heparin (0.5mg/100u if >1hr since heparin dose) slow IV stat; subsequent doses of protamine 1mg/kg (max 50mg). 1mg per 25ml pump blood. Heparin 1mg=100u (half life 1-2hr).
- Protein C, activated.** See drotrecogin alfa.
- Prothionamide.** TB: 15-20mg/kg (adult 0.75-1g) at night oral. Leprosy: 5-8mg/kg (adult 250-375mg) daily.
- Prothrombinex.** See coagulation factor, human.
- Protirelin.** NOT/kg: 200mcg IV stat.
- Protriptyline.** 0.1-0.4mg/kg (adult 5-20mg) 6-8H oral.
- Proxymetacaine.** 0.5% soltn: 1 drop/eye stat, then 1 drop every 10min for 5-7 doses.
- Pseudoephedrine.** 1mg/kg (adult 60mg) 6-8H oral. Slow rel: adult (NOT/kg) 120mg 12H.
- Pseudoephedrine 60mg + triprolidine 2.5mg (Actifed).** 10ml elixir=1tab. NOT/kg: 2.5ml (<2yr), 2.5-5ml (2-5yr), 0.5tab (6-12yr), 1tab (>12yr) 6-8H oral
- Psyllium.** Usu. 0.1-0.2g/kg (adult 5-10g) 8-24H oral.
- Pumactant (ALEC).** Prem babies (NOT/kg): disconnect ETT, rapidly inject 100mg in 1ml saline via catheter at lower end ETT, flush with 2ml air; repeat after 1hr and 24hr. Prophylaxis if intubated: 100mg into pharynx.
- Pyrantel.** Threadworm: 10mg/kg (adult 750mg) once oral, may repeat 2wkly x3 doses. Roundworm, hookworm: 20mg/kg (adult 1g) once, may repeat in 7 days. Necator: 20mg/kg (adult 1g) daily x2-3 doses.
- Pyrazinamide.** 20-35mg/kg (max 1.5g) daily oral, or 75 mg/kg (max 3g) x2/wk.
- Pyrethrins + piperonyl butoxide.** Lice: apply enough shampoo to wet hair, wash off in 15min; repeat in 10 days.

- Pyridostigmine.** Myasthenia gravis: 1mg/kg (adult 60mg) 4-6H oral, incr to max 2-3mg/kg (adult 120-180mg) 4-6H if reqd. 180mg slow rel tab (Timespan), adult (NOT/kg): 1-3 tab 12-24H oral. 1mg IV, IM or SC = 30mg oral.
- Pyridoxine.** With isoniazid or penicillamine (NOT/kg): 5-10mg daily IV or oral. Seizures: 10-15mg/kg daily IV or oral. Sideroblastic anaemia: 2-8mg/kg (max 400mg) dly IV or oral.
- Pyrilamine.** See mepyramine.
- Pyrimethamine.** Adult (NOT/kg): 25mg tab wkly oral
- Pyrimethamine 25mg + sulphadoxine 500mg (Fansidar).** <4yr ½ tab once, 4-8yr 1 tab, 9-14yr 2 tab, >14yr 3 tab. Prophylaxis: <4yr ¼ tab wkly, 4-8yr ½ tab, 9-14yr ¾ tab, >14yr 1 tab. See also dapsone + pyrimethamine.
- Quazepam.** 0.15-0.6mg/kg (adult 15-30mg) nocte oral
- Quetiapine.** Adult (NOT/kg) 12H oral/dose: 25mg day 1, 50mg day 2, 100mg day 3, 150mg day 4, then 150-250mg (range 75-400mg) 12H.
- Quinagolide.** 0.5mcg/kg (adult 25mcg) nocte, incr to 1.5-3 mcg/kg (adult 75-150mcg) nocte oral.
- Quinalbarbitone.** Sedativ 5mg/kg. Premed 10mg/kg
- Quinapril.** 0.2-0.8mg/kg (adult 10-40mg) daily oral. See also hydrochlorothiazide.
- Quinidine, base.** 10mg/kg stat, then 5mg/kg (max 333mg) 4-6H oral. IV: 6.3mg/kg (10mg/kg of gluconate) over 2hr, then 0.0125mg/kg/min. IM: 15mg/kg stat, then 7.5mg/kg (max 400mg) 8H. NOTE: 1mg base = 1.2mg sulphate = 1.3mg bisulphate = 1.6mg gluconate.
- Quinine, base.** Oral: 8.3mg/kg (max 500mg) 8H for 7-10 days. Parenteral: 16.7mg/kg (20mg/kg of dihydrochloride) IV over 4hr or IM, then 8.3mg/kg 8H IV over 2hr or IM for 2-3 days, then 8.3mg/kg 8H oral for 5 days. NOTE: 1mg base = 1.7mg bisulphate = 1.2mg dihydrochloride = 1.2mg ethyl carbonate = 1.3mg hydrobromide = 1.2mg hydrochloride = 1.2mg sulphate.
- Quinupristin.** See dalofpristin + quinupristin.
- Rabeprazole.** (NOT/kg): 20mg dly oral 4-8wk (DU), 6-12wk (GU), 4wk then 10-20mg dly (reflux). ZE: 60mg daily, incr if reqd to 12H. H.pylori: 20mg + clarithromycin 500mg + amoxicillin 1g all 12H for 7 days.
- Rabies vaccine, inactivated (Rabipur).** 1ml IM stat, 7 days later, and 28 days later (3 doses). Boost every 2yr. Postexposure: immune, 1ml IM day 0 and day 3; non-immune, give 1ml IM on days 0,3,7,14,30 and 90, with immunoglobulin.
- Raloxifene.** 1mg/kg (adult 60mg) daily oral.
- Raltegravir.** Adult (NOT/kg): 400mg 12H oral.
- Raltitrexed.** Initially 3mg/m<sup>2</sup> IV over 15min every 3wk
- Ramipril.** 0.05mg/kg (adult 2.5mg) oral dly, may incr over 4-6wk to 0.1-0.2mg/kg (adult 5-10mg) dly
- Ranitidine.** IV: 1mg/kg (adult 50mg) slowly 6-8H, or 2mcg/kg/min. Oral: 2-4mg/kg (adult 150mg) 8-12H, or 300mg (adult) at night.
- Ranitidine bismuth citrate.** 8mg/kg (adult 400mg) 12H oral; to eradicate H.pylori, add antibiotics.
- Rapacuronium.** Initially 2mg/kg (child), 1.5mg/kg (adult), 2.5mg/kg Caesar; maint. 33-50% initial.
- Ramelteon.** 8mg oral at bedtime.
- Ranibizumab.** 0.5mg by intravitreal injection every month.
- Ranolazine.** Adult (NOT/kg): 0.5-1g 12H oral.
- Rasagiline.** Adult (NOT/kg): 0.5-1mg daily oral.
- Rasburicase.** 0.15-0.2mg/kg IV daily for 5-7 days.
- Razoxane.** 2mg/kg (max 125mg) 8-24H oral; or 7.5-15mg/kg (max 750mg) dly for 2-3 d every 1-4wk. Kaposi sarc, leukaemia: max 0.33g/m<sup>2</sup> 8H oral.
- Reboxetine.** Adult (NOT/kg): 2-4mg 12H oral, incr gradually if reqd to max 10mg 12H.
- Recombinant antihæmophilic factor.** See Factor 8
- Remifentanyl.** 0.05-0.2mcg/kg/min. Ventilated: usually 0.5-1 mcg/kg/min; occasionally up to 8 mcg/kg/min if reqd.
- Repaglinide.** Adult (NOT/kg) before main meals, oral: initially 0.5mg, incr every 1-2wk to 4mg (max 16mg/day).
- Reproterol.** Aerosol 0.5mg/puff: 1-2 puffs 3-8H.
- Reserpine.** 0.005-0.01mg/kg (adult 0.25-0.5mg) 12-24H oral.
- Residonrate.** Adult (NOT/kg): 5mg daily oral; slow release 35mg once a week.
- Resonium.** See sodium polystyrene sulphonate.
- Retapamulin.** 1% ointment: apply 12H for 5 d.
- Reteplase.** Adult (NOT/kg) for myocard infarct: give heparin 5000u IV + aspirin 250-350mg oral; then reteplase 10u IV over 2min + 2nd dose 30min later; then heparin 1000u/hr for 24-72hr and aspirin 75-150mg/d till discharge.
- Retinol A.** See vitamin A.
- Reviparin.** Child >2mo: 100u/kg 12H SC. Adult: 1432u 2hr before surgery, then dly SC
- Ribavirin.** Inhalator (Viratek nebulizer): 20mg/ml at 25ml/hr (190mcg/l of gas) for 12-18hr/day for 3-7 days. Oral: 5-15mg/kg 8-12H. Hepatitis C: see interferon alfa-2b.
- Riboflavin.** NOT/kg: 5-10mg daily oral. Organic acidosis (NOT/kg): 50-200mg dly oral, IM or IV.
- Rifabutin.** Pulmonary TB: 3-5 mg/kg (adult 150-300mg) dly oral. Resistant pulm TB: 5-7.5mg/kg (adult 300-450mg) daily. Mycobact avium complex: 7.5-12mg/kg (adult 450-600mg) dly; prophylaxis 5mg/kg (adult 300mg) daily.



- Rifampicin.** 10-15mg/kg (max 600mg) daily oral fasting, or IV over 3hr (monitor AST). Prophylaxis: N.meningitidis 10 mg/kg daily (neonate), 10 mg/kg (max 600mg) 12H for 2d; H.influenzae 10mg/kg dly (neonate), 20mg/kg (max 600mg) daily for 4 days.
- Rifapentine.** Usually 10-15 mg/kg (adult 600mg) x2/wk for 2mo, then wkly for 4 months.
- Rifaximin.** Adult (NOT/kg): 200mg 8H for 3 days.
- Riluzole.** 1mg/kg (adult 50mg) 12H oral.
- Rimantadine.** 2.5mg/kg (adult 100mg) 12H oral.
- Rimexolone.** 1%. 1drop/eye 6H. Uveitis: 1drop 1H in daytime for 1wk, 2H for 1wk, 6H for 1wk, daily 1wk.
- Rimonabant.** Adult: 20mg oral before breakfast
- Risedronate.** Osteoporosis: 0.1mg/kg (adult 5mg) daily oral; slow release 35mg (adult) wkly. Paget's: 0.5mg/kg (adult 30mg) dly oral.
- Risperidone.** 0.02mg/kg (adult 1mg) 12H, incr if reqd to 0.15mg/kg (adult 2-4mg, max 8mg) 12H oral.
- Ritonavir.** 250mg/m<sup>2</sup> (adult 300mg) 12H, incr over 5 days if toleratd to 400mg/m<sup>2</sup> (infant 450mg/m<sup>2</sup>, adult 600mg) 12H oral.
- Rituximab.** Leukaemia: 260-370mg/m<sup>2</sup> by IV infsn wkly x4. Rheumatoid arthritis (adult, NOT/kg): 1g IV twice, 2wk apart.
- Rivastigmine.** Adult (NOT/kg): initially 1.5mg 12H, incr every 2wk to max 6mg 12H oral. Patch: apply 4.6mg (5cm<sup>2</sup>) daily for 4wk, then 9.5mg (10cm<sup>2</sup>) daily.
- Rizatriptan.** Adult (NOT/kg): 10mg oral, may rpt x1 in 2hr.
- Rocuronium.** 0.6-1.2mg/kg IV stat, then 0.1-0.2mg/kg boluses or 5-15mcg/kg/min.
- Ropinirole.** Adult (NOT/kg): 0.25mg dly x2d, 0.5mg x5 d, then 1mg dly; incr wkly to max 4mg dly oral. Restless legs: 0.25mg (max 4mg) 2hr nocte
- Ropivacaine.** 4-5mg/kg (adult max 200-250mg). Intrathecal: 1mg/kg (0.1ml/kg of 1%). Postop infsn 0.2-0.4mg/kg/hr (0.1-0.2ml/kg/hr of 0.2%).
- Rosiglitazone.** Adult (NOT/kg): 4mg daily oral, incr after 6-8 wk to 4mg 12H if reqd.
- Rosuvastatin.** 10mg daily oral, incr if reqd to 20mg then 40mg at 4wk intervals.
- Rotavirus vaccine, human (Rotarix).** Live, monovalent. 1ml oral at 6-14wk, and at least 4wk later at 14-24wk (2 doses).
- Rotavirus vaccine, human-bovine (RotaTeq).** Live, penta-valent. 2ml oral at age 2mo, 4mo, 6mo (3 doses).
- Rotigotine.** Adult, NOT/kg: 2mg patch dly for 1wk, then 4mg daily; incr if reqd to 6mg daily.
- Roxithromycin.** 2.5-4mg/kg (adult 150mg) 12H oral
- Rubella vaccine (Ervevax, Meruvax II).** Live. >12mo: 0.5ml SC once.
- Salbutamol.** 0.1-0.15mg/kg (adult 2-4mg) 6H oral. Inhaltn: mild resp soltn (5mg/ml, 0.5%) 0.5ml diluted to 4ml, or nebulae 2.5mg/2.5ml 3-6H; moderate 0.5% soltn 1ml diluted to 4ml, or nebulae 5mg/2.5ml 1-2H; severe (in ICU) 0.5% soltn undiluted continuous. Aerosol 100mcg/puff: 1-2 puff 4-6H. Rotahaler: 200-400mcg 6-8H. IM or SC: 10-20 mcg/kg (adult 500mcg) 3-6H. IV in child: amp 1mg/ml at 0.3-0.6ml/kg/hr (5-10mcg/kg/min) for 1hr, then 0.06-0.12ml/kg/hr (1-2mcg/kg/min). IV infusion incompatible with aminophylline, ketamine and magnesium.
- Salcatonin.** Hypercalcaemia: 5u/kg 12-24H IM, SC or IV over 6-12hr. Paget's: adult 50-100u dly. Cancer bone pain: 4u/kg (adult 200u) up to x4/d
- Salicylic acid.** Cradle cap: 6% soltn (Egocappol) 12H 3-5 days. Plantar warts: 15% soltn x1-2/day, 40% medicated disc 24-48H. See also benzoic acid + salicylic acid.
- Salicylsalicylic acid.** See salsalate.
- Salmeterol.** Aerosol, diskhaler (NOT/kg): 50-100mcg 12H. See also fluticasone + salmeterol.
- Salmonella typhi vaccine.** See typhoid vaccine.
- Salsalate.** 10-20mg/kg (adult 0.5-1g) 6H oral.
- Saquinavir.** Soft gel caps preferred. Child: 50mg/kg 8H oral; 33mg/kg 8H with nelfinavir. Adult (NOT/kg): 1200mg 8H, or 1600mg 12H oral.
- Saracenia purpurea (Sarapin).** Adult (NOT/kg): 2-10ml nerve block, 5-10ml local infiltration.
- Sargramostim (GM-CSF, Leucomax).** 3-5mcg/kg dly SC, or IV over 6hr. Keep wbc 5,000-10,000/mm<sup>3</sup>.
- Scopolamine.** See hyoscine hydrobromide.
- Secbutobarbitone.** 0.3-0.6mg/kg (adult 15-30mg) 6-8H, or 1-4mg/kg (adult 50-200mg) nocte oral.
- Secretin.** 1cu = 4chr units. 1-2cu/kg slow IV.
- Selegiline.** Adult (NOT/kg): 10mg daily, oral. Transdermal patch: 6mg daily; incr to max 9-12mg daily if reqd.
- Selenium sulphide.** 2.5% shampoo x2/wk for 2wk.
- Senna, Sennoside.** Tab 7.5mg, granules 15mg/5ml. Daily (NOT/kg): 6mo-2yr 7.5mg, 3-10yr 7.5-15mg, >10yr 1-30mg.
- Sermorelin (GHRH).** 1mcg/kg fasting in morning IV.
- Sertaconazole.** 2% cream: apply 12H for 4wk.
- Sertindole.** Adult 4mg dly, incr to 12-24mg dly oral
- Sertraline.** 0.5mg/kg (adult 25mg) dly oral, may incr to 1-2mg/kg (adult 50-100mg) dly; may give 3-4mg/kg (adult 150-200mg) dly for up to 8wk.
- Sevelamer.** 20-40mg/kg (adult 800-1600mg) 8H oral, titrated to serum phosphorus.

**Sibutramine.** Adult (NOT/kg): usually 10mg (range 5-15mg) daily oral.

**Sildenafil.** Pulm hypertension: 0.3mg/kg 3-6H incr until effective or systemic hypotension occurs (usual max 2-3 mg/kg/dose); adult (NOT/kg) usually 20mg 8H oral. 1hr before stopping NO: 0.4mg/kg oral once.

**Silver nitrate, stick.** Apply dly to affected area only.

**Silver sulfadiazine 1% + chlorhexidine 0.2%.**  
Cream: apply in 3-5mm layer.

**Simethicone.** See aluminium hydroxide compound

**Simvastatin.** Adult (NOT/kg): 10mg daily oral, incr if reqd every 4wk to max 80mg daily.

**Sinecatechins.** 15% ointmnt: apply 8H for up to 16wk

**Sirolimus.** 3mg/m<sup>2</sup> (adult 6mg) stat, then 1mg/m<sup>2</sup> (adult 2mg) daily oral.

**Sitagliptin.** 2mg/kg (adult 100mg) daily oral.

**Sitaxentan.** 2mg/kg (adult 100mg) daily oral.

**Sodium.** Deficit (ml saline) =  
$$\frac{Wt(kg) \times 4 \times (140 - [Na])}{100} \text{ / \% saline.}$$
  
To incr serum Na by 0.5 mmol/L/hr (max safe rate), infsn rate (ml/hr) =  $2 \times Wt(kg) \text{ / } (\% \text{ saline infused})$ ; hrs of infsn =  $2 \times (140 - \text{serum Na})$ .  
4ml/kg of X% saline raises serum Na by Xmmol/L. Need 2-6 mmol/kg/day. NaCl MW = 58.45, 1g NaCl = 17.1mmol Na, NaCl 20% = 3.4mmol/ml.

**Sodium aurothiomalate.** 0.25mg/kg wkly IM, incr to 1 mg/kg (max 50mg) wkly for 10wk, then every 2-6wk.

**Sodium benzoate.** Neonate: 250mg/kg over 2hr stat, then 10-20mg/kg/hr IV.

**Sodium bicarbonate.** See bicarbonate.

**Sodium calcium edetate (EDTA).** 25-40mg/kg 12H IM, IV over 1hr for 5 d; rpt aft 3 d if reqd. With dimercaprol: 12.5mg/kg 4H for 3-7 days.

**Sodium cellulose phosphate (Calciisorb).**  
Adult: 5g (NOT/kg) 8H oral.

**Sodium citrate.** Constipatn (adult, NOT/kg) usu. 450mg in 5ml as enema, often with sodium lauryl sulphoacetate, glycerol, sorbitol or sorbic acid.

**Sodium citrotertrate.** 40-80mg/kg (adult 2-4g) in 50ml water 8-12H oral.

**Sodium cromoglycate.** Inhalation (Intal): 1 cap (20mg) 6-8H, 2ml soltn (20mg) 6-8H, aerosol 1-10mg 6-8H. Eye drops 2%: 1 drop/eye 4-6H. Oral: 5-10mg/kg (max 200mg) 6H oral. Nasal 2% or 4%: 1 dose to each nostril 3-12H.

**Sodium ferric gluconate.** Fe 12.5mg/ml. 0.05ml/kg (adult 2ml) test dose IV over 1hr, then 0.25ml/kg (adult 10ml) IV over 1hr with each dialysis (usually for 8 doses).

**Sodium fluoride.** NOT/kg: <2yr 0.55mg oral dly, 2-4yr 1.1 mg, >4yr 2.2mg. Osteoporosis, Paget's, (NOT/kg): 20-40mg 8-12H.

**Sodium fusidate.** Tablets: 10-15mg/kg (adult 250-500mg) 8H oral. IV over 2-8hr: 10mg/kg (adult 500mg) 8H; severe infn 15mg/kg (adult 750mg). Peak level 30-200umol/L ( $\times 0.52 = \text{mcg/ml}$ ). For suspension, see fusidic acid.

**Sodium hyaluronate.** Adult (NOT/kg). Cystitis 800mcg/ml: 50ml into bladder wkly x4, then 4wkly. Ophthalmic: 10-15 mg/ml (1-1.5%) 0.2-0.6ml into anterior chamber; 0.18% drops 1/eye as reqd. Osteoarthritis 10-15mg/ml: 2-2.5ml intra-articular wkly x3-5.

**Sodium nitrite.** 3%: 0.2ml/kg (max 10ml) IV over 5 min

**Sodium nitropruside.** <30kg: 3mg/kg in 50ml 5%dex-hep at 0.5-4ml/hr (0.5-4mcg/kg/min) IV. >30kg: 3mg/kg made to 100ml in 5%dex-hep at 1-8ml/hr (0.5-4mcg/kg/min). If used >24hr, max rate 4mcg/kg/min. Max total 70mg/kg with normal renal function (or sodium thiocyanate <1725 umol/L,  $\times 0.058 = \text{mg/L}$ ). Protect from light.

**Sodium oxybate.** Narcolepsy (NOT/kg): 2.25g nocte, rpt 2-4hr later; incr if reqd by 0.75g every 2wk to max 4.5g + 4.5g (9g per night).

**Sodium phenylbutyrate.** 10-13g/m<sup>2</sup>/day divided into equal amounts with each feed/meal, oral.

**Sodium phosphate.** See phosphate, sodium.

**Sodium picosulphate.** 2.5mg (1-4yr), 2.5-5mg (4-10yr), 5-10mg (>10yr) at night oral.

**Sodium polystyrene sulphonate (Resonium).** 0.3-1 g/kg (adult 15-30g) 6H NG (give lactulose) or PR.

**Sodium stibogluconate.** Soltn 100mg/ml of pentavalent antimony. 20mg/kg (max 850mg) dly IV over 5-10min for 20 d (visceral) or at least 4wk (mucocutaneous); 10-15mg/kg 12H if toxicity or poor response. Early cutaneous: infiltrate lesions with 1-3ml, rpt x1-2 if reqd aft 1-2 d. Severe cutaneous: 20mg/kg dly IV over 5-10min until 3 d after cure (usually), for 4wk (L.braziliensis), or 3mo aft cure (Lamazonensis)

**Sodium tetradecyl sulphate.** NOT/kg: 0.25-1ml per vein as 1% (max 10 small veins) or 3% (max 4 large veins).

**Sodium thiosulphate.** 1ml/kg (adult 50ml) 25% soltn IV over 10min.

**Sodium valproate.** 5mg/kg (adult 200mg) 8-12H oral, incr if reqd to max 20mg/kg (adult 1g) 8-12H. Level 2hr after dose 300-700umol/l ( $\times 0.14 = \text{mg/l}$ ).

**Solifenacin.** Adult (NOT/kg): 5-10mg daily oral.

**Somatostatin.** See octreotide.

**Somatrem.** 4u/m<sup>2</sup> 3 days a wk IM.

**Somatropin.** 1mg = 3iu. Usually 2-3iu/m<sup>2</sup> on 5-7 days a wk SC, or 4-6iu/m<sup>2</sup> on 3 days a wk IM.

**Sorafenib.** Adult (NOT/kg): 400mg 12H (or 24-48H) oral.

**Sorbitol 70%.** 0.2-0.5ml/kg (adult 20-30ml) 8-24H oral.

With activated charcoal: 1g/kg (1.4ml/kg) NG, x1-2

**Sorbolene cream; pure, with 10% glycerin, or with 5% or 10% olive oil or peanut oil.**

Skin moisturiser: apply prn.

**Sotalol.** IV: 0.5-2mg/kg (adult 25-120mg) over 10 min 6H. Oral: 1-4mg/kg (adult 50-160mg) 8-12H.

**Sparfloxacin.** 10mg/kg (adult 400mg) stat, then 5mg/kg (adult 200mg) daily oral.

**Spectinomycin.** 40-80mg/kg (adult 2-4g) IM once.

**Spironolactone.** Oral (NOT/kg): 0-10kg 6.25mg 12H, 11-20kg 12.5mg 12H, 21-40kg 25mg 12H, over 40kg 25mg 8H. Female hirsutism 50mg 8H. IV: see potassium canrenoate.

**Stanolone.** 2.5% gel. Male: apply 5-10g dly to large area of skin and allow 5 min to dry. Female (lichen sclerosis): apply 2.5g to vulva on alternate days.

**Stanozolol.** 0.05-0.2mg/kg oral (adult 2.5-10mg) daily at first, then every 2-3 days.

**Stavudine (d4T).** 1 mg/kg (<30kg), 30mg (30-60 kg), 40mg (>60kg) 12H oral. Slow rel (adult, NOT/kg): 75mg (<60kg), 100mg (>60kg) dly oral

**Sterculia.** NOT/kg: 3.5-7g 12-24H oral.

**Stibogluconate.** See sodium stibogluconate.

**Streptokinase (SK).** Short term (myocard infarct): 30,000u/kg (max 1,500,000u) IV over 60min, rpt if occlusion recurs <5 days.

Long term (DVT, pulm emb, arterial thrombosis): 2,000 u/kg (max 100,000u) IV over 10min, then 1000u/kg/hr (max 100,000u/hr); stop heparin and aspirin, if PTT <x2 normal at 4hr give extra 10,000u/kg (max 500,000u) IV over 30min, stop SK if PTT >x5 normal then give 1000u/kg/hr. Local infns: 50 u/kg/hr (continue heparin 10-15u/kg/hr). Blocked IV cannula: 5000u/kg in 2ml in cannula for 2hr then remove, may rpt x2.

**Streptomycin.** 20-30mg/kg (max 1g) IM daily.

**Streptozocin.** 1-1.5g/m<sup>2</sup> wkly IV.

**Strontium ranelate.** Adult, NOT/kg: 2g dly nocte

**Succimer.** 350mg/m<sup>2</sup> 8H for 5d, then 12H x14d oral

**Succinyl choline.** See suxamethonium.

**Sucralfate.** 1g tab (NOT/kg): 0-2yr quarter tab 6H, 3-12 yr half tab 6H, >12yr 1 tab 6H oral.

**Sucrose.** Analgesia in infants: 0.17g/kg (0.5ml/kg of 33% soltn) 2min before procedure.

**Sufentanil.** 2-50mcg/kg slow IV; then infuse so that total dose is 1mcg/kg/hr of expected surgical time

**Sulbactam.** See ampicillin + sulbactam.

**Sulconazole.** 1% cream: apply 12H for 3wk after clinical cure.

**Sulfadiazine.** 50mg/kg (max 2g) 6H slow IV.

**Sulfadoxine.** See pyrimethamine + sulphadoxine.

**Sulfametopyrazine.** 40mg/kg (adult 2g) wkly oral.

**Sulfisoxazole.** See sulphafurazole.

**Sulindac.** 4mg/kg (adult 200mg) 12H oral.

**Sulphacetamide.** 100mg/ml 1 drop/eye 2-3H during the day.

**Sulphadoxine.** See pyrimethamine + sulphadoxine.

**Sulphafurazole.** 75mg/kg (adult 4g) stat, then 35mg/kg (adult 1.5g) 4-6H oral.

**Sulphamethizole.** 10mg/kg (adult 0.5-1g) 6H oral.

**Sulphamethoxazole + trimethoprim.**

See cotrimoxazole.

**Sulphasalazine.** Active colitis: 20mg/kg 6-12H (max 4g/day) oral; remission 7.5mg/kg (max 0.5g) 6-8H, suppos (NOT/kg) adult 0.5-1g 12H. Arthritis: 5mg/kg 12H, incr if reqd to 10mg/kg 8-12H (max 2g/day).

**Sulphinpyrazone.** 2-3mg/kg (max 200mg) 6-12H oral

**Sulpiride.** 4mg/kg (adult 200mg) 12H, slow incr if reqd to 4-24mg/kg (adult 0.2-1.2g) 12H oral.

**Sulthiame.** 1mg/kg (adult 50mg) 8-12H oral, may incr to 5mg/kg (adult 200mg) 8H.

**Sumatriptan.** Oral: 1-2mg/kg (adult 50-100mg) stat, may rpt twice. SC: 0.12mg/kg (max 6mg) stat, may rpt once after 1hr. Nasal: 10-20mg, may rpt x1 after 2hr.

**Sunitinib.** Adult (NOT/kg): 50mg (37.5-87.5mg) daily oral for 4wk, then 2wk off.

**Surfactant.** See beractant (Survanta), calfactant (Infasurf), colfosceril palmitate (Exosurf), pumactant (ALEC).

**Suxamethonium.** IV: neonate 3mg/kg, child 2mg/kg, adult 1mg/kg. IM: double IV dose.

**Tacrine.** Adult (NOT/kg): 10mg 6H oral for 6wk, may incr by 10mg every 6wk to max 40mg 6H.

**Tacrolimus.** IV infusion: 2mg/m<sup>2</sup>/day. Oral: 3mg/m<sup>2</sup> 12H. Trough level: whole blood 10-15ng/ml

**Tacrolimus ointment.** 2-16yr: apply 0.03% sparingly 12H for max 3wk, then daily. >16yr: apply 0.1% sparingly 12H for max 3wk, then 0.03% 12H.

**Tamoxifen.** Adult (NOT/kg): 20mg daily, incr to 40mg daily if no response after 1mo.

**Tamsulosin.** Adult 400mcg daily aftr breakfast oral.

**Tazarotene.** 0.05%, 0.1% gel, cream: apply thin layer to affected area daily (or on alternate days) in the evening.

**Tazobactam.** See piperacillin + tazobactam.

**Tegafur 100mg + uracil 224mg.** 100mg/m<sup>2</sup> tegafur + 224 mg/m<sup>2</sup> uracil (with 30mg calcium folinate) 8H oral for 28d, 7d off, then rpt cycle.

**Tegaserod.** Adult (NOT/kg): 6mg 12H for 4-12wk oral

**Teicoplanin.** 250mg/m<sup>2</sup> IV over 30min stat, then 125mg/m<sup>2</sup> IV, IM dly. Severe infn: 250mg/m<sup>2</sup> 12H x3 doses, then 250mg/m<sup>2</sup> IV or IM daily.

**Telbivudine.** Adult (NOT/kg): 600mg daily oral.

**Telithromycin.** Adult (NOT/kg): 800mg oral daily.

- Telmisartan.** 1mg/kg (adult 40mg) daily, incr if reqd to 2 mg/kg (adult 80mg) daily oral.
- Temazepam.** 0.3mg/kg (adult 20-40mg) oral.
- Temocillin.** 25-50mg/kg (adult 1-2g) 12H IV, IM.
- Temporfin.** 150mcg/kg IV over 10min; 96hr later give 652 nm laser for about 200 sec to give 20J/cm<sup>2</sup>; repeat once after 4wk if reqd.
- Temozolomide.** 200mg/m<sup>2</sup> dly oral for 5d per 28d cycle (150mg/m<sup>2</sup> for 1st cycle if previous chemo).
- Temsirolimus.** (Adult, NOT/kg): 25mg IV over 1hr wky
- Tenecteplase.** 1mg = 200u. Myocardial infarct (adult): 100u/kg (max 10,000u) IV over 10sec once; also give aspirin 150-325mg/day, and heparin to maintain APTT 50-75sec.
- Tenoposide.** 100-150mg/m<sup>2</sup> IV over 1hr wky.
- Tenofovir disoproxil fumarate.** 300mg of tenofovir DF = 245mg tenofovir D. Adult (NOT/kg): 300mg daily oral.
- Tenoxicam.** 0.2-0.4mg/kg (adult 10-20mg) dly oral
- Terazosin.** 0.02mg/kg test, then 0.04-0.4mg/kg (adult 2-20 mg) daily oral.
- Terbinafine.** 62.5mg (<20kg), 125mg (20-40kg), 250mg (adult) daily oral. 1% cream, gel: apply 12-24H to dry skin.
- Terbutaline.** Oral: 0.05-0.1mg/kg (adult 2.5-5mg) 6H. SC: 5-10mcg/kg (adult 0.25-0.5mg). IV: child 3-6mcg/kg/min for 1hr, then 0.4-1mcg/kg/min; adult 0.25mg stat over 10min, then 1-10mcg/kg/hr. Inhaltn: mild resp soltn (1%, 10mg/ml) 0.25ml dilutd to 4ml 3-6H; moderate 0.5ml of 1% dilutd to 4ml, or respule 5mg/2ml 1-2H; severe (in ICU) undiluted continuous. Aerosol 250mcg/puff: 1-2 puffs 4-6H.
- Terfenadine.** 30mg (6-12yr), 60mg (adult) 12H oral.
- Teriparatide.** Adult (NOT/kg): 20mcg SC daily.
- Terlipressin.** 0.04mg/kg (adult 2mg) IV, then 0.02-0.04mg/kg (adult 1-2mg) 4-6H for max 72hr. Slow onset, long action: continuous infsn may cause necrosis.
- Testolactone.** 5-10mg/kg (max 250mg) 6H oral.
- Testosterone.** Esters (NOT/kg): 100-500mg IM every 2-4wk. Implant: 8mg/kg (to nearest 100mg) every 16-24wk. Undecanoate (NOT/kg): 40mg dly oral, incr to 80-120mg dly. 1% gel: 5g tube (50mg testosterone) to skin dly. 30mg buccal tab: applied just above incisor 12H. Testosterone level: <16yr 5-10nmol/L, >16yr 10-30nmol/L.
- Tetanus toxoid (Tet-Tox).** 0.5ml IM stat, 6wk later, and 6mo later. Boost every 10yr, or if contaminated wound.
- Tetrabenazine.** 0.5-2mg/kg (adult 25-100mg) 12H oral
- Tetracaine.** See amethocaine.
- Tetracosactrin zinc injection (Synacthen Depot).** 600 mcg/m<sup>2</sup> (max 1mg) IM every 1-7 days.
- Tetracycline.** >8yr (NOT/kg): 250-500mg 6H oral. Acne (NOT/kg): 500mg 12H, reducing to 250mg 12H. Eye: apply 2-8H.
- Tetrahydrobiopterin.** Defective synthesis: 20mg/kg daily oral. Defective regeneration: 5mg/kg 6H oral. Loading test: 20mg/kg oral, 2mg/kg IV.
- Tetrahydrozoline.** 0.05%: 1 drop/eye 8-12H. See also macrogol + tetrahydrozoline.
- Thalidomide.** 4mg/kg (adult 200mg) 12H oral, reducing over 2-4wk to 0.5-1mg/kg (adult 25-50mg) 12H.
- THAM.** See trometamol.
- Theophylline.** 80mg theophylline = 100mg aminophylline). Loading dose: 8mg/kg (max 500mg) oral. Maintenance: 1st wk life 2mg/kg 12H; 2nd wk 3mg/kg 12H; 3wk-12mo ((0.1 x age in wk) + 3) mg/kg 8H; 1-9yr 4mg/kg 4-6H, or 10mg/kg s slow rel 12H; 10-16yr or adult smoker 3mg/kg 4-6H, or 7mg/kg 12H slow rel; adult non-smoker 3mg/kg 6-8H; elderly 2mg/kg 6-8H. Serum level: neonate 60-80umol/L, asthma 60-110 (x0.18 = mcg/ml).
- Thiabendazole.** 25mg/kg (max 1.5g) 12H oral 3d
- Thiamine.** Beriberi: 1-2mg/kg IV, IM or oral dly. Metabol dis (NOT/kg): 100mg 8H IV, IM, SC, oral.
- Thiethylperazine maleate.** >10kg: 0.2mg/kg (adult 10mg) 8-24H oral, IM, or PR.
- Thioguanine.** 100mg/m<sup>2</sup> daily oral; or 100mg/m<sup>2</sup> 12H for 5-7 days.
- Thiopentone.** 2-5mg/kg slowly stat (beware hypotension). IV infsn: amp 25mg/ml at 0.04-0.2ml/kg/hr (1-5mg/kg/hr). Level 150-200umol/L (x0.24 = mcg/ml).
- Thioridazine.** 0.5-3mg/kg (adult 25-150mg) 6-8H oral or IM.
- Thiosulphate.** See sodium thiosulphate.
- Thiotepa.** 10-14mg/m<sup>2</sup> IV every 1-4wk.
- Thiotepa.** 1 in 2000: 1 drop/eye 4-6H for 6wk.
- Thiothixene.** >12yr (NOT/kg): initially 2mg 8H oral, slow incr to 2-20mg per dose.
- Theonine.** 15-30mg/kg (adult 0.75-1.5g) 8H oral.
- Thrombin glue.** 10,000u thrombin in 9ml mixed with 1ml 10% calcium chloride in syringe 1, 10ml cryoprecipitate in syringe 2: apply to bleeding sites together. Do not inject.
- Thrombin, topical.** 100-2000u/ml onto bleeding surface.
- Thymidine.** 75g/m<sup>2</sup> every 4-6wk IV over 24hr.
- Thymoxamine.** Adult (NOT/kg): 40-80mg 6H oral.
- Thyrotropin alfa.** Adult (NOT/kg): 0.9mg IM 24H x2 doses, or 72H x3 doses.

- Thyroxine.** 50mcg tab. 100mcg/m<sup>2</sup> rounded to nearest quart tab (adult 100-200mcg) dly oral.
- Tiagabine.** Usu. 0.1mg/kg (adult 5mg) 12H, incr wkly to 0.1-0.5mg/kg (adult 5-15mg) 8H oral.
- Tiaprofenic acid.** 2-4mg/kg (adult 100-200mg) 8H oral.
- Tibolone.** Adult (NOT/kg): 2.5mg daily oral.
- Ticarcillin.** 50mg/kg (adult 3g) IV 6-8H (1st wk life), 4-6H or constant infsn (2+ wk). Cystic fib: 100mg/kg (max 6g) 8H IV.
- Ticarcillin + clavulanic acid.** Dose as for ticarcillin.
- Ticlopidine.** 5mg/kg (adult 250mg) 12H oral.
- Tigecycline.** 2mg/kg (adult 100mg) IV over 1hr stat, then 1mg/kg (adult 50mg) IV over 30min 12H.
- Tilactase.** 200u/drop: 5-15 drops/L added to milk 24hr before use. 3300u/tab: 1-3tabs with meals oral.
- Tiludronate disodium.** Adult 400mg dly x12 wk oral
- Timolol.** 0.1mg/kg (adult 5mg) 8-12H, incr to max 0.3mg/kg (adult 15mg) 8H. Eye drops (0.25%, 0.5%): 1 drop/eye 12-24H;
- Timolol 5mg/ml + travoprost 40mcg/ml.** 1 drop/eye daily.
- Tinidazole.** Giardia, trichomonas: 50mg/kg (adult 2g) daily for 2 days oral, or 25mg/kg (adult 1g) daily x5 days. Amoebiasis: 50mg/kg (adult 2g) daily for 3-5 days, usually followed by diloxanate furoate 10mg/kg (adult 500mg) 8H for 10 days.
- Tinzaparin.** 1mg =75 anti-Xa IU. Prophylaxis: 50u /kg SC 2hr before surgery, then dly for 7-10d. Treatment: 175u/kg SC daily for at least 6 days.
- Tioconazole.** 280mg/ml: apply to nails 12H for 6-12mo.
- Tioguanine.** Usu, 200mg/m<sup>2</sup> daily oral for 5-20d
- Tiopronin.** 3-10mg/kg (adult 150-500mg) 6-8H oral.
- Tiotropium.** NOT/kg: 18mcg cap daily by inhaler.
- Tipranavir.** Adult (NOT/kg): 500mg 12H with food (and ritonavir 200mg) oral.
- Tirilazad.** 1.5mg/kg 6H IV over 30min.
- Tirofiban.** 0.4mcg/kg/min x30min, then 0.1mcg/kg /min x2-5 d; also give heparin to APTT x2 normal
- Tissue plasminogen activator.** See alteplase.
- Tizanidine.** 0.01mg/kg (adult 0.5mg) 8H, incr gradually to 0.1-0.25mg/kg (adult 6-12mg) 8H oral.
- Tobramycin.** IV or IM. 1wk-10yr: 8mg/kg day 1, then 6 mg/kg daily. >10yr: 7mg/kg day 1, then 5mg/kg (max 240-360mg) daily.  
Neonate, 5mg/kg dose: <1.2kg 48H (0-7 days of life), 36H (8-30 days), 24H (>30 days); 1.2 - 2.5kg 36H (0-7 days of life), 24H (>7 days); term 24H (0-7 days of life), then as for 1wk-10yr. Trough level <1.0mg/L.  
Inhnltn: 80mg diluted to 4ml 12H; or TOBI
- Tocainide.** 5-10mg/kg (max 400-800mg) 8-12H IV over 30min or oral.
- Tocopherol.** See alpha-tocopheryl acetate, and vitamin E.
- Tolazamide.** 2-5mg/kg (adult 100-250mg) 6-24H oral
- Tolazoline.** Newborn: 1-2mg/kg slowly stat (beware hypotension), then 2-6mcg/kg/min (0.12-0.36mg/kg/hr) IV. Note: 1-2mg/kg/hr too much (Pediatrics 1986;77:307).
- Tolbutamide.** Adult (NOT/kg): initially 1g 12H oral, often reducing to 0.5-1g daily.
- Tolcapone.** Adult (NOT/kg): 100mg 8H oral; if no response, try maximum dose of 200mg 8H. Monitor ALT and AST.
- Tolfenamic acid.** 4mg/kg (adult 200mg) oral, may repeat once after 2hr.
- Tolmetin.** 5-10mg/kg (adult 400-600mg) 8H oral.
- Tolnaftate.** 1% cream, ointmnt, powdr, soltn: apply 8-12H.
- Tolterodine.** 0.05mg/kg (adult 2mg) 12H oral. Slow rel: adult 2-4mg daily oral.
- Topiramate.** 1mg/kg (adult 50mg) 12-24H oral, incr slowly if reqd to 4-10mg/kg (adult 100-500mg) 12H.
- Topotecan.** 1.5mg/m<sup>2</sup> daily x5 IV over 30min, repeat every 3wk for at least 4 courses.
- Torasemid.** 0.1-1mg/kg (adult 5-50mg) daily oral or IV. Rarely up to 4mg/kg (adult 200mg) daily in renal failure.
- Toremifene.** Adult (NOT/kg): 60mg daily oral.
- Tramadol.** 2-3mg/kg (adult 50-100mg) stat, then 1-2mg/kg (adult 50-100mg) 4-6H (usual max 400mg/day, up to 600 mg/day) oral or IV over 3min. IV infusion 2-8mcg/kg/min.
- Tramazoline.** Nasal: 82mcg each nostril x3-6/d See also dexamethasone + tramazoline.
- Trandolapril.** 0.01-0.1mg/kg (adult 0.5-4mg) daily oral.
- Tranexamic acid.** Oral: 15-25mg/kg (adult 1-1.5g) 8H for up to 4 days. IV: 10-15mg/kg (adult 0.5-1g) 8H.
- Tranlycypromine.** 0.2mg/kg (adult 10mg) 8-12H oral.
- Trastuzumab.** 4mg/kg IV over 90min load, then 2mg/kg IV over 30min wkly. Early cancer after chemo: 8 mg/kg IV over 90min, then 6mg/kg IV over 90min every 3wk.
- Travoprost.** 40mcg/ml (0.004%): 1drop/eye in evening. See also timolol + travoprost.
- Trazodone.** 1-4mg/kg (adult 50-200mg) 8H oral.
- Treprostinil.** 1.25mg/kg/min SC infsn, incr each wk by 1.25-2.5mg/kg/min to max 20-60mg/kg/min.
- Tretinoin.** 22.5mg/m<sup>2</sup> 12H oral. Cream or lotion 0.05%, gel 0.01%: apply daily for 3-4 months, then x1-3/wk.

- Triamcinolone.** Joint, tendon (NOT/kg): 2.5-15 mg stat. IM: 0.05-0.2mg/kg every 1-7 days. Cream or ointment 0.02%, 0.05%: apply sparingly 6-8H. Triamcinolone has no mineral-corticoid action, 1mg = 5mg hydrocortisone in glucocorticoid action.
- Triamterene.** 2mg/kg (adult 100mg) 8-24H oral.
- Triazolam.** 0.005-0.01mg/kg (adult 0.125-0.5mg) nocte oral. 30 min preop: 0.01-0.03 mg/kg (adult 0.5mg) oral.
- Tricofos.** 25-30mg/kg (adult 0.5-1g) nocte oral.
- Triclosan.** 0.5%-5% lotion: 2ml to wet skin for 30sec, rinse and rpt. Bath oil: 20ml in 20cm bath, soak 15min.
- Trientine.** 10mg/kg (adult 500mg) 6-12H oral.
- Triethylenethiophosphoramide.** See thiotepa.
- Trifluoperazine.** 0.02-0.4mg/kg (adult 1-10mg, occasionally 20mg) 12H oral. Caps: adult 15mg dly.
- Trifluridine.** 1% soltn: 1 drop/eye 2H (max 9 drops /d) until epithelialised, then 4H (max 5 drops/d) x7d
- Trihexyphenidyl.** See benzhexol.
- Triiodothyronine (T3).** See liothyronine.
- Trilostane.** 0.5-4mg/kg (adult 30-240mg) 6H oral.
- Trimepazine.** Antihistamine: 0.1-0.5mg/kg (adult 2.5-25mg) 6H oral. Sedation: 0.5-1mg/kg IM, 2-4mg/kg oral.
- Trimethobenzamide.** 5mg/kg (adult 250mg) 6-8H oral, IM, PR.
- Trimethoprim.** 3-4mg/kg (max 150mg) 12H, or 6-8mg/kg (usual max 300mg) dly oral, IV. Urine prophylaxis: 1-2mg/kg (adult 150mg) nocte
- Trimethoprim + sulphamethoxazole.** See cotrimoxazole.
- Trimethylglycine.** See betaine hydrochloride.
- Trimetrexate.** 45mg/m<sup>2</sup> IV over 90min dly x21d, with folinic acid 20mg/m<sup>2</sup> IV over 10min 6H x24 d
- Trimipramine.** 1-2mg/kg (adult 50-100mg) 8-24H oral
- Trioxysalen.** Adult: 5-10mg dly 2hr bef. UV exposure
- Tripelennamine.** 1.25mg/kg (adult 75mg) 6H oral.
- Tripotassium dicitratobismuthate.** See bismuth subcitrate.
- Triprolidine.** See pseudoephedrine + triprolidene.
- Triptorelin.** Adult (NOT/kg). Depot: 3.75-4.2mg IM every 28 days. Long acting: 11.25mg IM every 12wk.
- Trisodium edetate.** 40-70mg/kg (max 3g) IV over 6hr daily x5 d; max 3 courses each 2 d apart.
- Trometamol (THAM).** ml of 0.3 molar/18g/500ml soltn = (Wt in kg) x BE; give half this IV over 30min, then repeat if reqd.
- Tropicamide.** 0.5%, 1%: 1 drop/eye, rpt aftr 5min
- Tropisetron.** 0.1mg/kg (adult 5mg) slow IV just before chemotherapy, then oral 12-24H.
- Trosipium chloride.** 0.4mg/kg (adult 20mg) 12H oral
- Trovafloxacin.** 4mg/kg (adult 200mg) daily oral. Severe infn: 6mg/kg (adult 300mg) daily oral.
- Tryptophan, L isomer.** Adult (NOT/kg) 1-2g 8H oral.
- Tyloxapol.** See colfosceril palmitate.
- Tulobuterol.** 0.04mg/kg (adult 2mg) 8-12H oral.
- Typhoid vaccine, oral (Vivotif).** Live. 1 cap oral days 1, 3, 5 and (for better immunity) 7. Boost yearly.
- Typhoid vaccine, parenteral, polysaccharide (Typherix, Typhim Vi).** Inactivated. >5yr: 0.5ml IM once. Boost 3yrlly.
- Ubidacarenone.** 1-3mg/kg (adult 50-150mg) 12H oral
- Uracil.** See tegafur + uracil.
- Urea.** 10% cream: apply 8-12H.
- Urofollitrophin.** See follicle stimulating hormone.
- Urokinase.** 4000u/kg IV over 10min, then 4000u/kg/hr for 12hr (start heparin 3-4hr later). Blocked cannula: instill 5000-25000u (NOT/kg) in 2-3ml saline for 2-4hr. Empyema: 2ml/kg of 1500u/ml in saline, position head up/down and right side up/down 30min each, then drain. Pericardial effusion: 10,000u/ml, 1ml/kg (max 20ml), clamp 1hr, drain.
- Ursodeoxycholic acid.** 5-10mg/kg (adult 200-400mg) 12H oral.
- Ursodiol.** See ursodeoxycholic acid.
- Valaciclovir.** 20mg/kg (adult 1g) 8H oral. Genital herpes (NOT/kg): treatment 500mg 12H, prevention 500mg daily (<10 episodes/yr) 1g daily (>9 episodes/yr). Orolabial: 40mg/kg (adult 2g) 12H for 2 doses.
- Valcyte.** Adult (NOT/kg): 900mg 12H oral for 3wk, then 900mg daily.
- Valdecobix.** Adult(NOT/kg): 10mg daily (arthritis), 20mg 12H (dysmenorrhoea) oral.
- Valganciclovir.** Adult (NOT/kg): 900mg 12H oral with food for 21 days, then 900mg daily.
- Valproic acid, valproate.** See sodium valproate.
- Valrubicin.** Adult (NOT/kg): 800mg wkly x6 intravesical
- Valsartan.** 0.8-3mg/kg (adult 40-160mg) daily oral. See also amlodipine + valsartan.
- Vancomycin.** 10mg/kg (adult 500mg) 6H IV over 1hr, or 1g 12H in adult IV over 2hr. Newborn: 10mg/kg 8H IV over 1hr. C.difficile: 10mg/kg (adult 500mg) 6H oral. Intraventricular (NOT/kg): 10mg 48H. Trough 5-10mg/L (peak 20-40mg/L).
- Varenicline.** Adult (NOT/kg): 0.5mg oral daily for 3 days, 12H days 4-7; then 1mg 12H for 11wk (23wk if stopped smoking).



- Varicella vaccine (Varilix, Varivax).** Live. 9mo-12yr: 0.5ml SC once. >12yr: 0.5ml SC stat, and 4-8wk later. See also Herpes zoster vaccine, and Immunoglobulin – zoster.
- Vasopressin, aqueous.** IM, SC: 2.5-10u 6-12H. IV: put 2-5u in 1L fluid, and replace urine out put + 10% each hour. Hypotension (brain death, sepsis, post-bypass): 1u/kg in 50ml 5% dex-hep at 1-3ml/hr (0.02-0.06 units/kg/hr) + adrenaline 0.1-0.2mcg/kg/min. GI hge: 6u/kg in 50ml at 1-5ml/hr IV, 1ml/hr local IA. See desmopressin, lypressin.
- Vasopressin, oily.** 2.5-5u (NOT/kg) IM every 2-4 d.
- Vecuronium.** ICU: 0.1mg/kg prn IV. Theatre: 0.1mg/kg stat, then 0.5-2mcg/kg/min; up to 10mcg/kg/min occasionally.
- Venlafaxine.** Adult (NOT/kg): 37.5mg 12H oral, incr if reqd to max 150mg 12H. Slow rel: 75mg daily oral, incr if reqd to max 225mg daily.
- Verapamil.** IV: 0.1-0.2mg/kg (adult 5-10mg) over 10min, then 5mcg/kg/min. Oral: 1-3 mg/kg (adult 80-120mg) 8-12H.
- Veregen.** 15% ointment: apply 8H for up to 16wk.
- Versenate.** See sodium calcium edetate.
- Verteporfin.** 6mg/m<sup>2</sup> over 10min IV; 15min after start of infsn give diode laser of 689nm at 600mW/cm<sup>2</sup> for 83sec.
- Vidarabine.** Eye ointment: x5/day until epithelialised, then 12H 7 days. IV infsn: 10mg/kg/day 5-10 d (varicellazoster), 15mg/kg/day 10 days (herpes encephalitis).
- Vigabatrin.** 40mg/kg (adult 1g) dly oral, may incr to 80-150mg/kg (max 4g) dly (given in 1-2 doses).
- Viloxazine.** 2-5mg/kg (adult 100-250mg) morning, and 2-3mg/kg (adult 100-150mg) noon oral.
- Vinblastine.** 6.5mg/m<sup>2</sup> IV over 1 min every 1-4wk.
- Vincristine.** 1.5mg/m<sup>2</sup> wklly IV over 1 min.
- Vindesine.** 3-4mg/m<sup>2</sup> IV every 7-10 day if wbc count >2500/mm<sup>3</sup>.
- Vinorelbine.** 30mg/m<sup>2</sup> IV over 10min weekly.
- Vitamin A.** High risk (NOT/kg): 100,000iu (<8kg), 200,000iu (>8kg) oral or IM every 4-6mo. Severe measles: 400,000iu (NOT/kg) once. Cystic fibrosis: 1500u daily (<3yr) 5000u daily (3-10yr) 10000u daily (>10yr) oral. >10,000iu daily or >25000u per wk may be teratogenic.
- Vitamin A, B, C, D compound (Pentavite, infant).** <3yr (NOT/kg): 0.15ml daily, incr by 0.15ml/day to 0.45ml/day.
- Vitamin A, B, C, D compound (Pentavite, child).** <3yr (NOT/kg): 2.5ml daily. >3yr (NOT/kg): 5ml daily.
- Vitamin B group.** Amp: IV over 30 min. Tab: 1-2/d
- Vitamin B1.** See thiamine.
- Vitamin B2.** Metabolic disease: 50-150mg 12-24H oral
- Vitamin B6.** See pyridoxine.
- Vitamin B12.** See hydroxocobalamin.
- Vitamin C.** See ascorbic acid.
- Vitamin D2.** See ergocalciferol.
- Vitamin D3.** See cholecalciferol.
- Vitamin E.** 1u = 1mg. Preterm babies, Copelol E (NOT/kg): 40u (2 drops) daily oral. Cystic Fibrosis, malabsorption: 50-100u (<3yr) 200-400u (>3yr) daily oral. Cholestasis: 50u/kg daily oral, incr if reqd in 50u/kg increments. A-beta-lipoproteinaemia: 35-70 u/kg 8H oral. HUS: 0.25g/m<sup>2</sup> 6H oral. See alpha-tocopheryl.
- Vitamin K1.** See phytonadione.
- Vitamin K3.** See menaphthone sodium bisulphite.
- Vitamins, parenteral.** MVI-12 (for adult): 5ml in 1 L IV fluid. MVI Paediatric, added to IV fluid: 65% of a vial (<3kg), 1 vial (3kg to 11yr).
- Voriconazole.** Oral, IV over 2hr: 8mg/kg (child >2yr) 200mg (adult <40kg) 400mg (adult >40 kg) rpt after 12hr, then 6mg/kg (child >2yr) 100mg (adult <40kg) 200mg (adult >40kg) 12H. Increase maintenance by 50% if required.
- Vorinostat.** Adult (NOT/kg): 400mg daily oral; may need to decrease to 300mg daily, or 300mg on 5 days a week.
- Warfarin.** Usually 0.2mg/kg (adult 5mg) stat, 0.2mg/kg (adult 5mg) next day providing INR <1.3, then 0.05-0.2mg/kg (adult 2-5mg) daily oral. INR usually 2-2.5 for prophylaxis, 2-3 for treatment. Beware drug interactions.
- Xamoterol.** 4mg/kg (adult 200mg) 12-24H oral.
- Xipamide.** 0.5-1.5mg/kg (adult 20-80mg) dly oral
- Xylometazoline.** <6yr: 0.05% 1 drop or spray 8-12H. 6-12yr: 0.05% 2-3 drops or sprays 8-12H. >12yr: 0.1% 2-3 drops or sprays 6-12H.
- Yellow fever vaccine (Stamaril).** Live. >12mo: 0.5ml SC once. Boost every 10yr.
- Yohimbine.** 0.05-0.1mg/kg (adult 2.7-5.4mg) 8H oral.
- Zafirlukast.** NOT/kg: 10mg (>7yr) 20-40mg (adult) 12H oral.
- Zalcitabine.** Usually 0.015mg/kg (adult 1mg) 12H oral.
- Zaleplon.** Adult (NOT/kg): 10mg (5-20mg) nocte oral
- Zanamivir.** Adult (NOT/kg): 10mg 12H for 5 days inhaled. Prophylaxis: 10mg daily inhaled.
- Ziconotide.** Adult (NOT/kg): 2.4mcg/day by intrathecal infusion, incr every 24-48hr to max 21.6mcg/day.

**Zidovudine (AZT).** Preterm: 1.5mg/kg 12H IV, or 2mg/kg 12H oral to 2wk, then 2mg/kg 8H. Term: 2mg/kg 6H oral, 1.5mg/kg 6H IV. Child: usually 180mg/m<sup>2</sup> 12H oral; 120 mg/m<sup>2</sup> 6H IV, or 20mg/m<sup>2</sup>/hr IV (range 90-180 mg/m<sup>2</sup> 6-8H IV). Adult (NOT/kg): usually 200mg 8H oral, or 300mg 12H oral, or 150mg 8H IV. See abacavir + lamivudine + zidov.

**Zileuton.** Adult (NOT/kg): 600mg 6H oral.

**Zinc chloride.** 5.3mg/ml = 2.5mg/ml Zn = 38umol/ml Zn. 2-4umol/kg/d (<1yr), 1umol/kg/d (child), 40-60umol/d (adult). Serum zinc 11-22 umol/l.

**Zinc sulphate.** (220mg cap = 50mg Zn = 765umol Zn). Deficiency, acroderm enteropath: initially 3mg/kg (adult 220mg) 8-12H oral, adjusted to achieve serum zinc 11-22umol/L (0.7-1.4mg/L). Diarrhoea child (NOT/kg): 10-20mg daily oral.

**Ziprasidone.** Adult (NOT/kg): 20mg 12H, incr if reqd to max 80mg 12H oral.

**Zoledronate.** 0.025-0.05mg/kg (adult 4mg) IV over 15min; usually repeated every 4wk.

**Zolmitriptan.** Adult (NOT/kg): 2.5-5mg oral, rpt in 2hr if reqd; max 15mg in 24hr. Nasal: 5mg spray in each nostril, repeat in 2hr if reqd; max twice in 24hr.

**Zolpidem.** 0.1-0.4mg/kg (adult 5-20mg) nocte oral.

**Zonisamide.** 2mg/kg (adult 100mg) daily oral, incr if reqd after 2wk to 12H, then 3mg/kg (adult 150mg) 12h, then 4mg/kg (adult 200mg) 12H; rarely up to 6mg/kg (adult 300mg) 12H. Level 10-20mg/l.

**Zopiclone.** 0.1-0.3mg/kg (adult 5-15mg) nocte oral.

**Zotepine.** 0.5mg/kg (adult 25mg) 8H oral, adjusted every 4 days to 0.5-2mg/kg 8H.

**Zuclopenthixol.** 0.4-3.0mg/kg (adult 20-150mg) daily oral.





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