PAEDIATRIC PROTOCOLS

For Malaysian Hospitals

3rd Edition

Hussain Imam Hj Muhammad Ismail
Ng Hoong Phak
Terrence Thomas

Kementerian Kesihatan Malaysia

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Paediatric Protocol 3rd Edition

Kementerian Kesihatan Malaysia

Malaysia like the rest of the world has 3 more years to achieve the Millennium Developmental Goals (MDG). MDG 4 is concerned with under 5 mortality. Although we have done very well since Independence to reduce our infant and toddler mortality rates, we are now faced with some last lap issues in achieving this goal.

Despite urbanization there are still many children in the rural areas. This constitutes a vulnerable group in many ways. Among the factors contributing to this vulnerability is the distance from specialist care.

There is a need to ensure that doctors in the frontline are well equipped to handle common paediatric emergencies so that proper care can be instituted from the very beginning.

Although all doctors are now required to do 4 months of pre-registration training in Paediatrics, this is insufficient to prepare them for all the conditions they are likely to meet as Medical Officers in district hospitals and health clinics. Hence the effort made by the paediatricians to prepare a protocol book covering all the common paediatric problems is laudable. I would also like to congratulate them for bringing out a third edition within 4 years of the previous edition.

I am confident that this third edition will contribute to improving the care of children attending the Ministry's facilities throughout the country.

Dato'Sri Dr Hasan Bin Abdul Rahman
Director General of Health, Malavsia

It has been 7 years since we produced the first edition of a national protocol book for Paediatrics. This effort was of course inspired by the Sarawak Paediatric Protocols initiated by Dr Tan Poh Tin. The 2nd edition in 2008 has proven to be very popular and we have had to recruit the services of the Malaysian Paediatric Association (MPA) to produce extra copies for sale. It is now the standard reference for House officers in Paediatrics.

In producing a third edition we have retained the size and style of the current version, essentially only updating the contents. Again it is targeted at young doctors in the service many of whom seem to have had a suboptimal exposure to paediatrics in their undergraduate years. It is hoped that the protocol book will help them fill in the gaps as they prepare to serve in district hospitals and health clinics.

The Ministry of Health has once again agreed to sponsor the printing of 1000 books and 500 CDs for distribution to MOH facilities. We shall be soliciting the help of the MPA in producing extra books to be sold to those who wish to have a personal copy. As a result of the full PDF version being available on the MPA website, we have had requests from as far away as Kenya and Egypt to download and print the material for local distribution. We have gladly allowed this in the hope that it will contribute to better care of ill children in those and other neighbouring countries.

As previously this new edition is only possible because of the willingness of busy clinicians to chip in and update the content for purely altruistic reasons and we hope this spirit will persist in our fraternity. Prof Frank Shann has gracefully agreed for the latest edition of his drug dosages handbook to be incorporated into the new edition. The Director General of Health has also kindly provided a foreword to this edition.

We wish to thank all who have made this new edition possible and hope this combined effort will help in improving the wellbeing of the children entrusted to our care.

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TABLE OF CONTENTS

TABLE OF CONTENTS

TABLE OF CONTENTS

TABLE OF CONTENTS

Acknowledgements
Again, to Dr Koh Chong Tuan, Consultant Paediatrician at Island Hospital, Penang for his excellent work in proof reading the manuscript.

VITAL SIGNS

Respiratory (Breath) Rate			
Normal, Breath rate at rest		Abnormal	
Age (years)	Rate/min	*These values define Tachypnoea*	
<1	30-40	Age	Rate/min
1-2	25-35	< 2 months	> 60
2-5	25-30	2 mths - 1 year	> 50
5-12	20-25	1-5 years	> 40

Heart (Pulse) Rate			
	Abnormal	Normal	Abnormal
Age (years)	Low *(Bradycardia)*	Average	High *(Tachycardia)*
Newborn	< 70/min	125/min	> 190/min
1-11 months	< 80/min	120/min	> 160/min
2 years	< 80/min	110/min	> 130/min
4 years	< 80/min	100/min	> 120/min
6 years	< 75/min	100/min	> 115/min
8 years	< 70/min	90/min	> 110/min
10 years	< 70/min	90/min	> 110/min

Ref: Nelson Textbook of Pediatrics, 18th Edition

Blood Pressure		
	Hypotension *if below*	Normal (average)
Age (years)	5th centile for age	50th centile for age
< 1 year	65 - 75 mmHg	80 - 90 mmHg
1-2 years	70 - 75 mmHg	85 - 95 mmHg
2-5 years	70 - 80 mmHg	85 - 100 mmHg
5-12 years	80 - 90 mmHg	90 - 110 mmHg
> 12 years	90 - 105 mmHg	100-120 mmHg

Calculation for Expected Systolic Blood Pressure
= 85 + (2 x age in years) mmHg for 50th centile - Median Blood Pressure
= 65 + (2 x age in years) mmHg for 5th centile - Hypotension if below this value

Ref: Advanced Paediatric Life Support: The Practical Approach, Fifth Edition 2011

Blood Pressure in Hypertension				
Age	Significant Hypertension		Severe Hypertension	
1 week	Systolic	96 mmHg	Systolic	106 mmHg
1 wk - 1 mth	Systolic	104 mHg	Systolic	110 mmHg
Infant	Systolic	112 mmHg	Systolic	118 mmHg
	Diastolic	74 mmHg	Diastolic	82 mmHg
3-5 years	Systolic	116 mmHg	Systolic	124 mmHg
	Diastolic	76 mmHg	Diastolic	86 mmHg
6-9 years	Systolic	122 mmHg	Systolic	130 mmHg
	Diastolic	78 mmHg	Diastolic	86 mmHg
10-12 years	Systolic	126 mmHg	Systolic	134 mmHg
	Diastolic	82 mmHg	Diastolic	90 mmHg
13-15 years	Systolic	136 mmHg	Systolic	144 mmHg
	Diastolic	86 mmHg	Diastolic	92 mmHg
16-18 years	Systolic	142 mmHg	Systolic	150 mmHg
	Diastolic	92 mmHg	Diastolic	98 mmHg

ANTHROPOMETRIC MEASUREMENTS

Age	Weight	Height	Head size
birth	3.5 kg	50 cm	35 cm
6 months	7 kg	68 cm	42 cm
1 year	10 kg	75 cm	47 cm
2 years	12 kg	85 cm	49 cm
3 years	14 kg	95 cm	49.5 cm
4 years		100 cm	50 cm
5-12 years		5 cm/year	0.33 cm/year

Points to Note

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 *regain* their birth weight by the 2nd week, *double* this by 5 months age, and *triple* the birth weight by 1 year of age
- Weight estimation for children (in Kg):

  Infants: (Age in months X 0.5) + 4

  Children 1 – 10 years: (Age in yrs + 4) X 2

Head circumference

- Rate of growth in preterm infants is 1 cm/week, but reduces with age. Head growth follows that of term infants when chronological age reaches term
- 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)

Other normal values are found in the relevant chapters of the book.

References:

1. Advanced Paediatric Life Support: The Practical Approach Textbook, 5th Edition 2011
2. Nelson Textbook of Pediatrics, 18th Edition.

HAEMATOLOGICAL PARAMETERS

Age	Hb	PCV	Retics	MCV *fl*	MCH *pg*	TWBC	Neutrophil	Lymphocyte
	g/dL	%	%	Lowest	Lowest	*x1000*	Mean	Mean
Cord Blood	13-7-20.1	45-65	5.0	110	-	9-30	61	31
2 weeks	13.0-20.0	42-66	1.0	-	29	5-21	40	63
3 months	9.5-14.5	31-41	1.0	-	27	6-18	30	48
6 mths - 6 yrs	10.5-14.0	33-42	1.0	70-74	25-31	6-15	45	38
7 - 12 years	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 counts	
< 7 days age	neutrophils > lymphocytes
1 wk - 4 years	lymphocytes > neutrophils
4 - 7 years	neutrophils = lymphocytes
> 7 years	neutrophils > lymphocytes

Points to note

- **Differential WBC:** eosinophils: 2-3%; monocytes: 6-9 %
- **Platelets counts** are lower in first months of age; but normal range by 6 months
- **Erythrocyte sedimentation rate (ESR)** is < 16 mm/hr in children, provided PCV is at least 35%.

National Immunisation Schedule for Malaysia (Ministry of Health, Malaysia)

	Age (months)										School years		
Vaccine	birth	1	2	3	5	6	9	10	12	18	7 yrs	13 yrs	15 yrs
BCG	1										if no scar		
Hepatitis B	1	2				3							
DTaP			1	2	3					DT B^+			T B^+
IPV			1	2	3					B^+			
Hib			1	2	3					B^+			
Measles						Sabah							
MMR									1				
JE (Sarawak)							1	2		B*			
HPV												3 doses	

Legend: B^+, Booster doses; B, Booster at 4 years age; BCG, Bacille Calmette-Guerin; DTaP, Diphhteria, Tetanus, acellular Pertussis;*

DT, Diphtheria, Tetanus; T, Tetanus IPV, Inactivated Polio Vaccine; Hib, Haemophilus influenzae type B;

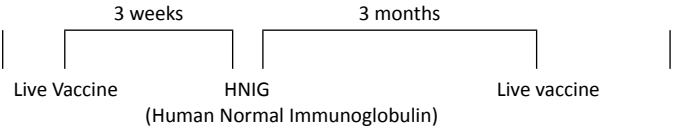
MMR, Measles, Mumps, Rubella; JE, Japanese Encephalitis, HPV, Human Papilloma Virus;

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. Vaccines are now packaged in combinations to avoid multiple injections to the child.
- sites of administration
  - oral – 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 lower antibody level production

Immunisation : *General* 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.
- A relative contraindication: avoid a vaccine within 2 weeks of elective surgery.
- **Live vaccine: Absolute contraindications**
  - *Immunosuppressed children* -malignancy; irradiation, leukaemia, lymphoma, primary immunodeficiency syndromes (but NOT asymptomatic HIV).
  - On *chemotherapy* or < 6 months after last dose.
  - On *High dose steroids*, i.e. Prednisolone ≥ 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 administer live vaccine.
  - If *given another LIVE vaccine including BCG < 4 weeks ago*. (Give live vaccines simultaneously. If unable to then give separately with a 4 week interval).
  - Within *3 months following IV Immunoglobulin* (11 months if given high dose IV Immunoglobulins, e.g. in Kawasaki disease).



  - 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 outweighs the risk to the foetus.
- **Killed vaccines are generally safe**. The only absolute contraindications are SEVERE local (induration involving > 2/3 of the limbs) or severe generalised reactions in the previous dose.

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 affected area).
- 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 syndrome, simple febrile convulsions, controlled epilepsy, mental retardation.
- Family history of convulsions.
- History of heart disease, acquired or congenital.
- Prematurity (immunise according to schedule irrespective of gestational age)

Vaccination: Special Circumstances

- Measures to protect **inpatients exposed to another inpatient with measles**:
  - Protect all **immunocompromised children** with Immunoglobulin (HNIG) 0.25-0.5 mls/kg. (Measles may be fatal in children in remission from leukaemia)
  - Check status of measles immunisation in the other children. Give measles monocomponent vaccine to **unimmunised children** within 24 hrs of exposure. Vaccination within 72 hours aborts clinical measles in 75% of contacts
  - Discharge the inpatient child with uncomplicated measles.
  - Do not forget to notify the Health Office.
- Immunisation in *children with HIV* (Please refer to Paediatric HIV section)
- In patients with **past history or family history of febrile seizures**, neurological or developmental abnormalities that would predispose to febrile seizures:-
  - Febrile seizures may occur 5 – 10 days after measles (or MMR) vaccination or within the first 72 hours following pertussis immunisation.
  - Give Paracetamol (120 mg or ¼ tablet) prophylaxis after immunisation (esp. DPT) 4-6 hourly for 48 hours regardless of whether the child is febrile. This reduces the incidence of high fever, fretfulness, crying, anorexia and local inflammation.
- Maternal Chicken Pox during perinatal period. (Please refer to Perinatally acquired varicella section)
- **Close contacts of immunodeficient children and adults** must be immunized, particularly against measles and polio (use IPV).
- In **contacts of a patient with invasive Haemophilus influenzae B disease**:
  - Immunise all household, nursery or kindergarden contacts < 4 years of age.
  - Household contacts should receive Rifampicin prophylaxis at 20 mg/kg once daily (Maximum 600 mg) for 4 days (except pregnant women - give one IM dose of ceftriaxone)
  - Index case should be immunised irrespective of age.

- Children with **Asplenia** (Elective or emergency splenectomy; asplenic syndromes; sickle cell anaemia) are susceptible to encapsulated bacteria and malaria.
  - Pneumococcal, Meningococcal A, C, Y & W-135, Haemophilus influenza b vaccines should be given.
  - For elective splenectomy (and also chemotherapy or radiotherapy): give the vaccines preferably 2 or more weeks before the procedure. However, they can be given even after the procedure.
  - Penicillin prophylaxis should continue 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 infants** may be immunised at the same chronological age as term infants. (Please refer section on The premature infants for more discussion)

Vaccine	Indication/Dose	Contraindication	Possible Side Effects	Notes
BCG	To be given at birth and to be repeated if no scar is present	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.	BCG adenitis may occur.	Intradermal. Local reaction: a papule at vaccination site may occur in 2 - 6 weeks. This grows and flattens with scaling and crusting. Occasionally a discharging ulcer may occur. This heals leaving a scar of at least 4 mm in successful vaccination.
Hepatitis B	All infants, including those born to HBsAg positive mothers All health care personnel.	Severe hypersensitivity to aluminium. The vaccine is also not indicated for HBV carrier or immuned patient (i.e. HBsAg or Ab positive)	Local reactions. Fever and flu-like symptoms in first 48 hours. Rarely, erythema multiforme or urticaria.	Intramuscular. Give with Hep B immunoglobulin for infants of HBsAg positive mothers.
Diphtheria, Tetanus (DT)	All infants should receive 5 doses including booster doses at 18 months and Standard 1	Severe hypersensitivity to aluminium and thiomersal	Swelling, redness and pain A small painless nodule may develop at injection site – harmless. Transient fever, headaches, malaise, rarely anaphylaxis. Neurological reactions rare.	Intramuscular

Vaccine	Indication/Dose	Contraindication	Possible Side Effects	Notes
Pertussis	All infants should receive 4 doses including booster at 18 months It is recommended that booster doses be given at Std 1 and at Form 3 due to increased cases of Pertussis amongst adolescents in recent years	Anaphylaxis to previous dose; encephalopathy develops within 7 days of vaccination Precautions: severe reaction to previous dose (systemic or local) and progressive neurological diseases.	Local reaction. Severe if involve 2/3 limbs Severe systemic reaction: Anaphylaxis (2 per 100 000 doses), encephalopathy (0 – 10.5 per million doses), high fever (fever>40.5), fits within 72 hours, persistent inconsolable crying (0.1 to 6%), hyporesponsive state. Acellular Pertussis vaccine associated with less side effects	Intramuscular. Static neurological diseases, developmental delay, personal or family history of fits are NOT contraindications.
Inactivated Polio Vaccine (IPV)	All infants to be given 4 doses including booster at 18 months.	Allergies to neomycin, polymyxin and streptomycin Previous severe anaphylactic reaction	Local reactions.	Intramuscular.
Haemophilus Influenzae type B (Hib)	All infants should receive 4 doses including booster at 18 months. Patients with splenic dysfunction, and post splenectomy.	Confirmed anaphylaxis to previous Hib and allergies to neomycin, polymyxin and streptomycin	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.	Intramuscular

Vaccine	Indication/Dose	Contraindication	Possible Side Effects	Notes
Measles	Sabah, Orang Asli population at 6 mths. Not usually given to children <12mth. If there is a measles outbreak, can be given to children 6 -11 mths age. This is later followed by MMR at 12 mths and 4-6 years age.	Avoid in patients with hypersensitivity to eggs, neomycin and polymyxin. Pregnancy. Children with untreated leukemia, TB and other cancers. Immunodeficiency.	Transient rash in 5%. May have fever between D5-D12 post vaccination. URTI symptoms. 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. (Natural infection 1:1000 - 5000)	Intramuscular. ** *Long term prospective studies have found no association between measles or MMR vaccine and inflammatory bowel diseases, autism or SSPE.*
Measles, Mumps, Rubella (MMR)	All children from 12 to 15 months. Booster at 4-6yrs (or at Std 1).	Severe reaction to hen's eggs and neomycin. Pregnancy	Measles: As above	Intramuscular. Can be given irrespective of previous history of measles, mumps or rubella infection.
Mumps			Rarely transient rash, pruritis and purpura. Parotitis in 1% of vaccinees, > 3 weeks after vaccination. Orchitis and retro bulbar neuritis very rare. Meningoencephalitis is mild and rare. (1:800,000 doses). (natural infection 1:400).	Intramuscular

Vaccine	Indication/Dose	Contraindication	Possible Side Effects	Notes
Rubella			Rash, fever, lymphadenopathy, thrombocytopenia, transient peripheral neuritis. Arthritis and arthralgia occurs in up to 3% of children and 20% of adults.	Given as MMR
Japanese Encephalitis (JE)	Given in Sarawak at 9, 10 and 18 months Booster at 4 years.	Immunodeficiency and malignancy, diabetes , acute exacerbation of cardiac, hepatic and renal conditions	Local redness, swelling, pain, fever, chills, headache, lassitude..	Inactivated vaccine. Subcutaneous. Protective efficacy > 95%.
Human Papilloma Virus (HPV)	Indicated for females aged 9-45 years.	Not recommended in pregnant patients.	Headache, myalgia, injection site reactions, fatigue, nausea, vomiting, diarrhoea, abdominal pain, pruritus, rash, urticaria, myalgia, arthralgia, fever.	2 vaccines available: Cervarix (GSK): bivalent. Gardasil (MSD): quadrivalent. - 3 dose schedule IM (0, 1-2month, 6 month). Recombinant vaccine. Protective efficacy almost 100% in preventing vaccine type cervical cancer in first 5 years.

Vaccine	Indication/Dose	Contraindication	Possible Side Effects	Notes
Pneumo-coccal (conjugate) vaccine: PCV 13/ PCV 7	Dosage: Infants 2-6 mth age. 3-dose primary series at least 1 mth apart from 6 wks of age. Booster: 1 dose between 12-15 mths of age. Unvaccinated: infants 7-11 mths 2 doses 1 month apart, followed by a 3rd dose at 12- 15 months; children 12-23 months 2 doses at least 2 months apart; healthy children 2 - 5 years: Single dose Unvaccinated high risk children 2-5 yrs age may be given 2 doses (6-8 wks apart)	Children who have severe allergic reaction to previous pneumococcal vaccine Healthy children under 6 weeks and more than 59 months of age	Decreased appetite, irritability, drowsiness, restless sleep, fever, inj site erythema, induration or pain, rash.	*Not in Blue Book* Immunogenic in children < 2 years Inactivated vaccine. Intramuscular High risk children: immunosuppression (includ-ing asymptomatic HIV), asplenia, nephrotic syndrome and chronic lung or heart disease.

Vaccine	Indication/Dose	Contraindication	Possible Side Effects	Notes
Pneumococcal (polysaccharide vaccine)	Recommended for children at high risk. > 2 years old. Single dose. Booster at 3-5 years only for high risk patients.	Age < 2 years old. Revaccination within 3 years has high risk of adverse reaction; Avoid during chemotherapy or radiotherapy and less than 10 days prior to commencement of such therapy – antibody response is poor. Pregnancy.	Hypersensitivity reactions.	Listed in Blue Book. Intramuscular, Subcutaneous Immunogenic in children ≥2 yrs. Against 23 serotypes. High risk: immunosuppression, asymptomatic HIV, asplenia, nephrotic syndrome, chronic lung disease. If these children are <2 yrs old, they should first receive pneumococcal conjugate vaccine; when > 2 yrs, then the polysaccharide vaccine is used.
Rotavirus	First dose given to infants ≥ 6 wks old. *Rotateq* (3 doses) Subsequent doses given at 4-10 wks interval. 3rd dose given ≤ 32 weeks age. *Rotarix* (2 doses). 2nd dose to be given by 24 weeks age. Interval between doses should be > 4 wks.	Prior hypersensitivity to any vaccine component. Uncorrected congenital GIT malformation, e.g. Meckel's diverticulum Severe combined immunodeficiency disease (reported prolonged shedding of vaccine virus reported in infants who had live Rotavirus vaccine)	Loss of appetite, irritability, fever, fatigue, diarrhoea, vomiting, flatulence, abdominal pain, regurgitation of food.	Oral live-attenuated vaccine. Protective efficacy 88-91% for any rotavirus gastroenteritis episode; 63-79% for all causes of gastroenteritis.

Vaccine	Indication/Dose	Contraindication	Possible Side Effects	Notes
Varicella Zoster	*12 mths to 12 yrs:* Single dose *> 12 yrs:* 2 doses ≥4 wks apart. Non immune susceptible health care workers who regularly come in contact with VZV infection Asymptomatic/mildly symptomatic children with HIV (with CD4% > 15%); 2 doses at 3 mths interval. Children in remission from leukemia for ≥1 yr, have >700/ml circulating lymphocytes may receive vaccine under paediatrician supervision (2doses).	Pregnant patients. Patients receiving high dose systemic immunosuppression therapy. Patients with malignancy especially haematological malignancies or blood dyscrasias. Hypersensitivity to neomycin.	Occasionally, papulovesicular eruptions, injection site reactions, headache, fever, paresthesia, fatigue	Live attenuated vaccine. Subcutaneous. 70 – 90% effectiveness.
Hepatitis A	For children >1 yr. 2 doses., given 6-12 months apart.	Severe hypersensitivity to aluminium hydroxide, phenoxyethanol, neomycin	Local reactions. Flu-like symptoms lasting 2 days in 10% of recipients	Intramuscular. Inactivated vaccine. Protective efficacy 94%.

Vaccine	Indication/Dose	Contraindication	Possible Side Effects	Notes
Cholera	Children 2-6 yrs: 3 doses at 1-6 wk interval. Children > 6 yrs: 2 doses at 1-6 wks interval. Booster dose >2 yrs.		Gastroenteritis	Oral inactivated vaccine. Protective efficacy 80-90% after 6 mths waning to 60% after 3 yrs.
Influenza	Single dose. Min age 6 mths. Unprimed individuals require 2nd dose 4 - 6 wks after 1st dose. Recommended for children with: chronic decompensated respiratory or cardiac disorders, e.g. cyanotic heart diseases chronic lung disease, HIV infection. In advanced disease, vaccination may not induce protective antibody levels.	Hypersensitivity to egg or chicken protein, neomycin, formaldehyde. Febrile illness, acute infection.	Transient swelling, redness, pain and induration locally. Myalgia, malaise and fever for 1 – 2 days starting within a few hours post vaccination. Very rarely, neurological (Guillain-Barre), glomerulonephritis, ITP or anaphylactic reaction occurs.	Intramuscular. Inactivated vaccine. Protective efficacy 70-90% Require yearly revaccination for continuing protection.

Vaccine	Indication/Dose	Contraindication	Possible Side Effects	Notes
Rabies	Pre-exposure: 3 doses at Day 0, 7, 28. Booster every 2-3 yrs. Post-exposure treatment: Fully immunised: 2 doses at Day 0, Day 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.		Headache, dizziness, malaise, abdominal pain, nausea, myalgia. Injection site reactions such as itching, swelling, pain.	Inactivated vaccine. (Available in Malaysia as Purified Vero Cell Rabies Vaccine (PVRV). Intramuscular.
Meningococcus A, C, Y & W-135	Single dose. Immunity up to 3 yrs.		Local reactions. Irritability, fever and rigors for 1-2 days. Very rarely, anaphylaxis.	Intramuscular.
Typhoid (Typhim Vi)	Single dose. Seroconversion in 85-95% of recipients; confers 60-80% protection beginning 2 wks after vaccination. Boosters every 3 yrs.	Children < 2yrs. (Immunogenicity < 2 yrs of age has not been established)	Local reactions. Myalgia, malaise, nausea, headaches and fever in 3% of recipients.	Intramuscular. Polysaccharide vaccine
Typhoid (Ty21a vaccine)	Three doses two days apart. Effective 7 days after last dose. Booster every 3 years.	Infant <6 mth. Congenital or acquired immunodeficiency. Acute febrile illness & acute intestinal infection.	Very rarely: mild GIT disturbances or a transitory exanthema.	Oral. Live attenuated vaccine.

Recommended Immunisation Schedule for Infants and Children *Not Immunised* at the Recommended Time

Time of Immunisation	Age at first visit	
	Between 6 wks -12 mths	12 months and older
1st visit	BCG, DPT/DTaP, Hib1, IPV1, HBV1	BCG, DPT/DTaP1, Hib1, IPV1, HBV1, measles (footnote 2) at 6 or 9 mths, MMR at 12 mths of age
2nd visit (1 mth later)		DPT/DTaP2, IPV2, HBV2, Hib2
3rd visit (1 mth later)	DPT/DTaP2,Hib2, IPV2, HBV2	DPT/DTaP3, IPV3,
4th visit (4 mths after 3rd visit)	DPT/DTaP3,Hib3, IPV3,	HBV3, DPT/DTaP4, IPV4,
2-8 mths later	HBV3, DTaP4, Hib4 & IPV4 (booster), measles in Sabah at 9 mths age, MMR at 12 mths age	Polio, DT/DTaP, MMR (at school entry)

Footnotes:

1. *For infants < 6 wks age, use "Recommended Immunisation Schedule for Infants & Children".*
2. *Measles vaccine should be given only after 9 mths. (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.*

Well children with *Normal hydration*

Very few well children require intravenous fluids (IV). Whenever possible use an enteral (oral) route for fluids.

These guidelines apply to children who are unable to tolerate enteral fluids.

The safe use of IV fluid therapy in children requires accurate prescribing of fluids and careful monitoring because incorrectly prescribed or administered fluids are hazardous.

If IV fluid therapy is required then **maintenance fluid requirements should be calculated using the Holliday and Segar formula based on weight.**

However this should be only be used as a starting point and the individuals' response to fluid therapy should be monitored closely by clinical observation, fluid balance, weight and a minimum daily electrolyte profile.

Prescribing Intravenous fluids

Fluids are given intravenously for the following reasons:

- Circulatory support in resuscitating vascular collapse.
- Replacement of previous fluid and electrolyte deficit.
- Maintenance of daily fluid requirement.
- Replacement of ongoing losses.
- Severe dehydration with failed nasogastric tube fluid replacement (e.g. on-going profuse losses, diarrhoea or abdominal pain).
- Certain co-morbidities, particularly GIT conditions (e.g. short gut or previous gut surgery)

Resuscitation

Fluids appropriate for bolus administration are:	
Crystalloids	0.9% Normal Saline
	Ringer's Lactate @ Hartmann's solution
Colloids	Gelafundin, Voluven
	4.5% albumin solution
Blood products	Whole blood, blood components

- Fluid deficit sufficient cause **impaired tissue oxygenation (i.e. clinical shock)** should be **corrected with a fluid bolus of 10-20mls/kg**.
- **Always reassess circulation** - give repeat boluses as necessary.
- **Look for the cause of circulatory collapse** - blood loss, sepsis, etc. This helps decide on the appropriate alternative resuscitation fluid.
- **Fluid boluses of 10mls/kg in selected situations** - e.g. diabetic ketoacidosis, intracranial pathology or trauma.
- **Avoid low sodium-containing (hypotonic) solutions** for resuscitation as this may cause hyponatremia.
- **Check blood glucose:** treat **hypoglycemia** with 2mls/kg of 10% Dextrose solution.

- **Measure Na, K and glucose at the outset and at least 24hourly** from then on. More frequent testing is indicated in ill patients or those with co-morbidities. Rapid results of electrolytes can be done with blood gases measurements.
- **Consider septic work-up or surgical consult in severely unwell patients with abdominal symptoms** (i.e. gastroenteritis).

Maintenance

- Maintenance fluid is the volume of daily fluid intake. It includes insensible losses (from breathing, perspiration, and in the stool), and allows for excretion of the daily production of excess solute load (urea, creatinine, electrolytes) in the urine.
- **Most children can safely be managed with solution of 0.45% saline with added glucose** (i.e. 0.45% saline in 5% glucose or 0.45% saline in 10% glucose) depending on glucose requirement.
- Sodium chloride 0.18 saline with glucose 5% should not be used as a maintenance fluid and is restricted to specialist area to replace ongoing loses of hypotonic fluids. These areas include high dependency, renal, liver and intensive care.
- Most children will tolerate standard fluid requirements. However some acutely ill children with inappropriately increased anti-diuretic hormone secretion (SIADH) may benefit from their maintenance fluid requirement being restricted to two-thirds of the normal recommended volume.
- **Children who are at high risk of hyponatremia should be given isotonic solutions (i.e. 0.9% saline ± glucose) with careful monitoring to avoid iatrogenic hyponatremia in hospital.**

  These include children with the following conditions:
  - Peri-or post-operative
  - Require replacement of ongoing losses
  - A plasma Na at lower normal range of normal (definitely if < 135mmol/L)
  - Intravascular volume depletion
  - Hypotension
  - Central nervous system (CNS) infection
  - Head injury
  - Bronchiolitis
  - Sepsis
  - Excessive gastric or diarrhoeal losses
  - Salt-wasting syndromes
  - Chronic conditions such as diabetes, cystic fibrosis and pituitary deficits.

Calculation of Maintanence Fluid Requirements

The following calculations approximate **the maintenance fluid requirement of well children according to weight in kg.** (Holliday-Segar calculator)

Weight	Total fluids	Infusion rate
First 10 Kgs	100 ml/kg	4 mls/kg/hour
Subsequent 10 Kgs	50 ml/kg	2 mls/kg/hour
All additional Kg	20 ml/kg	1 mls/kg/hour

Example: A Child of 29 kg will require:		
100mls/kg for first 10kg of weight	10 x 100	= 1000 mls
50mls/kg for second 10kg of weight	10 x 50	= 500 mls
20mls/kg for all additional weight	9 x 20	= 180 mls
	Total	= 1680 mls
	Rate	= 1680/24 = 70mls/hour

Composition of commonly used intravenous solution				
	Osmolality	Na content	Osmolality	Tonicity
Fluid	(mOsm/l)	(mmol/l)	compared to plasma	with ref to cell membrane
Na chloride 0.9%	308	154	IsoOsmolar	Isotonic
Na chloride 0.45%	154	77	HypoOsmolar	Hypotonic
Na chloride 0.9% + Glucose 5%	586	150	HyperOsmolar	Isotonic
Na chloride 0.45% + Glucose 5%	432	75	HyperOsmolar	Hypotonic
Na chloride 0.18% + Glucose 5%	284	31	IsoOsmolar	Hypotonic
Dextrose 5%	278	Nil	IsoOsmolar	Hypotonic
Dextrose 10%	555	Nil	HyperOsmolar	Hypotonic
Hartmann's	278	131	IsoOsmolar	Isotonic

Deficit

• A child's water deficit in mls can be calculated following an estimation of the degree of dehydration expressed as % of body weight.

Example: A 10kg child who is 5% dehydration has a water deficit of 500mls.		
Maintenance		
100mls/kg for first 10 kg	= 10 × 100	= 1000mls
Infusion rate/hour	= 1000mls/24 hr	= 42mls/hr
Deficit (give over 24hours)		
5% dehydration (5% of body water): 5/100 × 10kg × 1000mls		= 500mls
Infusion rate/hour (given over 24 hrs)	= 500mls/24 hr	= 21mls/hr

- **The deficit is replaced over a time period that varies according to the child's condition.** Precise calculations (e.g. 4.5%) are not necessary. The rate of rehydration should be adjusted with ongoing clinical assessment.
- **Use an isotonic solution for replacement of the deficit, e.g. 0.9% saline.**
- **Reassess clinical status and weight at 4-6hours,** and if satisfactory continue. If child is losing weight, increase the fluid and if weight gain is excessive decrease the fluid rate.
- Replacement may be rapid in most cases of gastroenteritis (best achieved by oral or nasogastric fluids), but **should be slower in diabetic ketoacidosis and meningitis, and much slower in hypernatremic states** (aim to rehydrate over 48-72 hours, the serum Na should not fall by >0.5mmol/l/hr).

Ongoing losses (e.g. from drains, ileostomy, profuse diarrhoea)

- These are best measured and replaced. Any fluid losses > 0.5ml/kg/hr needs to be replaced.
- Calculation may be based on each previous hour, or each 4 hour period depending on the situation. For example; a 200mls loss over the previous 4 hours will be replaced with a rate of 50mls/hr for the next 4 hours).
- Ongoing losses can be replaced with 0.9% Normal Saline or Hartmann's solution. Fluid loss with high protein content leading to low serum albumin (e.g. burns) can be replaced with 5% Human Albumin.

SODIUM DISORDERS

- The daily sodium requirement is 2-3mmol/kg/day.
- **Normal serum sodium is between 135-145mmol/l.**

Hypernatremia

- **Hypernatremia is defined as serum Na^+ > 150mmol/l,** *moderate* hypernatremia is when serum Na^+ is 150-160mmol/l, and *severe* hypernatremia is when serum Na^+ > 160mmol/l.
- It can be due to:
  - water loss in excess of sodium (e.g. diarrhoea)
  - water deficit (e.g. diabetes insipidus)
  - sodium gain (e.g. large amount of $NaHCO_3$ infusion or salt poisoning).

Clinical signs of Hypernatremic dehydration
Irritability
Skin feels "doughy"
Ataxia, tremor, hyperreflexia
Seizure
Reduced awareness, coma

- If the cause of the hypernatremia is central diabetes insipidus, it is advisable to consult Endocrinology team regarding management.
- In **hypernatremia the child appears sicker than expected for the degree of dehydration.**
- **Shock occurs late because intravascular volume is relatively preserved.** Signs of hypernatremic dehydration tend to be predominantly that of intracellular dehydration and neurological dysfunction.

Management

This will depend on the cause of hypernatremia.
For hypernatremic dehydration with Na^+> 150mmol/l

- **If the patient is in shock, give volume resuscitation with 0.9% Normal saline as required with bolus/es.**
- **Avoid rapid correction** as this may cause cerebral oedema, convulsion and death.
- Aim for correction of deficit over 48-72 hours and a fall of serum sodium concentration not more than 0.5mmol/l/hour.
- Give 0.9% saline to ensure the drop in sodium is not too rapid.
- Remember to also give maintenance and replace ongoing losses following the recommendation above.
- **Repeat blood urea and electrolytes** every 6 hours until stable.

Special considerations

- A slower rate will be required for children with chronic hypernatremia (present for more than 5 days).
- **Calcium and glucose need to be checked** as hypernatremia can be associated with hypocalcaemia and hyperglycemia, these conditions need to be corrected concurrently.

Hyponatremia

- **Hyponatremia is defined when serum Na^+ < 135mmol/l.**
- **Hyponatremic encephalopathy is a medical emergency** that requires rapid recognition and treatment to prevent poor outcome.
- As part of the general resuscitative measures, **bolus of 4ml/kg of 3% sodium chloride should be administered over 30 minutes.** This will raised the serum sodium by 3mmol/l and will usually help stop hyponatremic seizures.
- Gradual serum sodium correction should not be more than 8mmol/day to prevent osmotic demyelination syndrome.

Calculating sodium correction in acute hyponatremia	
mmol of sodium required	= (135-present Na level)× 0.6 × weight(kg)
The calculated requirements can then be given from the following available solutions dependent on the availability and hydration status:	
0.9% sodium chloride contains 154 mmol/l	
3% sodium chloride contains 513mmol/l	

- Children with **asymptomatic hyponatremia** do not require 3% sodium chloride treatment and if dehydrated may be managed with oral fluids or intravenous rehydration with 0.9% sodium chloride.
- Children who are hyponatremic and have a normal or raised volume status should be managed with fluid restriction.
- For Hyponatremia secondary to **diabetic ketoacidosis**; refer DKA protocol.

POTASSIUM DISORDERS

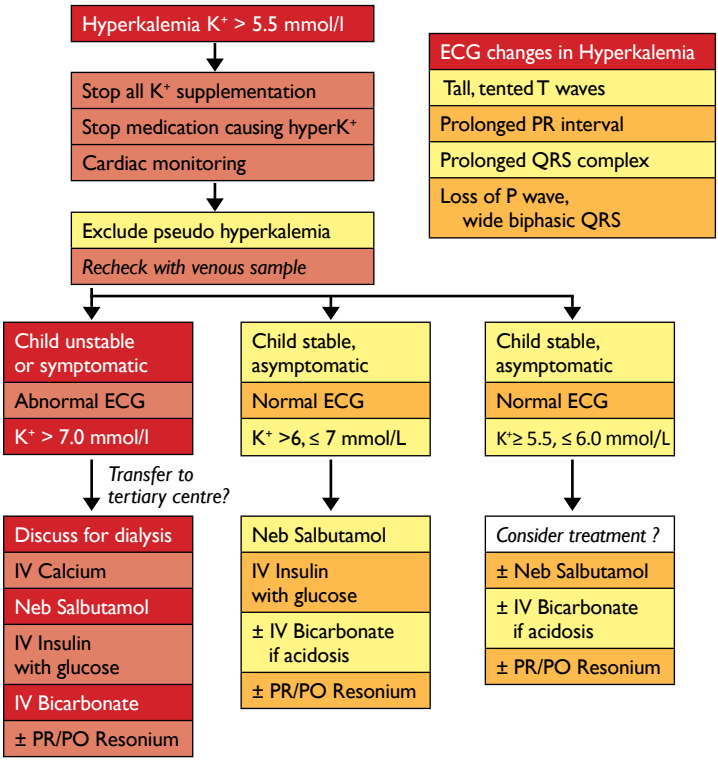
- The daily potassium requirement is 1-2mmol/kg/day.
- **Normal values of potassium are:**
  - **Birth - 2 weeks: 3.7 - 6.0mmol/l**
  - **2 weeks – 3 months: 3.7 - 5.7mmol/l**
  - **3 months and above: 3.5 - 5.0mmol/l**

Hyperkalemia

- Causes are:
  - Dehydration
  - Acute renal failure
  - Diabetic ketoacidosis
  - Adrenal insufficiency
  - Tumour lysis syndrome
  - Drugs e.g. oral potassium supplement, K^+ sparing diuretics, ACE inhibitors.

Treatment: ***see algorithm on next page***

Hyperkalemia Treatment Algorithm



Drug doses:

- IV Calcium 0.1 mmol/kg.
- Nebulised Salbutamol:
  Age ≤2.5 yrs: 2.5 mg; Age 2.5-7.5 yrs: 5 mg; >7.5 yrs: 10 mg
- IV Insulin with Glucose:
  Start with IV Glucose 10% 5ml/kg/hr (or 20% at 2.5 ml/kg/hr).
  Once Blood sugar level >10mmol/l and the K^+ level is not falling,
  add IV Insulin 0.05 units/kg/hr and titrate according to glucose level.
- IV Sodium Bicarbonate: 1-2 mmol/kg.
- PO or Rectal Resonium : 1Gm/kg.

Hypokalemia

- **Hypokalemia is defined as serum Na^+ > 3.4 mmol/l**
  (Treat if < 3.0mmol/l or Clinically Symptomatic < 3.4 mmol/l)
- Causes are:
  - Sepsis
  - GIT losses - diarrhoea, vomiting
  - Iatrogenic- e.g. diuretic therapy, salbutamol, amphotericin B.
  - Diabetic ketoacidosis
  - Renal tubular acidosis
- Hypokalaemia is often seen with chloride depletion and metabolic alkalosis.

ECG changes of Hypokalemia
These occur when K^+ < 2.5mmol/l
Prominent U wave
ST segment depression
Flat, low or diphasic T waves
Prolonged PR interval (severe hypoK^+)
Sinoatrial block (severe hypoK^+)

- **Refractory hypokalaemia** may occur with hypomagnesaemia.

Treatment

- Identify and treat the underlying condition.
- **Unless symptomatic, a potassium level of 3.0 and 3.4 mmol/l is generally not supplemented** but rather monitored in the first instance.
- The treatment of hypokalaemia does not lend itself to be incorporated into a protocol and as a result each patient will need to be treated individually.

Oral Supplementation

- Oral Potassium Chloride (KCL), to a maximum of 2 mmol/kg/day in divided doses is common but more may be required in practice.

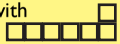
Intravenous Supplementation (1gram KCL = 13.3 mmol KCL)

- **Potassium chloride is always given by IV infusion, ***NEVER* **by bolus injection.**
- **Maximum *concentration* via a peripheral vein is 40 mmol/l** (concentrations of up to 60 mmol/l can be used after discussion with senior medical staff).
- **Maximum *infusion rate* is 0.2mmol/kg/hr** (in non-intensive care setting).

Intravenous Correction (1gram KCL = 13.3 mmol KCL)

- K^+ < 2.5 mmol/L may be associated with significant cardiovascular compromise. In the emergency situation, an IV infusion KCL may be given
  - Dose: initially 0.4 mmol/kg/hr into a central vein, until K^+ level is restored.
  - Ideally this should occur in an intensive care setting.

Age	Gross Motor	Fine Motor	Speech/Language	Social
6 wks	*Pull to sit:* Head lag, rounded back *Ventral Suspension:* Head briefly 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 weeks. Quiets to sound. Startles to sound.	Smiles responsively.
3 mths	*Pull to sit:* 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 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).		

Age	Gross Motor	Fine Motor	Speech/Language	Social
18 mths	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. Casting stops.
2 yrs	Goes up and down stairs alone, 2 feet per step. Walks backwards (21 months) Runs. Picks up toy without falling. Throws, kick ball without falling.	Tower of 6 cubes. Imitates cubes of train with no chimney.  Imitates straight line. Visual test: Snellen'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 yrs	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 yrs	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 O 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.

Age	Gross Motor	Fine Motor	Speech/Language	Social
4 yrs	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 yrs		Copies gate with cubes. Copies square. Draws recognisable man and house.		
5 yrs	Skips on both feet. Runs on toes.	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 yrs	Walks heel to toe Kicking, throwing, climbing.	Copies:  Goodenough test 12. Imitates or copies steps with 10 cubes		
Note: Goodenough test: 3 + a/4 years (a = each feature recorded in his picture).				

Age	Gross Motor	Fine Motor	Speech/Language	Social
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 sit.	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 stand.	Index approach. Uses index finger to poke at pea. Lets go of cube in hand.		Waves "Bye bye" Plays "Pat-a-Cake"
11 mths	Creeping on all fours. Pivoting. Cruising. Walks with *both* 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 phases; 2 - 3 words with meaning. Localising sound above head.	Casting (13 months) Less mouthing. Shy.
13 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

Chapter 5: 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.

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 or cannot do. **Note parental 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.

Key Developmental 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
Note: Parental concerns must always be taken seriously	

Assessment of children with suspected 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)

Physical examination

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

Investigations
(individualised according to history and physical findings)

- Visual and auditory testing
- T4, TSH
- Chromosomal Analysis
- Consider
  - Creatine kinase in boys
  - MRI Brain
  - Metabolic screen
  - Specific genetic studies (Fragile X, Prader Willi or Angelman syndrome)
  - Refer to a geneticist
  - EEG if history of seizures

Consider
Hypothyroidism
Chromosomal anomaly
Cerebral palsy
Congenital intrauterine infection
Congenital brain malformations
Inborn errors of metabolism
Autistic spectrum disorder
Attention deficit hyperactivity disorder
Prior brain injury, brain infections
Neuroctaneous disorders
Duchenne's muscular dystrophy

Assessment of Children with Suspected Hearing Impairment or Speech Delay

History

- Congenital infection
- Perinatal medications
- Severe neonatal jaundice
- Family history of deafness or speech delay
- Chronic ear infections
- Quality, quantity of speech

Physical examination

- Examine ears
- Dysmorphic features
- Distraction Test
- Assess expressive, receptive speech
- Neurological / development assessment

Warning Signs for Hearing Impairment	
1	Child appears not to hear
2	Child makes no attempt to listen.
3	Does not respond to name, "No" or clue words e.g. "Shoe", by 1 yr age
4	Any speech/language milestone delay

Consider
Congenital sensorineural deafness
Familial, genetic deafness
Congenital rubella infection
Oro-motor dysfunction

Management

- Formal hearing assessment
- Speech-language assessment and interventions

Hearing Tests at different ages		
Age	Test	Comments
Newborn screening	Automated Otoacoustic Emission (OAE) test	Determines cochlear function. Negative test in conductive hearing loss, middle ear infections, or in moderate to severe sensorineural hearing loss.
Any age	Brainstem Auditory Evoked Responses (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 and opening suckling rate.
> 2.5 years	Conditioned Play Audiometry	Earphones placed on child and various games are done when test tone is heard.
Older Children	Pure Tone Audiometry	Patient presses a response button or raises a hand when the test tone is heard

Assessment of Children with Suspected Visual Impairment

Children at risk

- Prematurity.
- Intrauterine Infection (TORCHES)
- Family history of cataracts, retinoblastoma or squint.
- Previous meningitis, asphyxia
- Dysmorphic babies

Warning Signs for Visual Impairment	
1	Does not fix on mother's face by 6 wks
2	Wandering eyes or roving eyes after 6 wks
3	Abnormal head postures
4	Leukocoria (white eye reflex)
5	Holds objects very close to eye.
6	Squint after 6 months of age.

Assessment of Children with Suspected Learning Difficulties

It is sometimes a challenge to identify the primary cause of the learning difficulty as conditions like dyslexia , ADHD and intellectual impairment share common symptoms.

A. History *(A thorough history is important)*

- Antenatal perinatal and postnatal complications
- High risk behaviour like substance abuse in mother
- Family history of development delay, learning difficulties etc.
- Detailed developmental milestones
- When learning problems were first noted (preschool achievement, etc. as children with dyslexia or ADHD will have symptoms in early childhood)
- Past and current education performance
- Areas of learning difficulties
- Specific: e.g. reading difficulties (dyslexia) , writing difficulties (dysgraphia) but extremely good in tasks that require visual stimulation, e.g. art, music
- General : more commonly seen in children with some degree of intellectual impairment or from an extremely understimulated environment
- Strength of the child perceived by parents and teachers
- Who is the main caregiver at home ?
- Social background of the family

B1. Review School concerns with the patient, parents & teachers (always ask for teachers report). Common symptoms

- Apathy towards school
- Avoidance or poor performance in specific subject areas
- Disruptive or negative behaviour in certain classes

B2. Review all school workbooks (not only report card)

C. Basic Cognitive (intellectual functioning) screening tool in a Pediatric Clinic:

- Ask child to tell about a recent event : birthday, visit to grandparents etc. (note whether language is fluent, coherent, organized)
- Ask parents whether child has difficulty taking retaining classroom instructions or instructions at home (short term memory)
- Observe the child using a pencil to copy symbols and words (visual perceptual motor disorder characterized by confusing symbol, easy distractibility , inability to copy information)
- Ask the child to perform a 3-step command (sequencing ability to communicate and understand information in a orderly and meaningful manner)
- Ask the child to repeat four words , remember them and repeat them again when asked in 5 -10 minutes (memory , attention)
- Ask the child to repeat three, then four digits forward then repeat three, then four digits backward (concentration)

D. Physical Examination

- Anthropometric measurement
- General alertness and response to surrounding
  (Children with dyslexia will be very alert and usually very enterprising)
- Dysmorphism
- Look for neurocutaneous stigmata
- Complete CNS examination including hand eye coordination
  as children may have a associated motor difficulties like dyspraxia
- Complete developmental assessment.
- Ask child to draw something he or she likes (this can help to get a clearer picture about intellect of the child)

Block and Pencil test (From *Parry TS: Modern Medicine, 1998*)

Age	Block Test	Pencil Test
3 - 3.5 yrs	Build a bridge 	Draw a circle 
3.5 - 4 yrs		Draw a cross 
3 - 4.5 yrs	Build a gate 	Draw a square 
5 - 6 yrs	Build steps 	Draw a triangle 

This test screens cognitive and perceptual development for age.
Block test: build the structure without child observing then ask the child to copy the structure.
Pencil test: Draw the object without child observing then ask the child to copy it.

E. Differential Diagnosis that need to be ruled out:

Common causes

- Autism
- ADHD or combination of both
- Specific learning difficulty like Dyslexia
- Limited environmental stimulation

Genetic or a chromosomal disorder

- Fragile X
- Hypothyroidism
- Intellectual impairment
- Tourette
- Neurofibromatosis

Neurological

- Seizures
- Neurodegenerative condition

Miscellanous causes

- Anaemia
- Auditory or visual impairment
- Toxins (fetal alcohol syndrome, prenatal cocaine exposure, lead poisoning)

F. Plan of Management

Dependent on the primary cause for learning difficulties

- Dyslexia screening test if available
- DSM 1V for ADHD or Autistic Spectrum Disorder
  (Refer CPG for management of children and adolescents with ADHD :2008)
- Refer Occupational therapist for school preparedness (pencil grip, attention span etc) or for associated problems like dyspraxia
- Refer speech therapist if indicated
- Assess vision and hearing as indicated by history and clinical examination
- Targeted and realistic goals set with child and parents
- One-to-one learning may be beneficial
- Registration as a *Child with Special Needs* as per clinical indication and after discussion with parents

G. Investigations

Clinical impressions guides choice. Consider:

- DNA analysis for Fragile X syndrome for males with Intellectual impairment
- Genetic tests, e.g. Prader Willi, Angelman, DiGeorge, Williams syndromes
- Inborn errors of metabolism
- TSH if clinically indicated
- Creatine Kinase if clinically indicated
- MRI brain study abnormal neurological examination
- EEG only if clinically indicated

When is IQ Testing Indicated?

When diagnosis is unclear and there is a need to determine options for school placement.

If unsure of diagnosis refer patient to a Pediatrician, Developmental Pediatrician, Pediatric Neurologist, Child Psychiatrist and Child Psychologist depending on availability of services in your area.

Some first signs suggestibe of dyslexia	
Preschool and Kindergarten	
Language	• May have difficulty pronouncing words and slow to add new vocabulary words • May be unable to recall the right word • Trouble learning nursery rhymes or playing rhyming • Trouble learning to recognize letters of the alphabet (important predictor of later reading skills: recognition of letters of alphabets starts before decoding)
Memory	• Difficulty remembering rote information (name, phone number, address)
Fine motor skills	• Fine motor skills may develop more slowly than in other children
Lower Grades in School	
Language	• Delayed decoding abilities for reading • Trouble following directions • Poor spelling and using of pronouns, verbs
Memory	• Slow recall of facts • Organizational problems • Slow acquisition of new skills
Attention	• Impulsive, easily distractible and careless errors
Fine motor skills	• Unstable pencil grip • Trouble with letter formation
Visual skills	• Confuses words, e.g. at –to, does –goes, etc • Consistent reading and spelling errors • Transposes number sequence, maths signs (+,- X/=)
Middle Grades of School	
Language	• Poor reading comprehension • Trouble with word problems • Lack of verbal participation in class
Memory	• Slow or poor recall of math facts and failure of automatic recall
Attention	• Inconsistency and poor ability to discern relevant details
Fine motor skills	• Fist-like or tight pencil grip • illegible, slow or inconsistent writing
Visual skills	• May reverse sequences (e.g.: soiled for solid)

Higher Grades in School	
Language	• Weak grasp of explanation • Poor written expressions • Trouble summarizing
Memory	• Trouble studying for test • Slow work pace
Attention	• Memory problems due to poor attention • Mental fatigue
Fine motor skills	• Less significant
Visual skills	• Misreads information • Trouble taking multiple choice questions • Difficulty with sequencing (maths, music and science: physics)

Essentials in making a diagnosis of dyslexia

History *(A thorough history is important)*

- When reading problems was first noted
- What were the problems?
- What is the current reading problem faced by the child at school
- Neurodevelopment (esp speech delay)
- Family history (esp. speech delay and learning disability)
- Significant birth and medical history
- Assessment of school work (esp. exam papers and teacher's report) .
- Strength of the child
- Any educational interventions or others attempted before

Physical Examination

Look for this, as some of these findings may be associated with features of dyslexia:

- Microcephaly
- Vision and Hearing problems
- Syndromic facies
- Neurocutaneous stigmata
- Neurodevelopmental examination

Neurodevelopmental assessment

Look specifically for problems in the following areas:

Gross motor

- Coordination (some can be "clumsy")
- Motor planning
- Visual motor & spatial functioning.

Fine motor
- Small muscle manipulation (dyspraxia)

Visual motor integration
- Spatial relationship
- Patterns in written material
- Meaning of maths symbols

Temporal sequential organization
- Auditory sequencing
- Understanding time
- Organization & planning

Language
- Receptive and Expressive language.
- Comprehension.
- Grammar
- Spoken and written instructions

Behavior
- Attention
- Adaptation
- Self monitoring

Investigations
Tailored to patients needs.
- IQ testing for those where diagnosis or underlying cause is unclear e.g. Borderline intellectual impairment with dyslexic features.

Differential Diagnosis
- Hearing and visual problems.
- Attention deficit hyperactivity disorder (ADHD)
- Global developmental delay
- Intellectual impairment

Minimum Interventions that can be done:
- Advocate for the educational needs of the child
- Network for services that child may need out of the school, e.g. one-to-one tuition
- Discuss with parents how to tackle child's difficulties, best school placements, registration as a *child with special needs*, etc.
- Refer to other disciplines e.g. Dyspraxia and Pencil grip: Occupational therapist
- May need referral to speech therapist

Suggestions for School Based Interventions

- A phonics-based reading program that teaches the link between spoken and written sounds
- A multi-sensory approach to learning, which means using as many different senses as possible such as seeing, listening, doing and speaking
- Arrangements with the child's school - for example, for them to take oral instead of written tests
- Learning via audiotape or videotape
- Arrange for extra time for exams
- Arrange for readers for UPSR students (need to write to JPN one year ahead of the UPSR exams)

Features of Dyslexia that can be elicited in the General Pediatric Clinic Setting
(tables in following pages)

- Assessment needs to be done in accordance to the child's cooperativeness level (may require 2-3 visits for a thorough assessment)
- This is not a validated assessment checklist, when in doubt refer to a Pediatrician, Developmental Pediatrician or an Educational Psychologist, depending on services available at your hospital.

At the end of the assessment, please answer these 2 questions below, and tick the appropriate column.

Question	Yes	No
1. Does the limitation in reading, spelling and writing cause significant learning difficulty in school?		
2. From your clinical assessment do you agree that the IQ of the child is appropriate for age?		

If the answer to the **both the above questions is "yes"** then the probable diagnosis is **Dyslexia**.
If unsure about diagnosis please refer to Pediatrician, Developmental Pediatrician or Educational Psychologist depending on services available in your area.

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Skill	Features	Examples	How to Test in Clinic
Reading	Unable to read appropriately for age	Give age appropriate passage or books	Listen to the child read aloud from his or her own grade level reader. (Keep a set of graded readers available in your clinic)
	Child may appear visibly tired after reading for only a short time		
	Reading will be slow, labored, inaccurate reading of even single words (ensure that there is no visual cues while doing this)	Single Word Reading • Boy • Chair • Kite • Hope	Show single words as suggested and ask child to read.
	Unable to read unfamiliar words or pseudo words and usually will try to guess or make up words because of some familiarity.	• Pilau = Pulau • Karusi = Kerusi • Maja = Meja	
Phonological processing / awareness	Difficulty in differentiating words that sounds alike	• Mana • Nama • Mama • Dapat • Padat	Consider the educational background of the child
Letter Indentification	Difficulty to name letters of the alphabet	A, B, C, D, E . . .	Prepare a table of alphabets and ask child to read out (ensure you point to the alphabets that you want the child to read). Take note that child maybe able to recite from memory

Skill	Features	Examples	How to Test in Clinic
Letter-Sound Association	Difficulty identifying words beginning with the same letter	• Doll, Dog, etc • Buku, buka, etc	
Segmentation	Difficulty in identifying word that would remain if a particular sound were removed	• What remains if the /k/ sound was taken away from "cat" = at • What remains if the /Ta/ sound taken away from "table"= ble • What remains if the /p/ sound was taken away from "paku" = aku • What remains if the sound /ma/ sound taken away from "mata" = mata	
Short term Verbal memory (eg, recalling a sentence or a story that was just told)	Difficulty recalling a sentence or a story that was just told	Narrate story to the child then ask questions like: • Apa nama kuching Ali? • Tompok suka makan apa? • Di mana Ali pergi memancing?	Have a short story which goes like this: "Ali ada seekor kuching bernama Tompok. Tompok suka makan ikan. Ali pergi memancing ikan di sungai dan memberikan ikan itu kepada Tompok."

Skill	Features	Examples	How to Test in Clinic
Rapid Naming	Difficulty in rapidly naming a continuous series of familiar objects, digits, letters, or colors	Use flash cards with pictures only, colours or numbers	Can use numbers for rapid naming or to test ability of remembering numbers in a reverse order. Ask child to name colours. If child not be able to do so ask child to point to a particular colour in a book. Usually the child will not have difficulty in doing so.
Expressive vocabulary or word retrieval	Difficulty in listing out name of animals or objects		Give me the names of animals you know
Rote memory	Difficulty in memorizing non-meaningful facts (facts that are not personally interesting and personally relevant)	• Multiplication tables • Days of the week or months of the year in order	Ask child to recite simple multiplication table or to say out days of the week or months of the year in order.
Sequencing steps in a task	Difficulty in performing task that needs sequencing	• Tying shoelaces • Printing letters: can't remember the sequence of pencil strokes necessary to form that letter. May write a in an odd way	

Skill	Features	Examples	How to Test in Clinic
Spelling	Difficulty in spelling even simple words that is age appropriate	• Buku, meja, mata, sekolah, etc	Ask child to do simple spelling with 2 syllables first if able to do then proceed to multisyllable words
Directionality	Left-Right confusion Up-Down confusion	• Substitution : b-p or d-q, n-u, and m-w • Confusion about directionality words: First-last, before-after, next-previous, over-under	
Dysgraphia	Poor, nearly illegible handwriting or difficulty in writing on a straight line. Difficulty in differentiating small or big letters. Unusual spatial organization of the page.	• Words may be widely spaced or tightly pushed together. • Margins are often ignored.	Observe school workbook for writing problems.
Copying	Difficulty in copying from blackboard Takes a long time to copy and copied work will have a lot of mistakes	• Tying shoelaces • Printing letters: can't remember the sequence of pencil strokes necessary to form that letter. May write a in an odd way	Observe school workbook which needs copying

Chapter 7: The H.E.A.D.S.S. Assessment

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 by the acronym **HEADSS** (**H**ome, **E**ducation /employment, peer group **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.

The HEADSS assessment Items are in listed in the following pages

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.

Item	Examples of Questions
Home	• Who lives at home with you? Where do you live? Do you have your own room? • How many brothers and sisters do you have and what are their ages? • Are your brothers and sisters healthy? • Are your parents healthy? What do your parents do for a living? • How do you get along with your parents, your siblings? • Is there anything you would like to change about your family?
Education	• Which school do you go to? What grade are you in? Any recent changes in schools? • What do you like best and least about school? Favourite subjects? Worst subjects? • What were your most recent grades? Are these the same or different from the past? • How much school did you miss last/this year? Do you skip classes? Have you ever been suspended? • What do you want to do when you finish school? • How do you get along with teachers? How do you get along with your peers? • Inquire about "bullying".
Employment	• Are you in any full time or part time job?
Eating	• What do you like and not like about your body? • Has there been any recent change in your weight? • Have you dieted in the last one year? How? How often? • How much exercise do you get on an average day ?Week? • Do you worry about your weight? How often? • Does it ever seem as though your eating is out of control? • Have you ever made yourself throw-up on purpose to control your weight?

Item	Examples of Questions
Activities	• Are most of your friends from school or somewhere else? Are they the same age as you? • Do you hang out with mainly people of your same sex or a mixed crowd? • Do you have a lot of friends? • Do you see your friends at school and on weekends, too? • Do you do any regular sport or exercise? Hobbies or interests? • How much TV do you watch? What are your favourite shows? • Dave you ever been involved with the police? Do you belong to a group or gang?
Drugs	• 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? • Have you or your friends ever tried any other drugs? Specifically, what? • Do you regularly use other drugs? How much and how often?
Sexuality	• Have you ever been in a relationship? When? • Have you had sex? Number of partners? Using contraception? • Have you ever been pregnant or had an abortion? • Have you ever been checked for a sexually transmitted infection (STI)? • Knowledge about STIs and prevention? • For females: Ask about menarche, last menstrual period (LMP), and menstrual cycles. Also inquire about breast self examination (BSE) practices. • For males: Ask about testicular self-examination (TSE) practices.

Item	Examples of Questions
Suicide, Depression	• Do you have difficulties to sleep? Has there been any change in your appetite recently? • Do you mix around well others? Do you have hopeless or helpless feelings? • Have you ever attempted suicide?
Safety	• Have you ever been seriously injured? Do you always wear a seatbelt in the car? • Do you use safety equipment for sports and or other physical activities (for example, helmets for biking)? • Is there any violence in your home? Does the violence ever get physical? • Have you ever been physically or sexually abused? • Have you ever been bullied? Is that still a problem? • Have you gotten into physical fights in school or your neighborhood? Are you still getting into fights?

Chapter 8: End of Life Care in Children

Introduction

Paediatric palliative care has been 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'. [1]

Causes of Paediatric Mortality (Malaysian Public Hospitals)

- In paediatric departments at Malaysian public hospitals, 70% of deaths occur in neonates and 30% are in older children. [2]
- Under Five Mortality Study data shows that 76% are hospital deaths; 24% are non hospital deaths.
- A third (33%) of hospital deaths were congenital malformations, deformations and chromosomal abnormalities; 5% had oncology disorders. It is difficult to ascertain the exact percentage who require palliative care in the latter group.

The data suggests that there is plenty of work to be done in paediatric palliative medicine and end of life care. Why is this important?

Impact of the lost of a child

- The care of dying children is different from adults as the dying process of a child affects many individuals with grief over the loss that is more intense, long lasting and complicated.[3] This is because children are generally expected to outlive their parents.
- Parental grief is the most severe form of grief [4]; with an associated increase in morbidity and mortality.[5] 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 psychiatric hospitalisation. [6] This risk is higher in bereaved mothers than bereaved fathers, the risk is highest in the 1st year following their child's death, and remains elevated for ≥ 5 years.[7]
- Care-related factors may influence parents' psychological outcomes.[8] Among factors that continued to affect parents 4-9 years following their child's death was the memory of the child having had unrelieved pain and experienced a 'difficult moment of death'. Interviews with 449 bereaved parents suggest that the child's physical pain and circumstances at the moment of death contributed to parents' long term distress.[9]

Quality of End of Life Care

Parents associated quality end of life care with physicians.[10]

- 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 contribute towards quality end of life care. A bereavement clinic follow up, or home visit, can be arranged in 6-12 weeks after 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 steps can be taken to help the patient and family. Existing medical orders and management strategies should be reviewed with the goal of enhancing comfort and decreasing noxious and invasive interventions.

Aspects of care that should be addressed are

- Discontinue parenteral nutrition. Enteral feeding reduced, discontinued or offered as a comfort measure; breastfeeding may be offered if desired by mother and baby; a lactation referral for breastfeeding mothers to stop milk production.
- Discontinue tests and treatments to minimize noxious or painful procedures.
- Intravenous access maintained for medications to decrease pain, anxiety or seizures. Alternatives to IV access are oral, sublingual or rectal medications.
- Discontinue antibiotics.
- Discontinue cardiac sustaining medications e.g. dopamine, adrenaline.
- Ventilator support: parents must be included in the decision to disconitnue mechanical ventilation support and should be provided with information about the expected sequence of events surrounding disconnection from the ventilator as well as the infant's physical response, including the possibility that the infant may not die immediately. [12]
- Moral and 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. discontinue 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 or wish list ; organ donation.
- Religious and spiritual needs of the parents and family.
- 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. hand prints, hair lock).
- Transitional care, family support, sibling support, staff support, organ donation, follow up support for family.

Neonatal Palliative Care Plan for the Infant 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 or 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 type 1.
- *Cardiac*
  Acardia, Inoperable heart anomalies, hypoplastic left heart syndrome, pentalogy of Cantrell (ectopia cordis).
- *Other structural anomalies*
  Certain cases of giant omphalocoele, 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 early.
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.

Neonatal Palliative Care Plan for the Infant with Lethal Anomalies

Comfort measures for babies:

- dry and warm baby, provide warm blankets.
- provide a 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)
- Suctioning of airway and secretions.
- 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 : _____

Note: 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:_____

References

Section 1 General Paediatrics

Chapter 1 Normal Values

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2.Nelson Textbook of Pediatrics, 18th Edition

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Introduction

- Transport of neonates involves **pre-transport intensive care level resuscitation and stabilisation and continuing intra-transport care** to ensure that the infant arrives in a stable state.
- Organized neonatal transport teams bring the **intensive care environment to critically ill infant before and during transport.**
- **Good communication and coordination** between the referring and receiving hospital is essential.
- **There is rarely a need for haste.**
- However, there must be a balance between the benefits of further stabilization versus anticipated clinical complications that may arise due to delay in the transport.

Special Considerations in Neonates
Apnoea
Premature and septic babies are especially prone to apnoea
Bradycardia
Hypoxia causes bradycardia followed by heart block and asystole
Oxygen toxicity to the lungs and retina
especially important in the premature infant
Reversal to fetal circulation (Persistent pulmonary hypertension of the neonate, PPHN)
Precipitating factors: hypoxia, hypercarbia, acidosis and sepsis
Hypothermia
Thermoregulation is less developed, infant has a larger body surface area to mass ratio. If bowels are exposed, heat and fluid loss are compounded by evaporation. The effects of hypothermia are acidosis and subsequent PPHN, impaired immune function and delayed wound healing.
Hypoglycemia
The neonate lacks glycogen stores in liver and fat deposits.

Mode of transport

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

- The best mode of transfer is “in utero”, e.g. a mother in premature labour should be managed in a centre with NICU facilities or for an antenatally detected surgical, the mother should be advised to deliver at a centre with paediatric surgical facilities.
- The advantages and disadvantages of road, air (helicopter / commercial airlines) and riverine transport must be considered in each child
- Transport incubators with monitors, ventilators, oxygen and suction equipment are ideal.

Air Transport

Patients can be transported by either commercial airlines with pressurised cabins or by helicopters flying without pressurised cabins at lower altitudes. There are special problems associated with air transport:

- *Changes in altitude* – Reduced atmospheric pressure causes decreased oxygen concentration and expansion of gases. This may be important in infants with pneumothorax, pneumoperitoneum, volvulus and intestinal obstruction. These must be drained before setting off as the gases will expand and cause respiratory distress. Infants requiring oxygen may have increased requirements and become more tachypnoeic at the higher altitude in non-pressurised cabins.
- *Poor lighting* - Can make assessment of child difficult .
- *Noise and Vibration* – May stress the infant and transport team; May also cause interference with the monitors, e.g. pulse oximeters. Use ear muffs if available. It is also impossible to perform any procedures during transport.
- *Limited cabin space* – Limits access to the infant especially in helicopters. Commercial aircraft and helicopters are unable to accommodate transport incubators. The infant is thus held in the arms of a team member.
- *Weather conditions and availability of aircraft* – Speed of transfer may be compromised by unavailability of aircraft/flight or weather conditions. Stress and safety to the infant 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: hospital – ambulance – helicopter – ambulance - hospital.
- *Finances* – Air transport is costly but essential where time is of essence.

Pre-transport Stabilisation

Transport is a significant stress and the infant may easily deteriorate during the journey. Hypothermia, hypotension and metabolic acidosis has a significant negative impact on the eventual outcome. Procedures are difficult to do during the actual transport. Therefore, pre-transport stabilization is critical.

The principles of initial stabilisation of the neonate

(see tables on following pages)

Airway
Breathing
Circulation, **C**ommunication
Drugs, **D**ocumentation
Environment, **E**quipment
Fluids – electrolytes, glucose
Gastric decompression

The principles of initial stabilisation of the neonate
Airway
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
Assess the need for intra-transport ventilation. Does the infant have: • Requirement of FiO2 60% to maintain adequate oxygenation. • ABG – PaCO2 > 60mmHg. • Tachypnoea and expected respiratory fatigue. • Recurrent apnoeic episodes. • Expected increased abdominal/bowel distension during air transport.
If there is a possibility that the infant needs mechanical ventilation during the transfer, it is safer to electively intubate and ventilate before transport. Check the position of the Endotracheal tube before setting off.
In certain conditions it may be preferable not to ventilate, e.g. tracheo-oesophageal fistula with distal obstruction. If in doubt, the receiving surgeon/paediatrician should be consulted. If manual ventilation is to be performed throughout the journey, possible fatigue and the erratic nature of ventilation must be considered.
Circulation
Assess: • Heart rate, Urine output, Current weight compared to birth weight - are good indicators of hydration status of the newborn infant. Also note that: • Blood pressure in infants drops just before the infant decompensates. • Minimum urine output should be 1-2 mls/kg /hr. • The infant can be catheterised or the nappies weighed (1g = 1 ml urine) • Ensure reliable intravenous access (at least 2 cannulae) before transport. • If the infant is dehydrated, the infant must be rehydrated before leaving.

The principles of initial stabilisation of the neonate

Communication

Good communication between referring doctor, transport team and neonatologist / paediatric surgeon aids proper pre-transfer stabilization, coordination, timing of transfer, and preparedness of receiving hospital.

- Inform receiving specialist, emergency department of receiving hospital.
- Provide Name and telephone contact of referring doctor and hospital
- Provide patient details
- Give a clear history, physical findings, provisional diagnosis, investigations
- Detail current management and status of the infant
- Discuss mode of transport, expected departure time, arrival at referral centre
- Decide on destination of the patient (e.g. A&E, NICU, Ward)

Drugs as required

- Antibiotics – needed in most sick neonates
- Analgesia or Sedation – if infant 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 for high risk infants and especially if parents are not accompanying child.
- Parents' contact address, telephone numbers, if not accompanying infant.
- 10 mls of Mother's blood for cross match, if she is not accompanying infant.

Environment

Maintain a **Neutral Thermal Environment**

Optimal temperature for the neonate (axilla) – 36.5 ^{0}C– 37.0 ^{0}C.

Prevention of heat loss involves maintaining an optimal ambient temperature as well as covering the exposed surfaces.

- Transport Incubator – would be ideal.
- Wrap limbs of the infant with cotton, metal foil or plastic.
- Do not forget a cotton-lined cap for the head.
- Remove all wet linen as soon as possible.
- Care of exposed membranes. (See section on Abdominal Wall Defects)
- Warm intravenous fluids.
- ELBW placed in polyethylene bags for newborn infants to prevent heat loss by evaporation.

The principles of initial stabilisation of the neonate

Environment (continued)

Special Consideration.
In **Hypoxic Ischaemic Encephalopathy**, *therapeutic hypothermia* may be indicated. Please discuss with receiving neonatal team prior to transfer.

Equipment *(see Table at end of chapter)*

Check all equipment: completeness and function before leaving hospital.

- Monitors- Cardiorespiratory monitor/ Pulse oximeter for transport. If unavailable or affected by vibration, a praecordial stethoscope and a finger on the pulse and perfusion will be adequate.
- Syringe and/or infusion pumps with adequately charged batteries. If unavailable, intravenous fluids prepared into 20 or 50ml syringes can be administered manually during the journey via a long extension tubing connected to the intravenous cannulae.
- Intubation and ventilation equipment; Endotracheal tubes of varying sizes.
- Oxygen tanks – ensure adequacy for the whole journey.
- Suction apparatus , catheters and tubings.
- Anticipated medication and water for dilution and injection.
- Intravenous fluids and tubings. Pre-draw fluids, medication into syringes if required during the journey.

Fluid therapy

Resuscitation Fluid

- Give boluses of 10 - 20 mls/kg over up to 2 hours as per clinical status
- Use Normal Saline or Hartmann's solution.
- If blood loss then use whole blood or pack red cells.

This fluid is also used to correct ongoing measured (e.g. orogastric) or third space losses as required. The perfusion and heart rates are reliable indicators of the hydration.

- If ongoing or anticipated losses in surgical neonates, e.g. gastroschisis, intestinal obstruction, , then use 0.45% Saline + 10% Dextrose
- Watch out for hyponatraemia and hypoglycemia.

Gastric decompression

- An orogastric tube is required in most surgical neonates, especially in intestinal obstruction, congenital diaphragmatic hernia or abdominal wall defects.
- The oral route is preferred as a larger bore tube can be used without compromising nasal passages (neonates are obligatory nasal breathers).
- As an orogastric tube is easily dislodged, check the position regularly.
- 4 hourly aspiration and free flow of gastric contents is recommended.

Immediately before Departure

- Check vital signs and condition of the infant.
- Check and secure all tubes.
- Check the equipment.
- **Re-communicate with receiving doctor about current status and expected time of arrival.**

Intra-transport Care

- **Transport Team.** Ideally, there should be a specialised neonatal transport team. Otherwise, a neonatal-trained doctor with/without a neonatal-trained staff nurse should escort the infant. A minimum of 2 escorts will be required for a ventilated/critically ill infant. The team should be familiar with resuscitation and care of a neonate.
- **Safety of the team must be a priority.** Insurance, life jackets and survival equipment should be available.
- **Monitoring.** Regular monitoring of vital signs, oxygenation and perfusion of the infant should be performed.
- **Fluids.** Intravenous fluids must be given to the ill infant to prevent dehydration and acidosis during the transport. Boluses need to be given as necessary depending on the haemodynamic assessment . If catheterised, the urine output can be monitored. The orogastric tube should be aspirated and kept on free drainage. Losses are replaced as required.
- **Temperature Regulation.** Check temperature intermittently. Wet clothes should be changed especially in the infant with abdominal wall defects. Disposable diapers and one way nappy liners are useful.

Arrival at the Receiving Hospital

- Reassessment of the infant
- Handover to the resident team

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, consider cessation of non-essential infusions.

Pre-Departure Checklist	
Equipment	
	Transport incubator (if available)
	Airway and intubation equipment are all available and working (ET tubes of appropriate size, laryngoscope, Magill forceps)
	Batteries with spares
	Manual resuscitation (Ambu) bags, masks of appropriate size
	Suction apparatus
	Oxygen cylinders-full and with a spare
	Oxygen tubing
	Nasal oxygen catheters and masks, including high-flow masks
	Infusion pumps
	Intravenous cannulae of various sizes
	Needles of different sizes
	Syringes and extension tubings
	Suture material
	Adhesive tape, scissors
	Gloves, gauze, swabs (alcohol and dry)
	Stethoscope, thermometer
	Nasogastric tube of different sizes
	Pulse oximeter
	Cardiac monitor if indicated
	Portable Ventilator if indicated
Patient Status	
	Airway is secured and patent (do a post-intubation chest X-ray before departure to make sure ET tube is at correct position.)
	Venous access is adequate and patent (at least 2 IV lines) and fluid is flowing well.
	Patient is safely secured in transport incubator or trolley.
	Vital signs are charted.
	Tubes - all drains (if present) are functioning and secured .

Pre-Departure Checklist *(continued)*	
Medications	
	Intravenous fluids • 0.9% Normal Saline • Hartmann's solution • 5% Albumin in Normal Saline • 0.18% Saline with 10% Dextrose • 0.45% Saline with10% Dextrose • 10% Dextrose water
	Inotropes • Dopamine • Dobutamine • Adrenaline
	Sedative/ Analgesia • Morphine • Midazolam
	Blood product if indicated
	Others • Atropine • Sodium bicarbonate • Sterile water for injection • Normal saline for injection • Antibiotics if indicated
Documentation	
	Patient notes, referral letter
	X-rays
	Consent form
	Vital signs chart
	Input, Output charts
	Maternal blood (for infant less than 6 months)

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.

Early and Late Complications in premature infants
Hypothermia
Respiratory distress syndrome, Apnoea
Hypotension, Patent ductus arteriosus
Intraventricular haemorrhage, Periventricular leukomalacia
Gastrointestinal: Paralytic ileus, Necrotizing enterocolitis
Hypoglycaemia, Hyperglycaemia
Neonatal Jaundice
Hypoprothrombinaemia
Fluid and Electrolyte disorders: hyponatraemia, hyperkalemia, metabolic acidosis
Septicaemia
Anaemia
Osteopaenia of prematurity
Retinopathy of prematurity
Chronic lung disease
Neuro-developmental disability
Psychosocial problems

Management

Before and During Labour

- Prewarmed incubator and appropriate equipment for neonatal intensive care should always be kept ready in the labour room or operating theatre.

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. For extremely low birth weight infant, from birth, the infant should be wrapped up to the neck with polyethylene plastic wrap or food plastic bag to prevent evaporative heat loss.

- **If infant's respiration is inadequate, keep the infant intubated with manual bag ventilation with oxygen during the transfer.**
- For those with mild respiratory distress, preferably initiate CPAP in labour room, and if tolerated CPAP during transport. Use a pulse oxymeter where available.

Admission Routine

- Ensure thermoneutral temperature for infant. An incubator or radiant warmer is necessary for more premature and ill infants.
- Ventilation in NICU is often necessary if ventilated during transfer. However, some infants take longer to adapt to extrauterine life and may not require ventilation especially those with no risk factors and given a full course of antenatal steroids. For the larger preterm infants above 1250 grams, review the required ventilation to maintain a satisfactory blood gas and consider extubation if the ventilator requirements are low, patient has good tone and good spontaneous respiration.
- Maintain SaO_2 between 89-92% for ELBW; 90-94% for the larger preterm
- Head circumference (OFC), length measurements, 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_2.

Immediate Care for Symptomatic infants

- 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 wks). Ensure hyperventilation is not present (a cause of hypotension). If the baby has good tone and is active, observe first as the BP may rise after first few hours of life towards a MAP approximating GA in weeks.
- Correct hypovolaemia: Give 10 ml/kg of Normal Saline over 20-30 mins, or packed cells if anaemic. Avoid repeat fluid boluses 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 or caffeine in premature infants <32-34 weeks.
- Maintain SaO_2 at 89-92% and PaO_2 at 50 –70 mmHg.

General Measures for Premature infants

- Monitor vitals signs (colour, temperature, apex beat, respiratory rate). Look for signs of respiratory distress (cyanosis, grunting, tachypnoea, nasal flaring, chest recessions, apnoea). In VLBL and ill infants pulse oximetry and blood pressure monitoring are necessary.
- Check Blood Sugar (see Hypoglycaemia protocol).
- Keep warm in incubator at thermoneutral temperature for age and birth weight. ELBW should preferably have humidified environment at least for the first 3 days.
- 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 vaccine is given on discharge.
  - For long stayers other immunisation should generally follow the schedule according to chronological rather than corrected age.
  - Defer immunisation in the presence of acute illnesses.
- Supplements:
  - At birth: IM Vitamin K (0.5 mg for BW<2.5 kg; 1 mg for BW ≥ 2.5 kg)
  - Once on full feeding, give Infant Multivitamin drops 1 mls OD (continue till fully established weaning diet). For preterm infants, use a formulation with Vit D 400 IU, 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 infants ≤ 32 weeks is 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 4-6 weeks of age is recommended for
  - All infants ≤ 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 35 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.

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.
- Normal caloric requirements in: **Term infants: 110 kcal/kg/day**
  Preterm infants : 120 – 140 kcal/kg/day
- Babies who have had a more eventful course need up to 180kcal/kg/day to have adequate weight gain.

Types 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 for **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 low 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 < 32 wks 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 ≥ 32 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 gained 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 the baby is able to suckle and mother is not with the baby, cup feeding is preferable to bottle feeding to prevent nipple confusion.

When to start milk?

- As soon as possible for the well term babies
- However, in very preterm infants there may be an increased risk for NEC if feeding is advanced too rapidly, although early feeds with EBM is to be encouraged. Studies suggest that rapid increments in feeds 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 breastfeeding 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.

What is the maximum volume?

- Target weight gain should be around 15g/kg/day (range 10-25g/kg/day). Less weight gain than this suggests a need to increase calories especially protein calories.. More weight gain than 30g/kg/day 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. (This should only be achieved by Day 10 to Day 14 respectively if baby had tolerated feeds well from Day 1)
  - If on EBM, when volume reaches 75 mls/kg/day: add HMF.
- Term infants: allow feeding on demand.

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.
- Preterm with poor weight gain can be given specially formulated post discharge formula for preterm infants. Preterm formula meant for newborn preterm infants should not be given to infants > 2 months post conceptual age in view of potential Vitamin A and D toxicity.

Vitamin and mineral supplementation

- *Vitamins*: a premature infant's daily breast milk/ breast milk substitute intake will not supply the daily vitamin requirement. Multivitamins 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.
  - 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 show that these babies are at risk of NEC. Thus feeds should be introduced slowly and initially use only EBM.

Composition of Various Milk

Component		Cow's milk	Standard formula	Mature breastmilk	Preterm formula	Preterm breastmilk
Carbohydrate	g/100ml	4.6	7.5	7.4	8.6	6.4
Fat	g/100ml	3.9	3.6	4.2	4.4	3.1
Protein	g/100ml	3.4	1.5	1.1	2.0	2.7
Casein : Lactalbumin ratio		4:1	2:3	2:3	2:3	2.3
Calories	KCal/100ml	67	67	70	80	74
Sodium	mmol/l	23	6.4	6.4	14	17
Potassium	mmol/l	40	14	15	19	17
Calcium	mg%	124	46	35	77	29
Phosphate	mg%	98	33	15	41	13
Iron	mg%	0.05	0.8	0.08	0.67	

Chapter 12: 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 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 growth rates without increased significant morbidity.

Indication for TPN

- Birth weight < 1000 gm
- Birth weight 1000-1500 gm and anticipated to be not on significant feeds for 3 or more days.
- Birth weight > 1500 gm and anticipated to be not on significant feeds for 5 or more days.
- Surgical conditions in neonates: necrotizing enterocolitis, gastroschisis, omphalocoele, tracheo-esophageal fistula, intestinal atresia, malrotation, short bowel syndrome, meconium ileus and diaphragmatic hernia.

Components of TPN

The essential components of parenteral nutrition are:

- Fluids
- Carbohydrate
- Protein
- Lipids
- Electrolytes
- Vitamins
- Trace minerals

Goal is to provide 120-130 KCal/kg/day.

- 10% dextrose solution provides 0.34 KCal/ml.
- 10% lipid solution gives 0.9 KCal/ml; 20% lipid solution gives 1.1 KCal/ml.
- Protein/Energy ratio: 3-4 gm/100 KCal is needed to promote protein accretion. A baby given only glucose will lose 1.5 grams body protein/day.

Thus it is important to start TPN within the first 24 hours of life in the smaller preterm infants <1250 grams birth weight.

Fluid

- Fluid is an essential component.
- Usually started at 60-80 ml/kg/day (if newborn), or at whatever stable fluid intake the baby is already receiving.
- Postnatal weight loss of 5 - 15 % per day in the ELBW is acceptable. Volumes are increased over the first 7 days in line with the fluids and electrolytes protocol with the aim to deliver 120-150 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 the secretion of insulin and insulin-like growth factors.
- Protein is usually started at 2g/kg/day of crystalline amino acids and subsequently advanced, by 3rd to 4th postnatal day, to 3.0 g/kg/day of protein in term and by 5th day 3.7 to 4.0 g/kg/day in the extremely low birthweight (ELBW) infants.
- 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.
- Hyperglycaemia occurs in 20-80% of ELBW as a result of decreased insulin secretion and insulin resistance, presumably due to 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 started at 6 mg/kg/min, advancing to 12-14 mg/kg/min and adjusted to maintain euglycaemia.
- If hyperglycaemia develops glucose infusion is decreased. Insulin infusion is generally not required if sufficient proteins are given and less glucose is administered during the often transient hyperglycaemia. Insulin infusion, if used for persistent hyperglycaemia with glycosuria, should be titrated to reduce risk of hypoglycaemia.

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. Some conditions inhibit lipid clearance e.g. infection, stress, malnutrition.
- Start lipids at 1g/kg/day, at the same time as amino acids are started, to prevent essential fatty acid deficiency; gradually increase dose 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 and provide a lower phospholipid-to-triglyceride ratio. 10% solution interferes with triglyceride (TG) clearance leading to higher TG and cholesterol values. Use of preparations containing lipids from fish oil and olive oil may reduce the risk of cholestasis with prolonged TPN.
- Heparin at 0.5 to 1 units/mL of TPN solutions (max 137 units/day) can facilitate lipoprotein lipase activity to stabilize serum triglyceride values.
- Lipid clearance monitored by plasma triglyceride (TG) levels. (Max TG concentration ranges from 150 mg/dl to 200 mg/dl).
- Exogenous lipid may interfere with respiratory function. Suggested mechanisms include impaired gas exchange from pulmonary intravascular accumulation or impaired lymph drainage resulting in oedema. Lipid may also aggravate pulmonary hypertension in susceptible individuals.
- The syringe and infusion line should be shielded from ambient light.

Electrolytes

- The usual sodium need of the newborn infant is 2-3 mEq /kg/day in term and 3-5 mEq/kg/day in preterm infants after the initial diuretic phase(first 3-5 days). Sodium supplementation should be started after initial diuresis(usually after the 48 hours), when serum sodium starts to drop or at least at 5-6% weight loss. Failure to provide sufficient sodium may be associated with poor weight gain.
- Potassium needs are 2-3 mEq/kg/day in both term and preterm infants. Start when urine output improves after the first 2-3 days of life.

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

- In extrauterine conditions, intrauterine calcium accretion rates is difficult to attain. Considering long-term appropriate mineralization and the fact that calcium retention between 60 to 90 mg/kg/d suppresses the risk of fracture and clinical symptoms of osteopenia, a mineral intake between 100 to 160 mg/kg/d of highly-absorbed calcium and 60 to 75 mg/kg/d of phosphorus could be recommended.
- 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 level does not give rise to major problems.

Trace Elements

- Indicated if PN is administered for ≥ 1 week. Commercial preparations are available.

Vitamins

- Both fat and water soluble vitamins are essential. It should be added to the 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 are only suitable for TPN ≤ 3 days duration and dextrose concentration ≤ 12.5%.
- Peripheral lines are also limited by osmolality (<600 mOsm/L) to prevent phlebitis.
- Percutaneous central line: confirm catheter tip position on X-ray prior to use.
- Ensure strict aseptic technique in preparation and administration of TPN.
- Avoid breakage of the central line through which the TPN is infused, though compatible drugs may be administered if necessary.

Caution

- **Hyperkalaemia.** Potassium is 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 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; requires 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
- Random blood sugar/dextrostix
- Liver function test, serum bilirubin

While on TPN, monitoring required :

Laboratory

- Full blood count, plasma sodium, potassium and creatinine. Daily for 1 week then 2-3 times a week until stable.
- Plasma calcium, magnesium, phosphate. Twice/wk 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 for infection.

Prevention of hospital acquired infection

- Aseptic precautions during preparation of PN.
- Use of laminar air flow.
- No compromise on disposables.
- Trained staff.
- No reuse of the PN solutions.
- No interruption of the venous line carrying PN.
- Use of bacterial filter in AA-glucose line.

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. Initial drop in weight is expected for newborn infants, term up to 10% BW in first 3-5 days, preterms up to 15% in first 1 week. Less weight loss is expected with use of humidified incubators. Abnormal weight gain/loss in the first days implies suboptimal fluid therapy.
- *General condition.*

  Note*:* ill, unstable, handles poorly e.g. desaturates on handling, stable, active, responsive to handling, improving, or good tone.
- *Cardiopulmonary system*
  - Check for:
    (i) Adequacy of the blood pressure – an estimate of normal BP for preterm infant is that of the gestational age at birth. However, there is no necessity to treat immediately if the baby is stable, responsive and of good tone. Review after one hour to check for improvement in the BP.
    (ii) Signs of poor perfusion (with poor peripheral pulses, rapid pulse, poor capillary refilling and cold peripheries) – but these signs have not been found to be very reliable for hypotension. Hypothermia can also be a cause of poor perfusion.
    (iii) Examine for presence of a patent ductus arteriosus (PDA) in preterm infants.
  - If BP is low and there has been a history of volume loss at birth or risk of sepsis, 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 in severely hypotensive infants. Caution: Risk of IVH in repeat doses especially in ELBW or ill preterm infants – check first for volume loss or reduced vascular volume due to extravascular fluid losses such as in sepsis or intestinal obstruction. Albumin is required only in severe sepsis such as in NEC.
  - Inotropic agents like adrenaline, dobutamine or dopamine may be needed. Consider hydrocortisone in ill preterm infant at birth if no response to volume or inotropes. Check that there is no iatrogenic hyperventilation as a cause of hypotension.
- *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 for preterm infants, i.e. of 20 mls/kg/day. More increments may be needed if evidence of dehydration, i.e. excessive weight loss and hypernatraemia >145 mmol/l.

- Generally, 10% Dextrose fluid is given on the 1st day; and Sodium and Potassium added on the second/third day.
- Total parenteral nutrition should be started as soon as possible for the infant below 1000 -1250 grams, preferably within the first day of life. Larger preterm infants may be started on parenteral nutrition if expected to not able to be fed enterally for 5 or more days (for eg congenital diaphragmatic hernia, omphalocele/gastrochiasis) .
- Empirically:
  - A preterm infant need 4-5 mmol/kg/day of sodium and 2-3 mmol/kg/day of potassium, after the first few days of life.
  - ELBW infants are prone for hyperkalaemia and adjustments should be made based on serum electrolytes.
  - Term infants need 2-3 mmol/kg/day of both sodium and potassium.
- Fluid and electrolyte therapy are influenced by underlying illness, complications: make neccesary adjustments based on these conditions, intake/output, weight, blood urea and electrolytes (BUSE).
  - Monitor BUSE; correct any imbalances after considering underlying cause.
  - Ensure the urine output is > 1 ml/kg/hr after the first day of life.5

- *Infection*
  - Is there a possibility of infection? Is the child on antibiotics?
  - Fungal infection should be considered if the infant is a preterm infant who has been on several courses of broad spectrum antibiotics and on total parenteral nutrition. Consider discontinuing antibiotics if the blood culture is negative and the patient improved “too quickly” after starting antibiotics, probably responding to other measures to improve dehydration or inadequate ventilatory support.
- *Feeding*
  - Enteral feeds can be given via oro or nasogastric tube. Orogastric tube is preferred in small infants as it prevents blockage of airway.
  - Encourage expressed breast milk to be started within the first 2 days of life.
- *Temperature Control*
  - ***Use of cling wrap/plastic wrap with cap for preterm infants soon after delivery will help maintain normothermia.***
  - Under the radiant warmer, 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. Transfer to a closed humidified incubator as soon as possible. Ensure thermoneutral environment. Humidity is essential to maintain temperature in the extremely preterm infants and reduce excessive weight loss in the first few weeks of life. Below is a humidification guide for preterm infants.

26 weeks gestation and below	27-30 weeks gestation
80% Humidity for at least 4 wks (may require higher % to cope with increased sodium)	80% Humidity for at least 2 wks
The infant's skin should have keratinised fully at the end of this period, therefore the humidity can be gradually reduced, as tolerated, to maintain a satisfactory axillary temperature	
Reduce the humidity gradually according to the infant's temperature (70% - 60% - 50%) until 20-30% is reached before discontinuing.	

- *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.
  - Group your blood taking together to minimise skin breaks/ breakage of indwelling arterial lines.
  - Observe limbs and buttocks prior to insertion of umbilical lines and at regular intervals afterwards to look for areas of pallor or poor perfusion due to vascular spasm.
- *Central nervous system*
  - Check fontanelle tension and size, condition of sutures i.e. overriding or separated, half-hourly to hourly head circumference monitoring (when indicated e.g. infants with subaponeurotic haemorrhage).
  - Sensorium, tone, movement, responses to procedures e.g. oral suctioning, and presence or absence of seizure should be noted.
- *Ventilation*
  - Check if ventilation is adequate. Is the child maintaining the optimum blood gases? Can we start weaning the child off the ventilator?
  - Overventilation is to be avoided as it may worsen the infant's condition.

Endotracheal tube (ETT) Care

Infant weight	ETT size	ETT position (oral)[1,2,3]
<1000g	2.5	
1000g-2000g	3.0	7 cm
2000g-3000g	3.5	8 cm
>3000g	3.5-4.0	9 cm

Footnotes:
1. oral ETT "tip-to-lip" distance; 2. or weight in kg + 6
3. for nasal ETT: add 2 cm respectively; For 1 kg and below - add 1.5 cm
Note:
The length of ETT beyond the lips should be checked as to be just sufficient for comfortable anchoring and not excessively long so as to reduce dead space.

Suction of ETT

- Performed only when needed, as it may be associated with desaturation and bradycardia.
- During suctioning, the FiO_2 may need to be increased as guided by the SaO_2 monitor during suctioning.
- Remember to reduce to the level needed to keep SaO_2 89-95%.

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

- Do not use iodine to prepare the skin for UAC or UVC placement .
- Do not allow the solution to pool under the infant as it may burn the skin particularly in the very low birthweight infant.
- Change any damp or wet linen under the infant immediately following the procedure.
- Sterile procedure is required for inserting the lines.
- For other than the time of insertion, wash hands or use alcohol rub before taking blood from the UAC.
- Ensure aseptic procedure when handling the hub or 3 way tap of the line to withdraw blood.
- **UAC position**
  - Length to be inserted measured from the abdominal wall is:
    3 X BW(kg) + 9 cm.
  - Confirm with X-ray to ensure that the tip of the UAC is between T6 to T9 or between L3-L4.
  - Reposition promptly if the tip is not in the appropriate position. The high positioning of the UAC is associated with less thrombotic events than the low position.
  - The UAC is kept patent with a heparin infusion (1U/ml) at 1 ml/hr and can be attached to the intra-arterial blood pressure monitor.

- **UVC position**
  - Length to be inserted measured from the abdominal wall is:
    ½ UAC length as calculated above +1 cm.
  - This usually put the tip above the diaphragm. However, this formula is not as accurate as using catheter length based on shoulder umbilical length. (Check available graph) . The shoulder umbilical length is taken as a perpendicular line dropped from the shoulder to the level of the umbilicus.
  - Placement of the catheter tip in the portal circulation or liver is not acceptable and catheter should be removed and a new catheter inserted under sterile technique. In an emergency situation, it can be withdrawn to the level of the umbilical vein to be used for a short period until an alternative venous access is available.
- Remember to add on the length of the umbilical stump for calculating the length of both UAC and UVC.

Ventilation

- Initial ventilator setting (in most situations):

Total Flow:	8 - 10 litres/min
Peak Inspiratory Pressure (PIP):	20-25 mmHg (lower in ELBW infants and those ventilated for non-pulmonary cause, i. e normal lungs)
Positive End Expiratory Pressure (PEEP):	4 - 5 mmHg
Inspiration Time:	0.3- 0.35 sec
Ventilation rate:	40- 60 / min
FiO_2:	60 to 70% or based on initial oxygen requirement on manual positive pressure ventilation.
When Volume Guarantee is used:	VG = 4 – 6 ml/kg

- 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	7.25 - 7.40
	PaO_2	50 - 70 mmHg for premature infants 60 - 80 mm Hg for term infants
	$PaCO_2$	40 - 60 (NB. the trend is not to 'chase' the $PaCO_2$ by increasing ventilator settings unless there is respiratory acidosis).
	SaO_2	89 - 92% for preterm infants.

- Changing of ventilator settings:
  - To produce an increase in PaO_2 either: -
    - Increase FiO_2 concentration.
    - Increase PEEP.
    - Increase PIP (increases minute volume).
    - *rarely*, increase I/E ratio (prolong inspiration).
  - To produce a decrease in $PaCO_2$ either: -
    - Increase Rate (increases minute volume).
    - Decrease I/E ratio (prolong expiration).
    - Increase PEEP in worsening lung disease.
    - Decrease PEEP in recovery phase.
    - Increase Targeted Volume in Ventilation
  - Do the opposite to decrease PaO_2 or to increase $PaCO_2$.
- Minute volume = tidal volume (volume per breath) x rate per minute. Minute volume should be about 0.1 – 0.3L/kg/min
- With volume-limited settings, minute volume can be calculated (use tidal volume = 4-6 ml/kg).
- With pressure-limited mode - increasing peak inspiratory pressure results in increased minute volume.

Sedation and Ventilation

- Avoid the use of paralysing agents as far as possible. Paralysis has been shown to result in poorer lung function, more dependent oedema and longer duration of ventilation.
- Use morphine infusion as an analgesia and sedative, if required.

Consider the following if the child *deteriorates* on ventilation:
Worsening of primary condition, e.g. RDS or congenital pneumonia
Mechanical problems : • ETT Dislodged or Obstructed • ETT displaced/ too deep • Pneumothorax • Ventilator tubes disconnected • Ventilator malfunction
Overventilation of the lung
Pneumonia such as nosocomial pneumonia
PDA or heart failure
Persistent pulmonary hypertension

High Frequency Oscillatory Ventilation (HFOV)

Indications

- When conventional ventilation fails HFOV should be considered. This is to be discussed with the specialist.
- Care should be taken not to overinflate the lungs as this can lead to further deterioration of child's condition – i.e. worsening saturation, hypotension.

Practical management

- Switching from conventional ventilation to HFOV :
  - Initial setting
    - Leave FiO_2 level at the same level as that on conventional ventilation.
    - MAP - For RDS, start at 2 cmH_2O above the MAP of conventional ventilation. In cases of air trapping, start MAP at same level as conventional ventilation and adjust according to CXR and blood gas.
    - Amplitude - 50-100% (Draeger Babylog 8000), Amplitude in Sensor Medic (start with twice MAP value); adjust until chest and upper abdomen vibrates but not whole abdomen.
    - Frequency - 10Hz.
    - Tidal volume - about 2 to 2.5ml/kg. (VThf on Draeger Babylog 8000)
  - Continuation of HFOV
    - Chest X-ray after 30-60 minutes, aim for lung expansion to 8-9th rib level
    - Hypoxia - increase MAP or FiO_2 if not already on FiO_2 of 1.0
    - Hyperoxia - reduce FiO_2 or decrease MAP (MAP to be reduced first if CXR shows diaphragm to be below T9 or flattened or hyperinflated lung fields)
    - Hypercapnia
      - Increase amplitude
      - Decrease frequency
      - Increase MAP (if persistent or lung volume still poor)

- Hypocapnia
  - Decrease amplitude.
  - Increase frequency.
  - Decrease MAP.
- Overinflation
  - Reduce MAP.
  - Consider discontinuing HFOV.

- Weaning
  - Reduce FiO2 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.

Guidelines for packed red blood cells (PRBCs) transfusion thresholds for preterm neonates.

< 28 days age, *and*	• Assisted ventilation with FiO_2 > 0.3: Hb 12.0 gm/dL or PCV < 40% • Assisted ventilation with FiO_2 < 0.3: Hb 11.0 g/dL or PCV < 35% • CPAP: Hb < 10 gm/dL or PCV <30%
> 28 days age, *and*	• Assisted ventilation: Hb < 10 gm/dL or PCV < 30% • CPAP: Hb < 8 gm/dL or PCV < 25%
Any age, breathing spontaneously, *and*	• On FiO_2 > 0.21: Hb < 8 gm/dL or PCV < 25%* • On Room Air: Hb < 7 gm/dL or PCV < 20%* **Consider transfusion if there is poor weight gain or metabolic acidosis as an indication of tissue hypoxia.*

Guidelines for platelet transfusions in non-immune thrombocytopaenic neonates

Platelet count < 30,000/mm^3	• Transfuse all neonates, even if asymptomatic
Platelet count 30,000/mm^3 - 50,000/mm^3	Consider transfusion in • Sick or bleeding newborns • Newborns <1000 gm or < 1 week of age • Previous major bleeding tendency (IVH grade 3-4) • Newborns with concurrent coagulopathy • Requiring surgery or exchange transfusion
Platelet count 30,000/mm^3 - 99,000/mm^3	• Transfuse only if actively bleeding.

Thromboembolism (TE) is being increasingly recognised as a significant complication of intravascular catheters in sick newborn infants. Many factors contribute to neonatal catheter-related thrombosis, including the small caliber of the vessel, endothelial damage, abnormal blood flow, design and site, duration of catheterisation and composition of the infusate, in addition to the increased risk of thrombus formation in sick infants. Sepsis and catheters are the most common correlates of thrombosis in the NICU.

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 ultrasonagraphy – portable, non-invasive, useful to monitor progress over time. False positive and false negative results may 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 4 mm/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. An urgent doppler ultrasound scan is needed 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 a paediatric haematologist, 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.
    - Known history of heparin induced thrombocytopaenia or allergy to heparin.

- Relative contraindications –
  - Platelet count < 50,000 x 10^9 /L.
  - Fibrinogen levels < 100mg/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 below.
    - Optimal duration is unknown but therapy is usually given for 5-14 days
    - Monitor thrombus closely during and following treatment.
    - Anti- Factor X activity (if available) aimed at 0.3-0.7 U/mL.
    - Baseline aPTT is prolonged at birth and aPTT prolongation is not linear with heparin anticoagulant effect. Therefore Anti factor X activity more effectively monitors UFH use in newborn infants.

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

- *A loading dose of 75 U/kg over 10 min followed by a maintainence 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 aPTT is in therapeutic range, a complete blood count and aPTT should be checked daily or as clinically indicated.*
- *For preterm infants, loading dose is 50U/kg.*
- *Initial maintenance dose for newborn < 28 weeks: 15U/kg/hr, newborn 28-36 weeks : 20U/kg/hr*

Abbreviations: aPTT, activated partial thromboplastin time.

- Complications: bleeding, heparin-induced thrombocytopaenia.
- Antidote: Protamine sulphate – see Table below for dosage.

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 thrombocytopaenia is rarely associated with LMWH.
  - Antidote: Omit 2 doses if an invasive procedure is required. Protamine is partially effective, dosage 1mg/100U heparin given within the last 3-4 hrs.

Age	Initial treatment dose	Prophylactic dose
< 2 months	1.5 mg/kg q12h	0.75 mg/kg q12h
> 2 months	1 mg/kg q12h	0.5 mg/kg q12h

Therapeutic dose range may vary from 0.95-3.5mg/kg/q12h.
Note :
- LMWH has specific anti-factor Xa activity.
- Therapy is monitored using anti-Factor Xa and not APTT (aim for anti-Factor Xa levels of 0.5-1U/mL), monitoring 4 hours after dosage adjustment; weekly once therapeutic level attained.
- Monitoring of anti-FXa levels may not be available in some laboratories.

- Thrombolytic agents
  - Consider thrombolytic agents (r-tPA: recombinant tissue plasminogen activator, streptokinase) if there is major vessel occlusion causing critical compromise of organs or limbs.
  - Supplemental plasminogen (in the form of FFP) enhances 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 hrs 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.

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

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 available in case of 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/dlL with cryoprecipitate (1 unit/5 kg); 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.

- Surfactant therapy for respiratory distress syndrome (RDS) is standard care for preterm infants, based on numerous randomised controlled trials demonstrating decreased mortality.
- Surfactant therapy reduces mortality rates most effectively in infants < 30 weeks and those of birthweight < 1250 gm.
- The guideline below is to address how to optimally use surfactant and in which subpopulation of preterm infants.
- The approach should be an individualised one based on clinical appraisal as given in the guideline below.
- Not all preterm infants have RDS and many of them initially have sufficient surfactant to establish relatively normal ventilation before other factors such as hypothermia, atelectasis or ventilation trauma inactivates the surfactant.
- The use of antenatal steroids has also reduced the incidence of RDS.

Who to give surfactant to?

- **Depressed preterm infants who have no spontaneous respiration after 30 seconds of ventilation** with T-piece resuscitator or resuscitation bag with CPAP attachment and pressure manometers, and thus require positive pressure ventilation (PPV).
- **Preterm infants below 28 weeks gestation** who are given only CPAP from birth in delivery room, i.e. the infant has spontaneous respiration and good tone at birth. Surfactant to be given within 30 minutes after birth. Decision as to whether to leave the patient intubated after surfactant depends on the lung compliance, severity of RDS and degree of prematurity
- **Preterm infants between 28-32 weeks** – to have CPAP from birth in delivery room. To assess requirement for surfactant in NICU based on oxygen requirement of FiO_2 > 30% and respiratory distress.
  To consider INSURE technique – INtubate, SURfactant, Extubate to CPAP
- **More mature or larger infants** should also be given surfactant if the RDS is severe i.e. arterial alveolar (a/A) PO_2 ratio of <0.22 or Fraction of inspired (FiO_2) > 0.5

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

- To be considered in **severe meconium aspiration syndrome with type II respiratory failure** – to be used prior to high frequency oscillatory ventilation and nitric oxide to allow the lungs to "open" optimally.

Timing of therapy

- Attempts to treat with surfactant before the infant can breathe resulted in more bronchopulmonary dysplasia than early treatment in delivery room because it interferes with initial stabilisation of the infant. Therefore surfactant delivery within the first minute of life is not indicated.

- The first dose has to be given as early as possible to the preterm infants requiring mechanical ventilation for RDS. The repeat dose is given 4-6 hours later if FiO_2 is still > 0.30 with optimal tidal volume settings forthose below 32 weeks and if FiO_2 > 0.40 and CXR still shows moderate to severe RDS ("white" CXR) for those infants > 32 weeks gestational age.

Types of surfactant and dosage

There are two types of surfactant currently available in Malaysia

- Survanta , a natural surfactant, bovine derived
  Dose : 4 ml/kg per dose.
- Curosurf , a natural surfactant, porcine derived (not in Blue Book)
  Dose: 1.25 mls/kg per dose.

Method of administration

- Insert a 5 Fr feeding tube that has been cut to a suitable length so as not to protrude beyond the tip of the ETT on insertion, through the ETT. If the surfactant is given soon after birth, it will mix with foetal lung fluid and gravity will not be a factor. Therefore no positional changes are required for surfactant given in delivery room.
- Surfactant is delivered as a bolus as fast as it can be easily be pushed through the catheter. Usually this takes 2 aliquots over a total of a few minutes. Continue PPV in between doses and wait for recovery before the next aliquot, with adjustments to settings if there is bradycardia or desaturation. Administration over 15 minutes has been shown to have poor surfactant distribution in the lung fields.
- Alternatively the surfactant can be delivered through the side port on ETT adaptor without disconnecting the infant from the ventilator. There will be more reflux of surfactant with this method.

Monitoring

- Infants should be monitored closely with a pulse oximeter and regular blood gas measurements. An indwelling intra-arterial line wiould be useful. Ventilator settings must be promptly wound down to reduce the risk of pneumothorax and ventilator induced lung injury. Consider extubation to CPAP if the oxygen requirement is less than 30% and there are minimal pressure requirements.

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 till the end of the first month and hence renal regulation of acid base may not be optimal.

Causes of Acidosis	
Metabolic acidosis	Respiratory acidosis
Renal failure	Asphyxia (injury to respiratory centre)
Septicaemia	
Hypoxia	Obstruction to respiratory tract e.g. secretions, blocked endotracheal tube
Hypothermia	
Hypotension	Respiratory distress syndrome (RDS)
Cardiac failure	Pneumonia
Dehydration	Pulmonary oedema
Hyperkalaemia	Apnoea
Hyperglycaemia	
Anaemia	
Intraventricular haemorrhage	
Drugs (e.g. acetazolamide)	
Metabolic disorders	
Causes of Alkalosis	
Metabolic alkalosis	Respiratory alkalosis
Sodium bicarbonate	Asphyxia (overstimulation of respiratory centre)
Pyloric stenosis	
Hypokalaemia	Over-ventilation while on mechanical ventilation
Drugs (e.g.thiazides and frusemide)	

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 $PaCO_2$ in respiratory acidosis increases cerebral blood flow and risk of intraventricular haemorrhage.

- Alkalosis
  - Over-excitability of the central nervous system.
  - Decreased cerebral blood flow - causing cerebral ischaemia, convulsions

Measurement of Acid Base Status

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

Normal values:

pH	7.34-7.45
$PaCO_2$	5.3-6.0 kpa (40-45 mmHg)
HCO_3^-	20-25 mmol/L
PaO_2	8-10 kpa (60-75 mmHg)
BE	± 5 mmol/L

Interpretation of Blood Gases

- pH < 7.34 : *acidosis*
  - If $PaCO_2$ and HCO_3 are low and base deficit is high: *metabolic acidosis.*
  - If $PaCO_2$ and HCO_3 are high and base excess is high: *respiratory acidosis.*
  - If both $PaCO_2$ and base deficit are high: *mixed metabolic and repiratory acidosis.*
- pH > 7.45: *alkalosis*
  - If $PaCO_2$ is low: *respiratory alkalosis*
  - If HCO_3 and base excess are high: *metabolic alkalosis*

  Acidosis and alkalosis may be partially or fully compensated by the opposite mechanism.
- Low $PaCO_2$: *hypocarbia*; high $PaCO_2$: *hypercarbia*

  Permissive hypercapnia (PCO_2 45-55 mmHg) is an important ventilation technique to reduce the risk of volume trauma and chronic lung disease.
- Low PaO_2: *hypoxaemia*; high PaO_2: *hyperoxaemia*

Management of Metabolic Acidosis and Alkalosis

- Treat underlying cause when possible.
- Do not treat acute metabolic acidosis by hyperventilation or by giving bicarbonate. This may correct pH but has deleterious effects on cardiac output and pulmonary blood flow. The use of sodium bicarbonate in acute resuscitative conditions is not advocated by the current body of evidence.
- Volume expansion (i.e., bolus 10 mL/kg of 0.9% Normal Saline) should not be used to treat acidosis unless there are signs of hypovolemia. A volume load is poorly tolerated in severe acidosis because of decreased myocardial contractility.
- $NaHCO_3$ should be used only in the bicarbonate-losing metabolic acidoses such as diarrhea or renal tubular acidosis.
- Dose of $NaHCO_3$ for treatment of metabolic acidosis can be calculated by:

  Dose in mmol of $NaHCO_3$ = Base deficit (mEq) x Body weight (kg) x 0.3
- Do not give $NaHCO_3$ unless infant is receiving assisted ventilation that is adequate. With inadequate ventilation, $NaHCO_3$ will worsen acidosis from liberation of CO_2.

- 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 $PaCO_2$ 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. .

(DOPE mnemonic: Displacement, Obstruction, Pneumothorax and Equipment Failure)

- A swift rise in $PaCO_2$ often accompanied by hypoxia following weaning is often an indication that the infant is not ready for weaning.
- A gradual rise in $PaCO_2$ 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 $PaCO_2$ in a infant on a ventilator means overventilation, hence treatment is to wean down the ventilation settings.

Interpretation of Blood Gases

Examples of Arterial Blood Gas (ABG) Interpretation

1. A 29 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
$PaCO_2$	6.6 kPa
PaO_2	7.5 kPa
HCO_3	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
$PaCO_2$	7.0 kPa
PaO_2	10.0 kPa
HCO_3	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
$PaCO_2$	8.0 kPa
PaO_2	8.0 kPa
HCO_3	35 mmol/L
BE	+10 mmol/L

Q: What does the ABG show?
A: Compensated respiratory acidosis

Q: What is a likely diagnosis?
A: Chronic lung disease.

4. An infant of 30 weeks' gestation and BW 1.3 kg is on a ventilator. ABG shows:

pH	7.35
$PaCO_2$	3.0 kPa
PaO_2	15.0 kPa
HCO_3	12 mmol/L
BE	-12 mmol/L

Q: Interpret the ABG
A: Compensated metabolic acidosis by respiratory alkalosis and hyperoxaemia

Q: What is your next course of action?
A: Reduce FiO_2, treat any contributory cause of acidosis and wean down ventilation settings.

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

pH	7.16
$PaCO_2$	10.0 kPa
PaO_2	6.0 kPa
HCO_3	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	7.2
$PaCO_2$	4.5 kPa
PaO_2	3.0 kPa
HCO_3	8 mmol/L
BE	-15 mmol/L

Q: What does the ABG show?
A: Metabolic acidosis with severe hypoxaemia.

Q: What is your next course of action ?
A: Consider prostaglandin infusion, confirm heart defect by Echocardiography, consider reducing ventilation.

Pearls
Conversion of kPa to mmHg is a factor of 7.5.

Chapter 17: Neonatal Encephalopathy

- Neonatal Encephalopathy (NE) is a clinical syndrome of disturbed neurological function, caused by failure to make a successful transition to extrauterine gas exchange
- Manifests in a difficulty in initiating and maintaining spontaneous respiration, depression of muscle tone and reflexes, depressed consciousness and often seizures.
- Occurs in 3.5 - 6/1000 live births; usually affects full term infants.
- 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 aetiologies such as CNS malformation, infection, multiple gestation, IUGR, maternal autoimmune disorders, metabolic disorders, drug exposure, and neonatal stroke as possible causes of the encephalopathy.
- Risk factors for neonatal encephalopathy were mainly seen in the antenatal period (69%) as compared to the intrapartum period (25%) in a large Western Australian study. Only 4% were due to intrapartum hypoxia.

HIE in newborn requires the presence of all 3 of the following criteria:
1. Presence of a clinically recognized encephalopathy within 72 hrs of birth.
AND
2. Three or more supporting findings from the following list:
• Arterial cord pH < 7.00
• Apgar score at 5 minutes of 3 or less
• Evidence of multiorgan system dysfunction within 72 hours of birth
• Evidence of foetal distress on antepartum monitoring: persistent late decelerations, reversal of end-diastolic flow on Doppler flow studies of the umbilical artery or a biophysical profile of 2 or less
• Evidence of CT, MRI, technetium or ultrasound brain scan performed within 7 days of birth of diffuse or multifocal ischaemia or of cerebral oedema.
• Abnormal EEG: low amplitude and frequency, periodic, paroxysmal or isoelectric.
AND
3. The absence of an infectious cause, a congenital malformation of the brain, an inborn error of metabolism or other condition, which could explain the encephalopathy.

- In HIE, the brain injury is caused by a deficit in oxygen supply.
- This can occur by
  - **Hypoxemia** - a decrease in oxygen saturation in the blood supply, *or*
  - **Ischaemia** - a decrease in the amount of blood perfusing the brain ***or both processes.***

Staging of Neonatal Hypoxic Ischaemic Encephalopathy (HIE)

This done using the Sarnat and Sarnat Staging system (facing page). This is mainly used in term infants or infants > 35 weeks gestation. It is not useful in premature infants.

Management

- Adequate and effective resuscitation.
- **Commence cooling therapy within 6 hours of life** for moderate to severe HIE in those more than or equal to 35 weeks gestation.
- Vital sign monitoring. Monitoring of blood gases, urine output, blood sugar and electrolytes.
- Management is supportive.
  - Avoid hyperthermia that may be 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).
- Cerebral protection measures
  - Maintain normal Blood Pressure. If necessary, consider use of inotrope infusion rather volume expander unless there is hypovolaemia.
  - Treat seizures (see chapter on Neonatal Seizures)
  - Mechanical ventilation to maintain normocarbia.
- Treat other systemic complications that arise:
  - **Renal.** *Acute tubular necrosis.*
    If oliguria with urine output < 1ml/kg/hr, check for prerenal cause and treat accordingly. If in established renal failure, restrict fluid and maintain normal electrolyte levels.
  - **Cardiac.** *Hypoxic damage to myocardium with cardiogenic shock and failure*.
    Use of inotropes and careful fluid balance.
  - **Lungs.** *Persistent Pulmonary Hypertension (PPHN)*.
    See relevant chapter on PPHN
  - **Gastrointestinal.** *Stress ulcers, feed intolerance, necrotizing enterocolitis.*
    Enteral feeding is preferable to parenteral but avoid rapid increase in volume of feeds to decrease risk of necrotizing enterocolitis.
  - **Haematology.** *Disseminated Intravascular Coagulation.*
    Correct coagulopathy as indicated.
  - **Others.** *SIADH, hypoglycaemia, hypocalcaemia, and hypomagnesaemia*
    Restrict fluids in SIADH. Correct hypoglycaemia and electrolyte imbalances.

Staging of Hypoxic Ischaemic Encephalopathy (HIE)

Only for term infants or > 35 weeks gestation. Not for use in premature infants.

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, then subsides
Complex reflexes			
Suck	Poor	Weak	Absent
Moro	Exaggerated	Incomplete	Absent
Grasp	Normal or exaggerated	Exaggerated	Absent
Doll's eyes	Normal	Overactive	Reduced or absent
Autonomic function			
Pupils	Dilated, reactive	Constrictive, reactive	Variable or fixed
Respirations	Regular	Variation in rate, depth; Periodic	Ataxic, apneic
Heart rate	Normal or tachycardia	Bradycardia	Bradycardia
Salivation	Sparse	Profuse	Variable
Electroencephalogram	Normal	*Early* Low voltage-continuous, *Later* Periodic, paroxysmal	*Early* Periodic, Burst suppression *Later* Isoelectric
Outcome	No impairment	25% Impaired	92% Impaired

Investigations

Investigation	Indication
Cranial Ultrasound	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.
Brain CT scan	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).
Brain MRI	MRI may provide prognostic information. Thalamic, basal ganglia abnormalities are associated with a risk of abnormal neuro-developmental outcome. Superior to CT scans.
Amplitude intergrated Electroencephalogram (aEEG)	Overall risks for death or disability were 95% for a severely abnormal aEEG, 64% for a moderately abnormal aEEG and 3 % for a normal or mildly abnormal aEEG.

Follow up

- All infants with NE should be followed up to look for development and neurological problems.
- Manage epilepsy (see Ch 44: Epilepsy), developmental delay, cerebral palsy, learning difficulty as appropriate.
- To evaluate hearing and vision on follow-up and manage appropriately.

Chapter 18: Neonatal Seizures

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

1. The seizures may be related to 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.

Etiology

Determination of etiology is critical because it gives the opportunity to treat specifically and also to make a meaningful prognosis.

Etiology	Onset[1]		Frequency[2]	
	0-3 days	>3 days	Preterm	Term
Hypoxic - ischemic encephalopathy	+		+++	+++
Intracranial hemorrhage	+	+	++	+
Intracranial infections	+	+	++	++
Brain malformations	+	+	+	++
Hypoglycaemia	+		+	+
Hypocalcaemia	+	+	+	+
Metabolic disturbances, inborn errors	+			+
Epileptic Syndromes	+	+		+

Footnote: 1, Postnatal age; 2, Relative frequency of seizures among all etiologies: +++ most common, ++ less common, + least common.

From JJ Volpe: Neurology of the Newborn 4th edition. Page 190

Notes:

- *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
- *Intracranial haemorrhage (ICH)*
  - Principally germinal matrix-intraventricular (GM-IVH), often with periventricular haemorrhagic (PVH) infarction in the premature infant
  - Severe GM-IVH: onset of seizures in first 3 DOL (usually generalized tonic type with subtle seizures).
  - With associated PVH usually develop seizures after 3 DOL.
  - In term infants ICH are principally subarachnoid (may occur with HIE) and subdural (often associated with a traumatic event, usually presenting with focal seizures in the first 2 DOL).

Classification of Neonatal Seizures		
Clinical Seizure	EEG seizure	Manifestation

Subtle	Common	• **Ocular phenomena**
		  • Tonic horizontal deviation of eyes common in term infants.
		  • Sustained eye opening with fixation common in preterm infants.
		  • Blinking.
		• **Oral-buccal-lingual movements**
		  • Chewing common in preterm infants.
		  • Lip smacking, cry-grimace.
		• **Limb movements**
		  • Pedaling, stepping, rotary arm movements
		• **Apnoeic spells** common in term infants

Clonic		
Focal	Common	Well localized clonic jerking, infant usually not unconscious
Multifocal	Common	Multifocal clonic movements; simultaneous, in sequence or non-ordered (non-Jacksonian) migration
Tonic		
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 BP are prominent features.
Myoclonic		
Focal, Multifocal	Uncommon	Well localized, single or multiple, migrating jerks usually of limbs
Generalized	Common	Single/several bilateral synchronous jerks or flexion movement more in upper than lower limbs.

- *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
- *Metabolic disorder*
  - *Hypoglycemia*. It may be difficult to establish hypoglycemia as the cause of seizures because of associated hypoxic-ischemic encephalopathy, hypocalcaemia or hemorrhage.
  - *Hypocalcaemia* has 2 major peaks of incidences:
    - First 2 - 3 days of life, in low birth weight infants, infant of a diabetic mother or history of hypoxic-ischemic encephalopathy. A therapeutic response to IV calcium will help in determe if low serum calcium is the cause of the seizures. Early hypocalcaemia is more commonly an associated factor rather than the cause of seizures.
    - Later-onset hypocalcaemia is associated with endocrinopathy (maternal hypoparathyroidism, neonatal hypoparathyroidism) and heart disease (+/- Di George Syndrome); rarely with nutritional disorders (cow's milk, high phosphorus synthetic milk). Hypomagnesemia is a frequent accompaniment.
  - Other metabolic disorders, e.g. intoxication with lidocaine, hypo- and hyper-natraemia, hyperammonemia amino acidopathy, organic acidopathy, non-ketotic hyperglycinemia, mitochondrial diosrders, pyridoxine dependency (recalcitrant seizures cease with IV pyridoxine) and glucose transporter defect (GLUT1 deficiency: low CSF glucose but normal blood glucose - treated with a ketogenic diet).

Seizures versus Jitteriness and Other Non-epileptic Movements

Jitteriness and other normal movement during sleep (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 newborns may be mistaken for seizures.

Clinical Manifestation	Jitteriness	Seizure
Abnormality of gaze or eye movement	0	+
Movements exquisitely stimulus sensitive	+	0
Predominant movement	Tremors[1]	Clonic, jerking[2]
Movements stop with passive flexion of affected limb	+	0
Autonomic changes (tachycardia, high BP, apnoea, salivation, cutaneous vasomotor phenomena)	0	+

Footnote: 1, Tremors – alternating movements are rhythmical and of equal rate and amplitude; 2, Clonic, jerking – movements with a fast and slow component

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Management

- Ensure adequate respiratory effort and perfusion.
- Correct metabolic and electrolyte disorders.
- No consensus on the treatment of minimal or absent clinical manifestations.
- Anticonvulsant treatment prevents potential adverse effects on ventilatory function, circulation and cerebral metabolism (threat of brain injury).
- Little evidence for use of any anticonvulsant drugs currently prescribed in the neonatal period. Also lack of consensus on optimal treatment protocol.
- 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.
- Anticonvulsant drugs may not treat electroencephalographic seizures even if they are effective in reducing or eliminating the clinical manifestations (electro-clinical dissociation).
- Uncertainty exists over when to commence anticonvulsant drugs. Consider anticonvulsant drugs to treat seizures when seizures:
  - Are prolonged – greater than 2-3 minutes.
  - Are frequent– greater than 2-3 per hour.
  - Disrupt of ventilation and/or blood pressure homeostasis.
- Administer anti convulsant drugs:
  - Intravenously to achieve rapid onset of action and predictable blood levels.
  - To achieve serum levels in the high therapeutic range.
  - To maximum dosage before introducing a second drug.
- Requirement for maintenance and duration of therapy is not well defined. Keep duration of anti convulsant drug treatment as short as possible. However, this depends on diagnosis and likelihood of seizure recurrence.
- Maintenance therapy may not be required if loading doses of anticonvulsant drugs control clinical seizures.
- Babies with prolonged or difficult to treat seizures and those with abnormality on EEG may benefit from continuing anticonvulsant treatment.

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 re-evaluate in one 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.

Prognosis

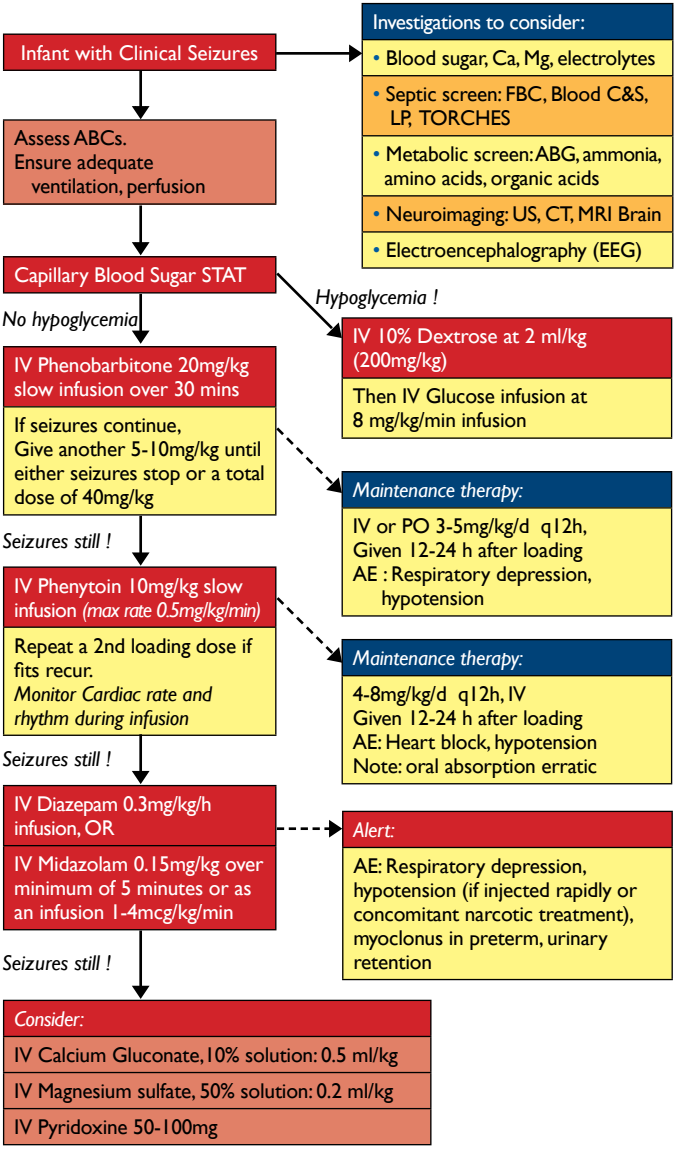
Prognosis according to aetiology of neonatal seizures

Neurological disorder	Normal Development (%)[1]
Hypoxic Ischemic Encephalopathy	50
Severe Intraventricular Haemorrhage with periventricular hemorrhagic infarction	10
Hypocalcaemia *Early onset* (depends on prognosis of complicating illness, if no neurological illness present prognosis approaches that of later onset) *Later onset* (nutritional type)	 50 100
Hypoglycemia	50
Bacterial meningitis	50
Malformation of Cortical Development	0

Footnote: 1, Prognosis based cases with the stated neurological disease when seizures are a manifestation. This will differ from overall prognosis of the disease.

From JJ Volpe: Neurology in the Newborn: 4th edition. Page 202

Management of Neonatal Seizures



Introduction

The authors of several literature reviews have concluded that there is not a specific plasma glucose concentration or duration of hypoglycemia that can predict permanent neurologic injury in high-risk infants.

- Neonatal glucose concentrations decrease after birth, to as low as 30 mg/dL (1.7 mmol/dL) during the first 1 to 2 hours after birth, and then increase to higher and relatively more stable concentrations, generally above 45 mg/dL (2.5 mmol/L) by 12 hours after birth.
- From birth to 4 hours, glucose level of above 25 mg/dL (1.5 mmol/L) is acceptable if the infant is asymptomatic.
- **Hypoglycaemia is defined as < 2.6 mmol/L after first 4 hours of life.**
- There is no specific plasma glucose concentration or duration of hypoglycemia that predicts permanent neurologic injury in high-risk infants.

High Risk Infants

- Infants of Diabetic Mothers.
- Small for Gestational Age infants.
- Preterm infants including late preterm infants.
- Macrosomic infants / Large for gestational age infants > 4.0kg.
- Ill infants including those with:
  - Hypoxic-ischemic encephalopathy.
  - Rhesus disease.
  - Polycythaemia.
  - Sepsis.
  - Hypothermia.

Clinical Features

Symptoms of hypoglycaemia include:

- Jitteriness and irritability.
- Apnoea and cyanosis.
- Hypotonia and poor feeding.
- Convulsions.

Note: Hypoglycaemia may be asymptomatic therefore monitoring is important for high risk cases.

Management

Prevention and Early Detection – at birth.

- Identify at risk infants.
- Well infants who are at risk:
  - Immediate feeding – first feed can be given in Labour Room.
  - Supplement feeding until breastfeeding established.
- Unwell infants:
  - Set up dextrose 10% drip.
- Regular glucometer monitoring:
  - On admission and at 1, 2 and 4 hours after admission.
  - 3 -6 hourly just prior to feeding once stable for 24-48 hours.

Hypoglycaemia

- Repeat the capillary blood sugar sampling and send RBS stat.
- Examine and document any symptoms.
- Note when the last feeding was given.
- If on IV drip, check that IV infusion of glucose is adequate and running well.
- Blood Sugar Level <1.5mmol/l or if the baby is symptomatic:
  - GIve IV 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 and asymptomatic:
  - Give supplementary feed (EBM or formula) as soon as possible.
  - If BSL remains < 2.6 mmol/l and baby refuses feeds, give dextrose 10% drip.
  - If baby is on dextrose 10% drip, consider stepwise increment of glucose infusion rate by 2 mg/kg/min until blood sugar is > 2.6 mmol/L.
- Glucose monitoring (capillary blood sugar - dextrostix, glucometer):
  - If blood sugar is < 2.6 mmol/l, re-check glucometer $^1/_2$ hourly.
  - If blood sugar > 2.6 mmol/l for 2 readings: Monitor hourly x 2, Then 2 hourly X 2, Then to 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.

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 awaiting RBS result.
- Increase volume by 30ml/kg/day and/or increase dextrose concentration to 12.5% or 15% . Concentrations >12.5% must be infused through a central line.
- **If hypoglycaemia still persists despite glucose delivery >8-10 mg/kg/min, consider glucagon 40 mcg/kg stat then 10-50mcg/kg/h.** 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 **IV Hydrocortisone 2.5 -5 mg/kg /dose bd**. There may be hyperinsulinaemia in growth retarded babies as well.

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

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

Recurrent or resistant hypoglycaemia

- Consider this if failure to maintain normal blood sugar levels despite a glucose infusion of 15 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.

Differential diagnoses include:

- Hyperinsulinaemic states (e.g.Beckwith-Wiedemann syndr, Nesidioblastosis)
- Adrenal insufficiency.
- Galactosaemia.
- Metabolic (e.g. fatty acid oxidation disorders) and mitochondrial disorders.

Investigations

- Insulin , cortisol, growth hormone levels
- Serum ketones
- Urine for organic acids

Take blood investigations before an increase in rate of glucose infusion when hypoglycaemia persists despite glucose infusion. Further investigation is directed by the results of these tests and the differential diagnosis above.

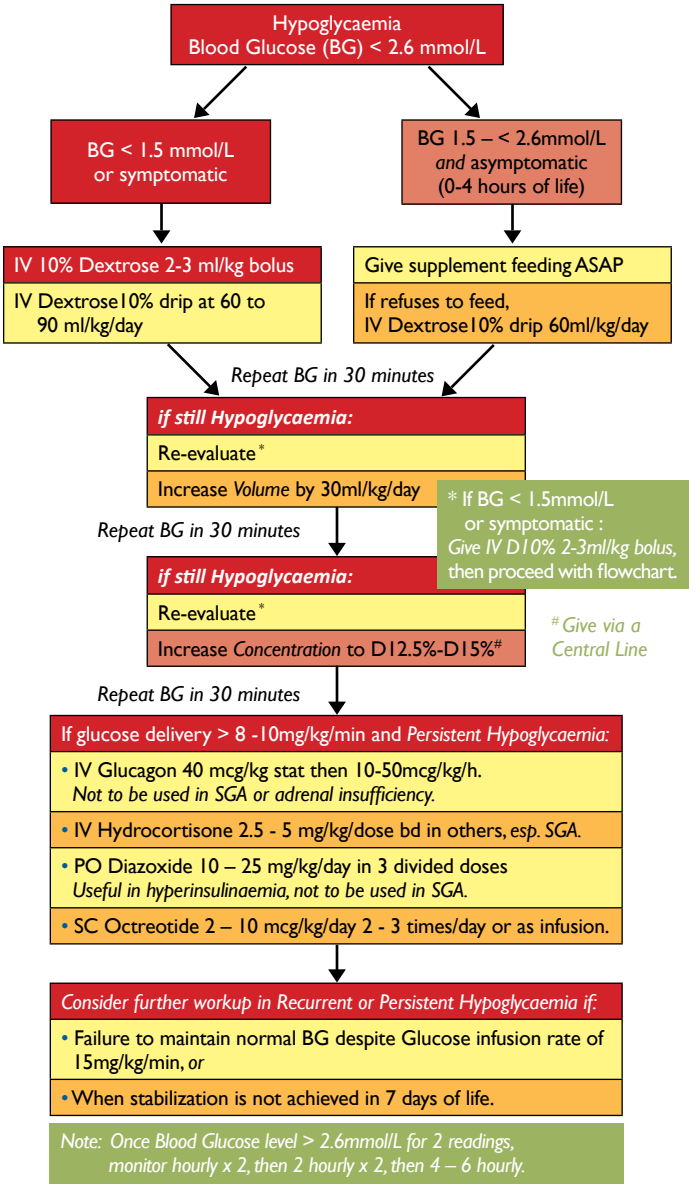
Medical treatment

- As per protocol for **Management of Persistent Hypoglycaemia**.
- PO Diazoxide 10-25mg/kg/day in three divided doses
  - Reduces insulin secretion, therefore useful in hyperinsulinaemia.
  - Not to be used in SGA infants.
- SC Octreotide (synthetic somatostatin) 2-10 µg/kg/day bd/tds or as infusion.

Pearls and Pitfalls in Management

- Depending on severity of hypoglycaemia, maintain some oral feeds as milk has more calories than 10% dextrose. Breastfeeding should be encouraged as it is more ketogenic.
- Feed baby with as much milk as tolerated and infuse glucose at a sufficient rate to prevent hypoglycaemia. The glucose infusion is then reduced slowly while milk feeds is 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 IV fluid is appropriate for patient, taking into consideration concomitant problems like cardiac failure, cerebral oedema and renal failure. If unable to increase volume further, increase dextrose concentration.
- RBS should be taken to correlate with low capillary blood sugar level as some glucose monitors are not as accurate for neonatal blood which has a higher haematocrit. Management can be instituted first whilst waiting for RBS results to be available.

Management of Persistent Hypoglycaemia



Introduction

Jaundice can be detected clinically when the level of bilirubin in the serum rises above 85 µmol/l (5mg/dl).

Risk factors for Bilirubin Encephalopathy
Preterm infants
Small for gestational age
Sepsis
Acidosis
Hypoxic-ischemic encephalopathy
Hypoalbuminaemia
Jaundice < 24 hours of age

Causes of neonatal jaundice

- Haemolysis due to ABO or Rh-isoimmunisation, G6PD deficiency, microspherocytosis, drugs.
- Physiological jaundice.
- Cephalhaematoma, subaponeurotic haemorrhage.
- Polycythaemia.
- Sepsis septicaemia, meningitis, urinary tract infection, intra-uterine infection.
- Breastfeeding and breastmilk jaundice.
- Gastrointestinal tract obstruction: increase in enterohepatic circulation.

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: 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.

Management

Indications for referral to hospital:

- Jaundice within 24 hours of life.
- Jaundice below umbilicus (corresponds to serum bilirubin 200-250 µmol/L).
- Jaundice extending to soles of feet:
  Urgent referral, may need exchange transfusion !
- Family history of significant haemolytic disease or kernicterus.
- Any unwell infant with jaundice.
- Prolonged Jaundice of >14 days.
  - Refer infants with **conjugated hyperbilirubinaemia** urgently to a hospital.
  - Infants with unconjugated hyperbilirubinaemia can be investigated and referred only if the jaundice does not resolve or a definitive cause found. (ref **Ch 22: Prolonged Jaundice in the Newborn**).

Investigations

- Total serum bilirubin
- G6PD status
- Others as indicated:
  - Infant's blood group, maternal blood group, Direct Coombs' 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)

Clinical Assessment of Neonatal Jaundice

Zone	Jaundice *(detected by blanching the skin with finger pressure)*	Estimated Serum Bilirubin (μmol/L)
1	Head and neck	68 -135
2	Over upper trunk above umbilicus	85 - 204
3	Lower trunk and thighs	136 - 272
4	Over arms, legs and below knee	187 - 306
5	Hands, feet	> 306

Note: This may be difficult in dark skinned infants

DO NOT rely on Visual Assessment of Skin alone to Estimate the Bilirubin Level

Treatment

Avoid sunlight exposure due to risk of dehydration and sunburn.

Phototherapy

- Phototherapy lights should have a minimum irradiance of 15 μW/cm²/nm. Measure intensity of phototherapy light periodically using irradiance meters. "Intensive phototherapy" implies irradiance in the blue-green spectrum of at least 30 μW/cm²/nm measured at the infant's skin directly below the center of the phototherapy unit.
- Position light source 35-50 cm from top surface of the infant (when conventional fluorescent photolights are used).
- Expose infant adequately; Cover infant's eyes.
- Monitor serum bilirubin levels as indicated.
- Monitor infant's temperature 4 hourly to avoid chilling or overheating.
- Ensure adequate hydration and good urine output. Monitor for weight loss. Adjust fluid intake (preferably oral feeds) accordingly. Routine fluid supplementation is not required with good temperature homeostasis.
- Allow parental-infant interaction.
- Discontinue phototherapy when serum bilirubin is below phototherapy level.
- Turn off photolights and remove eyepads 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.

- In infants without haemolytic disease, the average increase of bilirubin level in rebound jaundice after phototherapy is < 1 mg/dl (17 µmol/L). Hospital discharge need not be delayed to observe for rebound jaundice, and in most cases, no further measurement of bilirubin is necessary.

Intensive phototherapy (KIV Exchange transfusion) indications:
Total bilirubin >300 umol/L
Early onset jaundice (First 24 hours)
Rapidly rising jaundice (more than 8.5µmol/L/hr)
If the total serum bilirubin does not decrease or continues to rise in an infant receiving intensive phototherapy, this strongly suggests hemolysis.

Guidelines for Phototherapy and Exchange Transfusion (ET) in hospitalized infants of ≥ 35 weeks' gestation *(derived from fig 1, next page)*

Hours of Life	Total Serum Bilirubin levels mg/dL (µmol/L)					
	Low risk ≥ 38 wk and well		***Medium risk*** ≥ 38 wk + risk factors or 35 to <38 wk and well		***High risk*** 35 to <38 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)

Note:
- Start conventional phototherapy at TSB 3 mg/dL (50 µmol/L) below the levels for intensive phototherapy.
- Risk factors – isoimmune hemolytic disease; G6PD deficiency, hypoxic-ischemic encephalopathy, significant lethargy, temperature instability, sepsis, acidosis or albumin < 3.0 g/dL

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

Fig 1: Guidelines for Intensive Phototherapy in infants ≥ 35 wks gestation

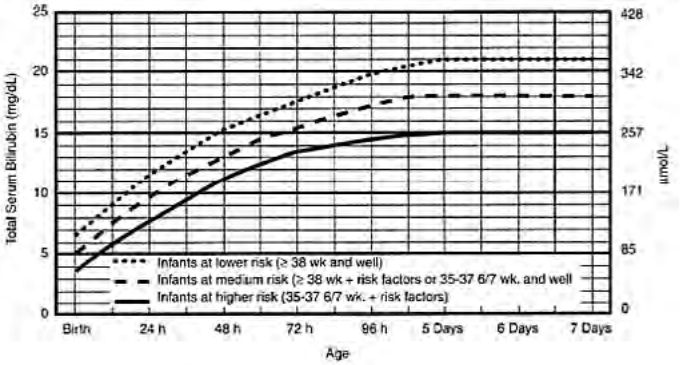
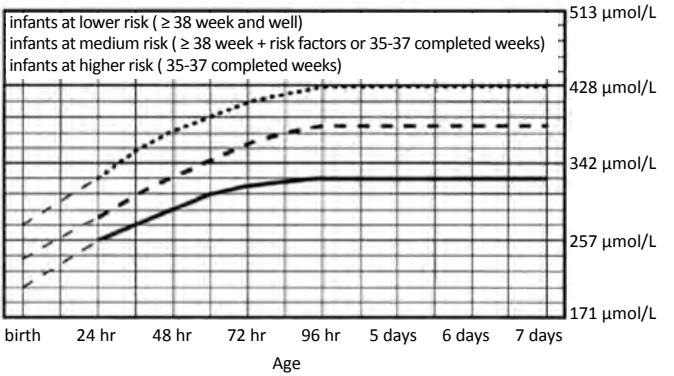


Fig 2: Guidelines for Exchange Transfusion in infants ≥ 35 wks gestation



Notes:

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. Do an Immediate exchange transfusion if infant shows signs of acute bilirubin encephalopathy (hypertonia, retrocollis, ophisthotonus, fever, high pitched cry) or if total serum bilirubin is ≥ 5 mg/dL (85 µmol/L) above these lines
3. For infants < 35 weeks gestational age- refer NICE (National Institute for Clinical Excellence) Guidelines 2010 for recommended levels of phototherapy and ET.

Figures 1 & 2 adapted from American Academy of Paediatrics. Pediatrics, 2004. 114:297-316

Additional Notes

- **Failure of phototherapy** has been defined as an inability to observe a decline in bilirubin of 1-2 mg/dl (17-34 µmol/L) after 4-6 hours and/or to keep the bilirubin below the exchange transfusion level.
- **Do an immediate exchange transfusion if infant shows signs of acute bilirubin encephalopathy** (hypertonia, retrocollis, opisthotonus, fever, high pitch cry) or if TSB is ≥5 mg/dL (85 umol/L) above exchange levels stated above.
- **Use total bilirubin level.** Do not subtract direct or conjugated bilirubin.
- During birth hospitalisation, ET is recommended if the TSB rises to these levels despite intensive phototherapy.
- Infants who are of lower gestation will require phototherapy and ET at lower levels, (please check with your specialist).

Intravenous Immunoglobulins (IVIG)

- High dose intravenous immunoglobulin (IVIG) (0.5 - 1 gm/kg over 2 hours) reduces the need for exchange transfusions in Rh and ABO hemolytic disease.
- Give as early as possible in hemolytic disease with positive Coombs test or where the serum total bilirubin is increasing despite intensive phototherapy.
- Dose can be repeated in 12 hours if necessary. If exchange transfusion is already indicated, IVIG should be given after ET.

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. Supplementary feeds may be given to ensure adequate hydration, especially if there is more than 10% weight loss from birth weight.
- Interruption of breastfeeding in healthy term newborns is discouraged and frequent breast-feeding (at least 8-10 times/24 hours) should be continued. Supplementing with water or dextrose water does not lower bilirubin level.
- G6PD status should be known before discharge. Observe infants with G6PD deficiency, for 5 days if not jaundiced and longer with moderate jaundice.
- 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.
- If phototherapy in infants with hemolytic diseases is initiated early and discontinued before the infant is 3 - 4 days old, monitor for rebound jaundice and adequacy of breast feeding within the next 24-48 hours.

Follow-up

- All infants discharged < 48 hours after birth should be seen by a healthcare professional in an ambulatory setting, or at home within 2-3 days of discharge.
- For infants with risk factors for severe neonatal jaundice, early follow up to be arranged to detect rebound jaundice after discharge.
- Infants with serum bilirubin > 20 mg/dl (340 µmol/L) and those who require exchange transfusion should be followed for neurodevelopmental outcome. Do a Hearing assessment (using BAER, not OAE) at 0-3 months of corrected age.
- Infants with hemolytic diseases not requiring ET should be closely followed up for anaemia until the risk of ongoing hemolysis is minimal.

Agents to be avoided in Infants with G6PD Deficiency	
Foods and Herbs to be avoided	
Fava Beans *(Kacang Parang)*	
Chinese herbs/medicine: *Chuen Lin, San Chi, 13 herbs, 12 herbs*	
Avoid Other traditional herbs/medications unless with medical advice	
Other Chemicals to be avoided	
Naphthalene (moth balls)	
Mosquito coils and insect repellants which contains pyrethium	
Drugs to be avoided or contraindicated	
Acetanilide	Doxorubicin
Furazolidene	Methylene Blue
Nalidixic acid	Niridazole
Nitrofurantoin	Phenozopyridine
Promaquine	Sulfamethoxazole
Bactrim	
Drugs that can be safely given in therapeutic doses	
Paracetamol	Ascorbic Acid
Aspirin	Chloramphenicol
Chloroquine	Colchicine
Diphendramine	Isoniazid
Phenacetin	Phenylbutazone
Phenytoin	Probenecid
Procainamide	Pyrimethamine
Quinidine	Streptomycin
Sulfisoxazole	Trimethoprim
Tripelennamine	Vitamin K
Mefloquine	

Introduction

- **Exchange transfusion (ET) is indicated for severe hyperbilirubinaemia.**
- Kernicterus has a 10% mortality and 70% long term morbidity.
- Neonates with significant neonatal jaundice should be monitored closely and treated with intensive phototherapy.
- Mortality within 6 hours of ET ranged from zero death to 3 - 4 per 1000 exchanged term infants. Causes of death includes kernicterus itself, necrotising enterocolitis, infection and procedure related events.

Indications

- Double volume exchange
  - Blood exchange transfusion to lower serum bilirubin level and reduce the risk of brain damage associated with kernicterus.
  - Hyperammonimia
  - To remove bacterial toxins in septicaemia.
  - To correct life-threatening electrolyte and fluid disorders in acute renal failure.
- Partial exchange transfusion
  - To correct polycythaemia with hyperviscosity.
  - To correct severe anaemia without hypovolaemia.

Preparation of infant

- Signed Informed Consent from parent.
- Ensure resuscitation equipment is ready and available.
- Stabilise and maintain temperature, pulse and respiration.
- Obtain peripheral venous access for maintenance IV fluids.
- Proper gentle restraint.
- Continue feeding the child; Omit only the LAST feed before ET.
  If < 4 hours from last feed, empty gastric contents by NG aspiration before ET.

Type of Blood to be used

- **Rh isoimmunisation: ABO compatible, Rh negative blood.**
- **Other conditions: Cross-match with baby and mother's blood.**
- In Emergencies if Blood type unkown (rarely): 'O' Rh negative blood.

Procedure (Exchange Transfusion)

- Volume to be exchanged is 2x the infant's total blood volume (2x80mls/kg).
- Use (preferably irradiated) **Fresh Whole Blood preferably < 5 days old** or reconstituted Packed Red Blood Cells and FFP in a ratio of 3:1.
- Connect baby to a cardiac monitor.
- Take baseline observations (either via monitor or manually) and record down on the Neonatal Exchange Blood Transfusion Sheet.
  The following observations are recorded every 15 minutes:
  apex beat, respiration, oxygen saturation.
- Doctor performs the ET under aseptic technique using a gown and mask.

- Cannulate the umbilical vein to a depth of NOT > 5-7cm in a term infant for catheter tip to be proximal to the portal sinus (for push-pull technique ET through UVC). Refer to section on procedure for umbilical vein cannulation.
- Aliquot for removal and replacement – 5-6 mls/ kg (Not more than 5-8% of blood volume) Maximum volume per cycle - 20 mls for term infants, not to exceed 5 ml/kg for ill or preterm infants.
- At the same time the nurse keeps a record of the amount of blood given or withdrawn, and medications given (see below).

Isovolumetric or continuous technique

- Indication: where UVC cannulation is not possible e.g. umbilical sepsis, failed cannulation.
- Blood is replaced as a continuous infusion into a large peripheral vein while simlutaneously removing small amount blood from an arterial catheter at regular intervals, matching the rate of the infusion closely
  - e.g. in a 1.5 kg baby, total volume to be exchanged is 240 mls. Delivering 120mls an hour allowing 10 ml of blood to be removed every 5 mins for 2 hours.
- Care and observation for good perfusion of the limb distal to the arterial catheter should be performed as per arterial line care

Points to note

- **Pre-warm blood to body temperature using a water bath.** Avoid other methods, e.g. placing under radiant warmer, massaging between hands or placing under running hot water, to minimise preprocedure hemolysis of donor blood. Shake blood bag gently every 5-10 cycles to prevent settling of red blood cells.
- Rate of exchange: 3 -4 minutes per cycle *(1 minute 'out', 1 minute 'in', 1-2 minute 'pause' excluding time to discard blood and draw from blood bag).*
- Syringe should be held vertical during infusion 'in' to prevent air embolism.
- Total exchange duration should be 90-120 minutes utilising 30-35 cycles.
- Begin the Exchange with an initial removal of blood, so that there is always a deficit to avoid cardiac overload.
- Routine administration of calcium gluconate is not recommended.
- Remove the UVC after procedure unless a second ET is anticipated and there was difficulty inserting the UVC.
- Continue intensive phototherapy after the procedure.
- Repeat ET may be required in 6 hours for infants with high rebound SB.
- Feed after 4 hours if patient is well and a repeat ET not required.
- If child is anemic (pre-exchange Hb <12 g/dL) give an extra aliquot volume of blood (10 mls/kg) at the end of exchange at a rate of 5 mls/kg/hr after the ET.
- If the infant is on any IV medication , to readminister the medication after ET.

Investigations

- Pre-exchange (1st volume of blood removed)
  - Serum Bilirubin.
  - FBC.
  - Blood C&S (via peripheral venous blood; UVC to reduce contamination).
  - HIV, Hepatitis B (baseline).
  - Others as indicated.
- Post-exchange
  (Discard initial blood remaining in UVC before sampling)
  - Serum Bilirubin.
  - FBC.
  - Capillary blood sugar.
  - Serum electrolytes and Calcium.
  - Others as indicated.

Complications of ET
Catheter related
• Infection
• Haemorrhage
• Necrotising enterocolitis
• Air embolism
• Vascular events
• Portal, Splenic vein thrombosis (late)
Haemodynamic problems
• Overload cardiac failure
• Hypovolaemic shock
• Arrhythmia (catheter tip near sinus node in right atrium)
Electrolyte/Metabolic disorders
Hyperkalemia
Hypocalcemia
Hypoglycaemia or Hyperglycaemia

Post ET Management

- Maintain intensive phototherapy.
- Monitor vital signs:
  Hourly for 4 - 6 hours, and
  4 hourly subsequently.
- Monitor capillary blood sugar:
  Hourly for 2 hours following ET.
- Check serum Bilirubin:
  4 - 6 hours after ET.

Follow-up

- Long term follow-up to monitor hearing and neurodevelopmental assessment.

Partial Exchange Transfusion

- To correct hyperviscosity due to polycythaemia.
  Assuming whole blood volume is approximately 80 ml/kg

$$\text{Volume exchanged (mL)} = \text{Blood volume} \times \frac{(\text{Initial PCV} - \text{Desired PCV})}{\text{Initial PCV}}$$

- To correct severe anemia without hypovolaemia

$$\text{Packed Cell vol (ml) required} = 80 \text{ ml} \times \text{Bwt(kg)} \times \frac{[\text{Desired Hb} - \text{Initial Hb}]}{22\text{g/dL} - \text{Hb}_w}$$

Where Hb_w is reflection of the Hb removed during partial exchange transfusion:
Hb_w = [Hb desired + Hb initial]/2

Definition

- Visible jaundice (or serum bilirubin SB >85 µmol/L) that persists beyond 14 days of life in a term infant or 21 days in a preterm infant.

Causes of Prolonged Jaundice	
Unconjugated Hyperbilirubinaemia	Conjugated Hyperbilirubinaemia
Septicaemia	*Biliary tree abnormalities:*
Urinary tract infection	• Biliary atresia - extra, intra-hepatic
Breast milk jaundice	• Choledochal cyst
Hypothyroidism	• Paucity of bile ducts
Hemolysis:	• Alagille syndrome, non-syndromic
• G6PD deficiency	Idiopathic neonatal hepatitis syndrome
• Congenital spherocytosis	Septicaemia
Galactosaemia	Urinary tract infection
Gilbert syndrome	Congenital infection (TORCHES)
	Metabolic disorders
	• Citrin deficiency
	• Galactosaemia
	• Progressive familial intrahepatic cholestasis (PFIC)
	• Alpha-1 antitrypsin deficiency
	Total Parenteral Nutrition
The early diagnosis and treatment of biliary atresia and hypothyroidism is important for favourable long-term outcome of the patient.	

Unconjugated hyperbilirubinaemia

- Admit if infant is unwell. Otherwise follow-up until jaundice resolves.
- Important investigations: Thyroid function, urine FEME and C&S, urine for reducing sugar, FBC, reticulocyte count, peripheral blood film, G6PD screening.
- Exclude urinary tract infection and hypothyroidism.
- **Congenital hypothyroidism is a Neonatal Emergency.** (Check Screening TSH result if done at birth). See **Ch 54 Congenital Hypothyroidism.**
- Where indicated, investigate for galactosaemia
- Breast milk Jaundice is *a diagnosis of exclusion*. Infant must be well, gaining weight appropriately, breast-feeds well and stool is yellow. Management is to continue breast-feeding.

Conjugated hyperbilirubinaemia

- Defined as conjugated bilirubin > 25 µmol/dL.
- Investigate for biliary atresia and neonatal hepatitis syndrome.
- Other tests : LFT, coagulation profile, lipid profile, Hepatitis B and C virus status, TORCHES, VDRL tests, alpha-1 antitrypsin level.
- Admit and observe stool colour, for 3 consecutive days. **If pale, biliary atresia is a high possibility: consider an urgent referral to Paediatric Surgery.**
- Other helpful investigations are:
  - Serum gamma glutamyl transpeptidase (GGT) – Good discriminating test between non obstructive and obstructive causes of neonatal hepatitis. A significantly elevated GGT (few hundreds) with a pale stool strongly favours biliary obstruction whereas, a low/normal GGT with significant cholestasis suggests non obstructive causes of neonatal hepatitis.
  - Ultrasound of liver – Must be done after at least 4 hours of fasting. Dilated intrahepatic bile ducts (poor sensitivity for biliary atresia) and an absent, small or contracted gall bladder even without dilated intrahepatic ducts is highly suspicious of extra hepatic biliary atresia in combination with elevated GGT and pale stool. A normal gall bladder usually excludes biliary atresia BUT if in the presence of elevated GGT and pale stool, biliary atresia is still a possibility. An experience sonographer would be able to pick up Choledochal Cyst, another important cause of cholestasis.

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 by 4-6 weeks 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 if there is failure to achieve or maintain bile drainage.

Further investigations

Aim to exclude other (especially treatable) causes of a Neonatal Hepatitis Syndrome early which include:

Metabolic causes (see also **Ch 88 Inborn Errors of Metabolism**)

- Classical Galactosaemia
  - Dried blood spots for total blood galactose and galactose-1-uridyl transferase level (GALT). Usually sent in combination with acylcarnitine profile in a single filter paper to IMR biochemistry.
  - Urine reducing sugar may be positive in infants who are on lactose containing formula or breastfeeding.
  - A recent blood transfusion will affect GALT assay accuracy (false negative) but not so much on the total blood galactose and urine reducing sugar.
  - Treatable with lactose free formula.

- Citrin deficiency
  - An important treatable cause of neonatal hepatitis among Asians.
  - Investigations MAY yield elevated total blood galactose but normal galactose-1-uridyl transferase (GALT) *(i.e. secondary Galactosemia).*
  - Elevated plasma citrulline (in plasma amino acids & acylcarnitine profile).
  - Treatable with lactose free formula with medium chain triglyceride (MCT) supplementation.
  - *Note: Use lithium heparin container to send plasma amino acids.*
- Tyrosinaemia type I
  - Treatable with NTBC *(2-(2-nitro-4-trifluoromethylbenzoyl)-1,3-cyclohexanedione).*
  - Urine organic acids specifically looking for presence of succinylacetone is highly specific. Take particular attention of sending urine organic acids *frozen and protected from light* (i.e. covered plain urine container) to maintain the accuracy of the test.
- Neonatal Haemochromatosis
  - This needs to be excluded in infants presenting with liver failure within first weeks of life.
  - Significantly elevated serum ferritin (few thousands) is characteristic.
  - Diagnosis is confirmed by presence of iron deposits in extra hepatic tissue, e.g. lip tissue (iron deposits in minor salivary glands). Lip biopsy can be safely performed even in severely coagulopathic infants where liver biopsy is contraindicated.
  - Treatment with combination of immunoglobulins, desferral and anti-oxidant cocktails is potentially life saving (avoid liver transplant which at present not an option for neonatal onset liver failure).
  - Antenatal intravenous immunoglobulin prevents recurrence in subsequent children.
- Primary bile acid synthesis disorder
  - Suspect if cholestasis, low GGT and low cholesterol.
  - Serum bile acids is a good screening tool (ensure patient is not on ursodeoxycholic acid < 1 week prior to sampling).
  - Definite diagnosis requires urine bile acids analysis (available at specialized laboratory in UK).
  - Treatment with cholic acid (not ursodeoxycholic acid) confers excellent outcome on all subtypes.
- Peroxisomal biogenesis disorders
  - Cholestasis may be part of the manifestation.
  - Plasma very long chain fatty acids (VLCFA) is elevated.
- Mitochondrial depletion syndrome
  - Suspect in presence of other neurological signs e.g. rotatory nystagmus, hypotonia and elevated blood lactate. Metabolic/genetic consult for further diagnostic evaluation.

Infective causes

- Septicaemia
- Urinary tract infection
- Herpes simplex virus infection
  - Consider in infants with liver failure within first few weeks of life.
  - IV Acyclovir therapy while waiting for Herpes IgM results in affected infants may be justified.
- Hepatitis B virus infection
  - Can potentially present as early infantile liver failure but incidence is rare.
  - Presence of positive Hepatitis B surface antigen, positive Hepatitis B virus envelope antigen and high viral load confirms the diagnosis.

Alagille syndrome

- Consider in infants who have cardiac murmurs or dysmorphism.
- One of the parents is usually affected (AD inheritance, variable penetrance)
- Affected infants might not have typical dysmorphic features at birth due to evolving nature of the syndrome.
- Important screening tests include :
  - Slit eye lamp examination: look for posterior embryotoxon.
    May also help to rule out other aetiologies in neonatal hepatitis syndrome, e.g. retinitis in congenital infection, cataract in galactosaemia.
  - Vertebral x ray: To look for butterfly vertebrae.
  - Echocardiography: look for branched pulmonary artery stenosis.
    Other known abnormalities - ASD, valvular pulmonary stenosis.
  - Gene test: JAG1 gene mutation which can be done at IMR (EDTA container) *(Consult Geneticist Prior to Testing)*

Idiopathic Neonatal Hepatitis Syndrome

- Follow up with LFT fortnightly.
- Watch out for liver failure and bleeding tendency (vitamin K deficiency).
- Repeat Hepatitis B and C virus screening at 6 weeks.
- Most infants with idiopathic neonatal hepatitis in the absence of physical signs of chronic liver disease usually make a complete recovery.

Definition

- **Apnea of prematurity** is defined as sudden cessation of breathing that lasts for at least 20 seconds or is accompanied by bradycardia or oxygen desaturation (cyanosis) in an infant younger than 37 weeks' gestational age.
- It usually ceases by 43 weeks' postmenstrual age but may persist for several weeks beyond term, especially in infants born before 28 weeks' gestation with this risk decreasing with time.

Classification

Types:

- *Central:* absence of respiratory effort with no gas flow and no evidence of obstruction.
- *Obstructive:* continued ineffective respiratory effort with no gas flow
- *Mixed central and obstructive:* most common type

Aetiology

Symptomatic of underlying problems, commoner ones of which are:

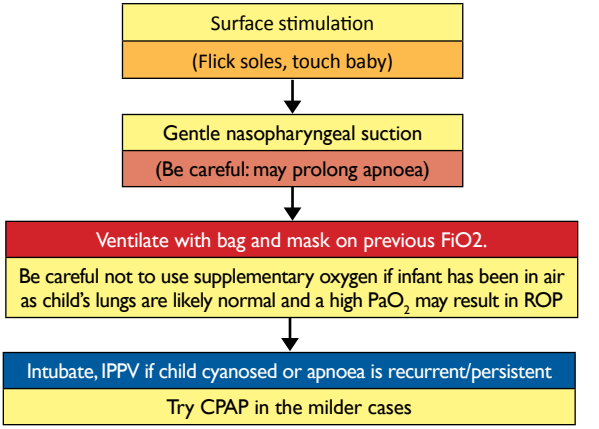
- Respiratory conditions (RDS, pulmonary haemorrhage, pneumothorax, upper airway obstruction, respiratory depression due to drugs).
- Sepsis
- Hypoxaemia
- Hypothermia
- CNS abnormality (e.g. IVH, asphyxia, increased ICP, seizures)
- Metabolic disturbances (hypoglycaemia, hyponatraemia, hypocalcaemia)
- Cardiac failure, congenital heart disease, anaemia
- Aspiration/ Gastro-oesophageal reflux
- Necrotising ennterocolitis, Abdominal distension
- Vagal reflex: Nasogastric tube insertion, suctioning, feeding

Differentiate from 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.
- Benign respiratory pattern for which no treatment is required.
- Respiratory pauses appear self-limited, and ventilation continues cyclically.
- Periodic breathing typically does not occur in neonates in the first 2 days of life

Management

- Immediate resuscitation.



- Review possible causes (as above) and institute specific therapy, e.g. septic workup if sepsis suspected and commence antibiotics Remember to check blood glucose via glucometer.
- Management to prevent recurrence.
  - Nurse baby in thermoneutral environment.
  - Nursing prone can improve thoraco-abdominal wall synchrony and reduce apnoea.
  - Variable flow NCPAP or synchronised NIPPV can reduce work of breathing and reduce risk of apnoea.
  - Monitoring:
    - Pulse Oximeter
    - Cardio-respiratory monitor
  - Drug therapy
    - Methylxanthine compounds:
    - Caffeine citrate (preferred if available)
    - IV Aminophylline or Theophylline.
- Start methylxanthines prophylactically for babies < 32 weeks gestation. For those > 32 weeks of gestation, give methylxanthines if babies have apnoea. To stop methylxanthines if :
  - gestation > 34 weeks
  - Apnoea free for 1 week when the patient is no longer on NCPAP
- Monitor for at least 1 week once the methylxanthines are stopped. After discharge , parents should be given advice for prevention of SIDS:
  - Supine sleep position.
  - Safe sleeping environments.
  - Elimination of prenatal and postnatal exposure to tobacco smoke.

Definition

Neonatal sepsis generally falls into two main categories:

- Early onset: usually acquired from mother with ≥ 1 obstetric complications.
- Late onset: sepsis occurring > 72hours after birth.
  Usually acquired from the ward environment or from the community.

Clinical Features

Risk Factors of Infants and Mother

- Any stage
  - Prematurity, low birth weight.
  - Male gender.
  - Neutropenia due to other causes.
- Early Onset Sepsis
  - Maternal GBS (*Group B Streptococcus*) carrier (high vaginal swab [HVS], urine culture, previous pregnancy of baby with GBS sepsis).
  - Prolonged rupture of membranes (PROM) (>18 hours).
  - Preterm labour/PPROM.
  - Maternal pyrexia > 38˚ C, maternal peripartum infection, clinical chorioamnionitis, discoloured or foul-smelling liquor, maternal urinary tract infection.
  - Septic or traumatic delivery, fetal hypoxia.
  - Infant with galactosaemia (increased susceptibility to *E. coli*).
- Late Onset Sepsis
  - Hospital acquired (nosocomial) sepsis.
    - Overcrowded nursery.
    - Poor hand hygiene.
    - Central lines, peripheral venous catheters, umbilical catheters.
    - Mechanical ventilation.
    - Association with indomethacin for closure of PDA, IV lipid administration with coagulase-negative *Staphylococcal* (CoNS) bacteriemia.
  - Colonization of patients by certain organisms.
  - Infection from family members or contacts.
  - Cultural practices, housing and socioeconomic status.

Signs and symptoms of Sepsis

- Temperature instability: hypo or hyperthermia
- Change in behaviour : lethargy, irritability or change in tone
  ('baby just doesn't seem right or doesn't look well)
- Skin: poor perfusion, mottling, pallor, jaundice, scleraema, petechiae
- Feeding problems: poor feeding, vomiting, diarrhea, abdominal distension
- Cardiovascular: tachycardia, hypotension,
- Respiratory: apnoea, tachypnoea,cyanosis, respiratory distress,
- Metabolic: hypo or hyperglycaemia, metabolic acidosis
- Evaluate neonate (late onset sepsis) carefully for primary or secondary foci, e.g. meningitis, pneumonia, urinary tract infection, septic arthritis, osteomyelitis, peritonitis, omphalitis or soft tissue infection.

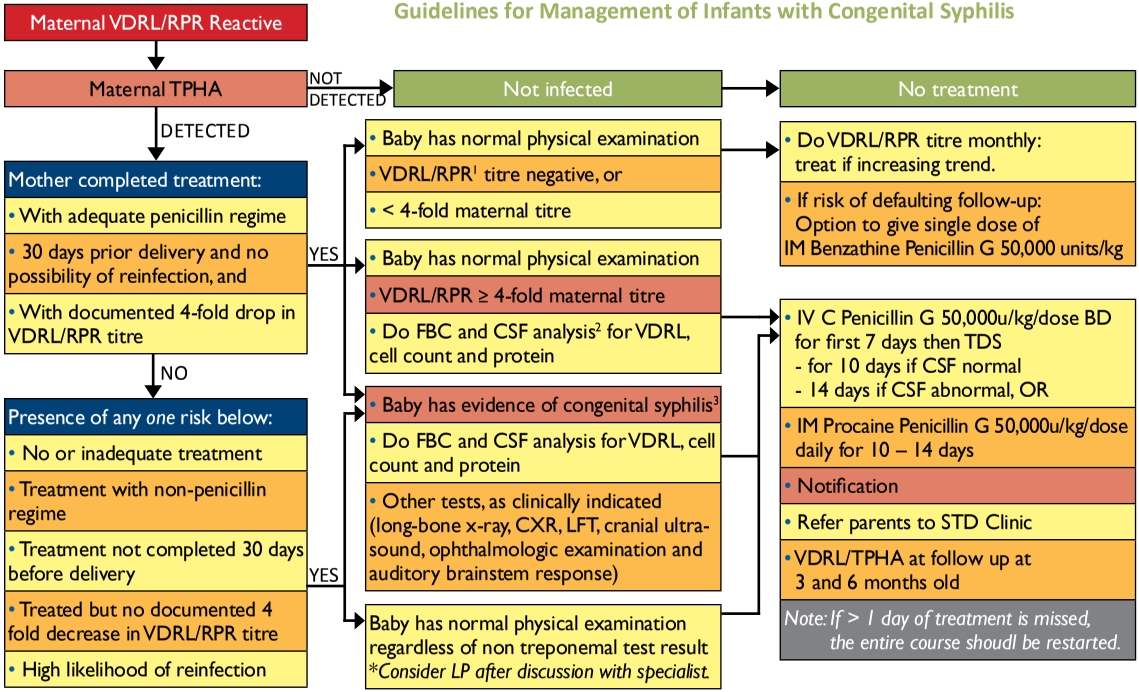
Investigations

- FBC: Hb, TWBC with differential, platelets, Blood culture (>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 first 2 weeks of life.
- Where indicated:
  - Lumbar puncture, CXR, AXR, Urine Culture.
  - Culture of ETT aspirate (Cultures of the trachea do not predict the causative organism in the blood of the neonate with clinical sepsis.)

Management

- Empirical 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. Stop antibiotics if cultures are sterile, infection is clinically unlikely.
- Empirical antibiotic treatment *(Early Onset)*
  - IV C.Penicillin/Ampicillin and Gentamicin
  - Specific choice when specific organisms suspected/confirmed.
  - Change antibiotics according to culture and sensitivity results
- Empirical antibiotic treatment – *(Late Onset)*
  - For community acquired infection, start on
    - Cloxacillin/Ampicillin and Gentamicin for non-CNS infection, and
    - C.Penicillin and Cefotaxime for CNS infection
  - For hospital acquired (nosocomial) sepsis
    - Choice depends on prevalent organisms in the nursery and its sensitivity.
    - For nursery where MRCoNS/ MRSA are common, consider Vancomycin; for non-ESBL gram negative rods, consider cephalosporin; for ESBLs consider carbapenams; for *Pseudomonas* consider Ceftazidime.
    - Anaerobic infections (e.g. Intraabdominal sepsis), consider Metronidazole.
    - Consider fungal sepsis if patient not responding to antibiotics especially if preterm/ VLBW or with indwelling long lines.
- Duration of Antibiotics
  - 7-10 days for pneumonia or proven neonatal sepsis
  - 14 days for GBS meningitis
  - At least 21 days for Gram-negative meningitis
- Consider removing central lines
- Complications and Supportive Therapy
  - Respiratory: ensure adequate oxygenation (give oxygen, ventilator support)
  - Cardiovascular: support BP and perfusion to prevent shock.
  - Hematological: monitor for DIVC
  - CNS: seizure control and monitor for SIADH
  - Metabolic: look for hypo/hyperglycaemia, electrolyte, acid-base disorder
- Therapy with IV immune globulin had no effect on the outcomes of suspected or proven neonatal sepsis.

Guidelines for Management of Infants with Congenital Syphilis



Footnotes to algorithm on previous page:

1. *VDRL/RPR test on venous blood sample as umbilical cord may be contaminated with maternal blood and could yield a false-positive result.*
2. *Clinical features of congenital syphilis: non-immune hydrops, IUGR, jaundice, hepatosplenomegaly, rhinitis, skin rash, pseudoparalysis of extremity.*
3. *Recommended value of 5 WBCs/mm^3 and protein of 40mg/dL as the upper limits of normal for "non traumatic tap".*

Follow up of patients

- All sero-reactive infants should receive careful follow up examination and serologic testing (VDRL/RPR) every 2-3 month until the test becomes non-reactive or the titre has decreased 4-fold.
- VDRL/RPR titre should decline by age of 3 month and should be non-reactive by age of 6 month if the infants was not infected or was infected but adequately treated.
- If the VDRL/RPR titre are stable or increase after 6-12 month, the child should be evaluated and treated with a 10-day course of parenteral Penicillin G.
- For infants whose initial CSF evaluations are abnormal should undergo a repeat lumbar puncture in 6 months. A reactive CSF VDRL test or abnormal CSF indices that cannot be attributed to other ongoing illness required re-treatment for possible neurosyphilis. If CSF is improving, monitor with follow-up serology.

Additional Notes:

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

Definition

Conjunctivitis occurring in newborn during 1st 4 weeks of life with clinical signs of erythema and oedema of the eyelids and palpebral conjunctivae, purulent eye discharge with one or more polymorph nuclear per oil immersion field on a Gram stained conjunctival smear.

Diagnosis

- Essentially a clinical diagnosis
- Laboratory diagnosis to determine aetiology
  - Eye swab for Gram stain (fresh specimen to reach laboratory in 30 mins)
  - Gram stain of intracellular gram negative diplococci - high sensitivity and specificity for *Neisseria gonorrhoea.*
  - Eye swab for culture and sensitivity.
  - Conjunctival scrapping for indirect fluorescent antibody identification for *Chlamydia*.

Aetiology

Bacterial

Gonococcal

- Most important bacteria by its potential to damage vision.
- Bilateral purulent conjunctival discharge within first few days of life.

Treatment:

- Systemic:
  - Ceftriaxone 25-50mg/kg (max. 125mg) IV or IM single dose. or
  - Cefotaxime 100 mg/kg IV or IM single dose.
    (preferred if premature or hyperbilirubinaemia present)
- Disseminated infections :
  - Ceftriaxone 25-50mg/kg/day IV or IM in single daily dose for 7days, or
  - Cefotaxime 25mg/kg/dose every 12 hours for 7 days.
- Documented meningitis : 10-14 days
- Local: Irrigate eyes with sterile normal saline initially every 15 mins and then at least hourly as long as necessary to eliminate discharge. Frequency can be reduced as discharge decreases. Topical antibiotics optional.

Non- Gonococcal

- Includes *Coagulase negative staphylococci, Staphylococcus aureus, Streptococcus viridans, Haemophilus, E.coli, Klebsiella species* and *Pseudomonas*. Most are hospital acquired conjuctivitis.

Treatment:

- Local: Chloramphenicol, gentamicin eye ointment 0.5%, both eyes (Change according to sensitivity ,duration according to response), or In non- responsive cases refer to ophthalmologist and consider Fucithalmic, Ceftazidime 5% ointment bd to qid for a week.
- Eye toilet (refer as above).

Chlamydial

- Replaced N. gonorrhoea as most common aetiology associated with sexually transmitted infections (STI).
- Unilateral or bilateral conjunctivitis with peak incidence at 2 weeks of life

Treatment:

- Erythromycin 50mg/kg/d in 4 divided doses for 2 weeks
  Caution - association with hypertrophic pyloric stenosis
  May need to repeat course of erythromycin for further 2 weeks if poor response as elimination after first course ranges from 80-100%
- If subsequent failure of treatment, use Trimethoprim-sulfamethazole 0.5ml/kg/d in 2 doses for 2 wks (Dilution 200mg SMZ /40mg TM in 5 mls).
- Systemic treatment is essential. Local treatment may be unnecessary if systemic treatment is given.

Herpes simplex virus

- Herpes simplex keratoconjunctivitis usually presents with generalized infection with skin, eyes and mucosal involvement.
- May have vesicles around the eye and corneal involvement

Systemic treatment

- IV acyclovir 30mg/kg/d divided tds for 2 weeks.

Important Notes

- Refer patients to an ophthalmologist for assessment.
- Ophthalmia neonatorum (all forms) is a notifiable disease
- Check VDRL of the infant to exclude associated congenital syphilis and 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 in 2 weeks with a repeat eye swab gram stain and C&S.

Chapter 27: Patent Ductus Arteriosus in the Preterm

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
- Intraventricular haemorrhage (IVH)
- Pulmonary haemorrhage
- Renal impairment
- Necrotising enterocolitis
- Chronic lung disease

Management

- Confirm PDA with cardiac ECHO if available
- Medical
  - Fluid restriction. Care with fluid balance to avoid dehydration
  - No role for diuretics
  - IV or oral Indomethacin 0.2mg/kg/day daily dose for 3 days
    or
    IV or oral Ibuprofen 10mg/kg first dose, 5mg/kg second and third doses, administered by syringe pump over 15 minutes at 24 hour intervals.
  - Indomethacin or ibuprofen is contraindicated if
    - Infant is proven or suspected to have infection that is untreated.
    - Bleeding, especially active gastrointestinal or intracranial.
    - Platelet count < 60 x 10^9/L
    - NEC or suspected NEC
    - Duct dependant congenital heart disease
    - Impaired renal function: creatinine > 140 µmol/L, 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 PDA in this group will close spontaneously.

Pearls and Pitfalls in Management

- There is a higher success rate in closure of PDA if indomethacin is given in the first two weeks of life.
- When using oral indomethacin, ensure that suspension is freshly prepared and well mixed before serving.
- IV indomethacin is unstable once the vial is opened.

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.

PPHN can be:

- Idiopathic - 20%
- Associated with a variety of lung diseases:
  - Meconium aspiration syndrome (50%)
  - Pneumonia/sepsis (20%)
  - RDS (5%)
  - Congenital diaphragmatic hernia (CDH)
  - Others: Asphyxia, Maternal diabetes, Polycythemia

Diagnosis

- *History*
  - 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 praecordial impulse
  - Low parasternal murmur of tricuspid incompetence
- *Radiography*
  - Lung fields
    Normal, parenchymal lesions if lung disease is present, or oligaemia
  - 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 output.
- The *Hyperoxic test* may play a role in diagnosis if 2D echocardiography is not available. However, severe PPHN is likely to produce a similar result to cyanotic CHD.

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.
- Infants 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 10-20 mcg/kg/hr. Morphine is a safe sedative and analgesic even in the preterm infants.
  - Midazolam – not recommended for preterms < 34 weeks gestational age, assocated with adverse long term neurodevelopmental outcomes.
- Ventilation
  - Conventional ventilation – adopt 'gentle ventilatory' approach by
    - Avoidance of hyperventilation (i.e. hypocarbia and hyperoxia).
      Hypocarbia is associated with periventricular leukomalacia. Aim for a PCO_2 of 45-55mmHg.
      Hyperoxia leads to chronic oxygen dependency and bronchopulmonary dysplasia. Keep PO_2 within normal limits of 60 -80 mmHg.
    - Ventilating to achieve a tidal volume of 3 to 5mls/kg.
    - 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 / High Frequency Jet Ventilation
    Effective in newborns with PPHN secondary to a pulmonary pathology.

- Circulatory support

  Inotropes for circulatory support improve cardiac output and enhances systemic oxygenation. Its use is poorly substantiated in PPHN, especially with the use of inhaled nitric oxide (iNO), which through its pulmonary vasodilating effect helps to improve cardiac output and the systemic blood pressure. Aim to keep the mean arterial pressure > 50 mmHg in term infants.

  However, inotropes are still recommended in institutions without facilities for iNO:

Dopamine	5 – 20 mcg/kg/min
Dobutamine	5 – 20 mcg/kg/min
Adrenaline	0.1 – 1.0 mcg/kg/min

- Vasodilators
  - Inhaled nitric oxide (iNO)- selective pulmonary vasodilator.
    - In term and near term infants (>34 weeks gestational age) reduces need for Extra Corporeal Membrane Oxygenation (ECMO)(Dose: 5-20 ppm).
    - insufficient evidence to support use in preterm infants < 34 weeks age.
  - Prostacycline and Sildenafil. These are not recommended for routine use as their safety and efficacy had not been tested in large randomized trials. Sildenafil in the treatment of PPHN has significant potential especially in resource limited settings.
- Extracorporeal membrane oxygenation (ECMO)

  ECMO is effective in PPHN. It is expensive as it requires trained personnel, specialized equipment and a good nursing-cot ratio.
- Practices not recommended for routine use:
  - Sodium bicarbonate.

    There is lack of sufficient evidence to recommend its routine use
  - Magnesium sulphate

    Anecdotal efficacy in PPHN but not yet been tested in large randomized trials to justify its use routinely.
  - Muscle relaxant agents

    No evidence for use in PPHN. Use had been known to increase mortality rates.

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%)**, as these infants have not acquired maternal protecting antibodies. 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 as prophylaxis:
  - Varicella Zoster immunoglobulin (VZIG) as soon as possible within 96 hours of initial exposure (to reduce the occurrence of complications and fatal outcomes). Attenuation of disease might still be achieved with administration of VZIG up to 10 days.
  - If Zoster immunoglobulin is not available give IV Immunoglobulin 400 mg/kg (this is less effective), AND
  - IV Acyclovir 15 mg/kg/dose over 1 hour every 8hrly (total 45 mg /kg/day) for 5 days.
  - On sending home, warn parents to look out for new vesicles or baby being unwell for 28 days after exposure. If so, parents to bring the infant to the nearest hospital as soon as possible (62% of healthy such neonates given VZIG after birth)
- If vesicles develop to give IV Acyclovir 10-15 mg/kg/dose over 1 hour every 8hrly (total 30-45 mg /kg/day) for 7-10 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.
- It has been generally accepted that passive immunization of the neonate can modify the clinical course of neonatal varicella but it does not prevent the disease and, although decreased, the risk of death is not completely eliminated.
- Infants whose mothers develop Zoster before or after delivery have maternal antibodies and they will not need ZIG.
- Recommend immunisation of family members who are not immune.

Postnatal exposure to varicella in the hospital

- Give VZIG within 96 hours to those who have been exposed if they fit the following criteria:
  - All babies born at < 28 weeks gestation or who weighed < 1000g at birth irrespective of maternal history of chickenpox.
  - All preterm babies born at ≥28 weeks gestation whose mothers have not had chickenpox or whose status is unknown.
  - All immunocompromised patients, e.g. immunosuppressive therapy, have malignant disease or are immunodeficient.
- Isolate patient who has varicella infection and susceptible patients who have been exposed to the virus. Treatment of symptomatic patients with acyclovir as above.
- Screen exposed, susceptible hospital staff for skin lesions, fever, headache and systemic symptoms. They are potentially infective 10-21 days after exposure and should be placed on sick leave immediately should any symptoms or skin lesion arise. If possible they can also be reassigned during the incubation period to areas where the patients are not as susceptible or non-patient care areas.

Other notes

- In hospitals, airborne transmission of VZV has been demonstrated when varicella has occurred in susceptible persons who have had no direct contact with the index case-patient.
- Incubators are not positive pressure air flow & therefore do not provide isolation. Neonates may not be protected given that they are frequently open for nursing purposes.
- All staff should preferably be screened and susceptible staff vaccinated for varicella before commencing work in neonatal, oncology and ICU wards. If not,they should receive post exposure vaccination as soon as possible unless contraindications exist such as pregnancy. VZIG is an option for exposed susceptible pregnant staff to prevent complications in the mother rather than to protect the foetus.
- The use of VZIG following exposure does not necessarily prevent varicella and may prolong the incubation period by > 1 week and hence signs or symptoms should be observed for 28 days post exposure.
- VZIG is not presently recommended for healthy full term infants who are exposed postnatally, even if their mothers have no history of varicella infection. To emphasise to parents to bring back early for treatment with acyclovir if any skin lesion appear within the next 3 weeks.

References

Section 2 Neonatology

Chapter 9 Transport of a Sick Newborn

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Chapter 30: 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.
- 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 a bronchodilator.

Important Points to Note in:	
Clinical History	*Physical Examination*
Current symptoms	*Signs of chronic illness*
Pattern of symptoms	Harrison's sulci
Precipitating factors	Hyperinflated chest
Present treatment	Eczema / dry skin
Previous hospital admission	Hypertrophied turbinates
Typical exacerbations	*Signs in acute exacerbation*
Home/ school environment	Tachypnoea
Impact on life style	Wheeze, rhonchi
History of atopy	Hyperinflated chest
Response to prior treatment	Accessory muscles
Prolonged URTI symptoms	Cyanosis
Family history	Drowsiness
	Tachycardia
Note: Absence of Physical Signs Does Not Exclude Asthma!	

- In pre-school children, epidemiological studies have delineated children with wheezing into 3 different phenotypes:
  Transient wheezers, Persistent wheezers and Late-onset wheezers.
- These phenotypes are only useful when applied retrospectively.

- Hence, there are recommendations to define pre-school wheezing into two main categories:
  - *Episodic (viral) wheeze.* Children who only wheeze with viral infections and are well between episodes.
  - *Multiple trigger wheezers* are children who have discrete exacerbations and symptoms in between these episodes. Triggers are smoke, allergens, crying, laughing and exercise.
- The presence of atopy (eczema, allergic rhinitis and conjunctivitis) in the child or family supports the diagnosis of asthma . However, the absence of these conditions does not exclude the diagnosis.
- Thus, because of the difficulty to diagnose asthma in young children, an asthmatic predictive index can be helpful in predicting children who were going to be asthmatics. The possibility of those with negative index not becoming asthmatic by 6 years old was 95% whereas those with a positive index have a 65% chance of becoming asthmatic by 6 years old.

A Clinical Index to define Risk of Asthma in young children with Recurrent Wheeze:	
Positive index (> 3 wheezing episodes / year during first 3 years) plus 1 Major criterion or 2 Minor criteria.	
Major criteria	• Eczema[1]
	• Parental asthma[1]
	• Positive aeroallergen skin test[1]
Minor criteria	• Positive skin test[1]
	• Wheezing without upper respiratory tract infection
	• Eosinophilia (> 4%)
Footnote: 1, Doctor Diagnosed	

- The child who presents with chronic cough alone (daily cough for > 4 weeks) and has never wheezed is unlikely to have asthma. These children require further evaluation for other illnesses that can cause chronic cough.

MANAGEMENT OF CHRONIC ASTHMA

Patients with a new diagnosis of asthma should be properly evaluated as to their degree of asthma severity:

Evaluation of the background of newly diagnosed asthma	
Category	Clinical Parameters
Intermittent	• Daytime symptoms less than once a week
	• Nocturnal symptoms less than once a month
	• No exercise induced symptoms
	• Brief exacerbations not affecting sleep and activity
	• Normal lung function
Persistent (Threshold for preventive treatment)	
Mild Persistent	• Daytime symptoms more than once a week
	• Nocturnal symptoms more than twice a month
	• Exercise induced symptoms
	• Exacerbations > 1x/month affecting sleep, activity
	• PEFR / FEV_1 > 80%
Moderate Persistent	• Daytime symptoms daily
	• Nocturnal symptoms more than once a week
	• Exercise induced symptoms
	• Exacerbations > 2x/month affecting sleep, activity
	• PEFR / FEV_1 60 - 80%
Severe Persistent	• Daytime symptoms daily
	• Daily nocturnal symptoms
	• Daily exercise induced symptoms
	• Frequent exacerbations > 2x/month affecting sleep, activity
	• PEFR / FEV_1 < 60%

Note

- *This division is arbitrary and the groupings may merge. An individual patient'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.*
- *PEFR = Peak Expiratory Flow Rate; FEV_1 = Forced Expiratory Volume in One Second.*

- 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.
- Patients who are already on treatment should be assessed at every clinic visit on their control of asthma

Levels of Asthma Control (GINA 2006)			
Characteristics	*Controlled* All of the following:	*Partly Controlled* *Any* measure present in *any* week:	*Uncontrolled*
Daytime symptoms	None	> 2 per week	≥ 3 features of partly controlled asthma present in any week
Limitation of activities	None	Any	
Nocturnal symptoms or Awakenings	None	Any	
Need for Reliever	None	> 2 per week	
Lung function test	Normal	< 80% predicted or personal best	
Exacerbations	None	≥ 1 per year	One in *any* week

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 bedrooms, 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 β_2-agonist prior to strenuous exercise, as well as optimizing treatment, are usually helpful.

Drug Therapy

Drug Therapy: Delivery systems available & recommendation for different ages.				
Age (years)	Oral	MDI + Spacer	MDI + Mask + Spacer	Dry Powder Inhaler
< 5	+	+	-	-
5 – 8	-	+	-	-
> 8	-	+	+	+
Note: *MDI = Meter dose inhaler* *Mask used should be applied firmly to the face of the child*				

Treatment of Chronic Asthma

Asthma management based on levels of control is a step up and step down approach as shown in the table below:

Management Based On Control				
← Reduce			Increase →	
STEP 1 Intermittent	**STEP 2** Mild Persistent	**STEP 3** Moderate Persistent	**STEP 4** Severe Persistent	**STEP 5** Severe Persistent
As needed rapid acting β_2-agonist	As needed rapid acting β_2-agonist			
Controller Options	*Select one*	*Select One*	*Add one / more*	*Add one / both*
	Low dose inhaled steroids	Low dose ICS + long acting β_2-agonist	Medium / High dose ICS + long acting β_2-agonist	Oral Glucocorticoids lowest dose
	Leukotriene modifier	Medium / High dose ICS	Leukotriene modifier	Anti-IgE
		Low dose ICS + Leukotriene modifier	SR Theophylline	
		Low dose ICS + SR Theophylline		
Footnote: ICS, Inhaled Corticosteroids; SR, Sustained Release.				

Drug Dosages for Medications used in Chronic *Asthma*		
Drug	Formulation	Dosage
Relieving Drugs		
β_2-agonists		
• 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	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
Preventive Drugs		
Corticosteroids		
• Prednisolone	Oral	1-2 mg/kg/day in divided doses
• Beclomethasone Diproprionate • Budesonide	Metered dose inhaler Dry powder inhaler	<400 mcg/day : low dose 400-800 mcg/day : Moderate 800-1200 mcg/day: High
• Fluticasone Propionate	Metered dose inhaler Dry powder inhaler	<200 mcg/day : Low 200-400 mcg/day : Moderate 400-600 mcg/day : High
• Ciclesonide	Metered dose inhaler	160 microgram daily 320 microgram daily
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
Long acting β_2-agonists		
• Salmeterol	Metered dose inhaler Dry powder inhaler	50-100 mcg/dose BD 50-100 mcg/dose BD
Combination		
Salmeterol / Fluticasone	Metered dose inhaler Dry powder inhaler	25/50mcg, 25/125mcg, 25/250mcg 50/100mcg,50/250mcg, 50/500mcg
Budesonide /Formoterol	Dry powder inhaler	160/4.5mcg, 80/4.5mcg
Antileukotrienes (Leukotriene modifier)		
Montelukast	Oral	4 mg granules 5mg/tablet on night chewable 10mg/tablet ON

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 above.
- Step-down; review treatment every 3 months and if control sustained for at least 4-6 months, consider gradual treatment reduction.

Monitoring

During each follow up visit, three issues need to be assessed. They are:

- Assessment of asthma control based on:
  - Interval symptoms.
  - Frequency and severity of acute exacerbation.
  - Morbidity secondary to asthma.
  - Quality of life.
  - Peak Expiratory Flow Rate (PEFR) or FEV_1 monitoring.
- Compliance to asthma therapy:
  - Frequency.
  - Technique.
- Asthma education:
  - Understanding asthma in childhood.
  - Reemphasize compliance to therapy.
  - Written asthma action plan.

Patients with High Risk Asthma are at risk of developing near fatal asthma (NFA) or fatal asthma (FA) . This group of patients need to be identified and closely monitored which includes frequent medical review (at least 3 monthly), objective assessment of asthma control with lung function on each visit, review of asthma action plan and medication supply, identification of psychosocial issues and referral to a paediatrician or respiratory specialist.

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

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

Initial ABG is indicated only in acute severe asthma.

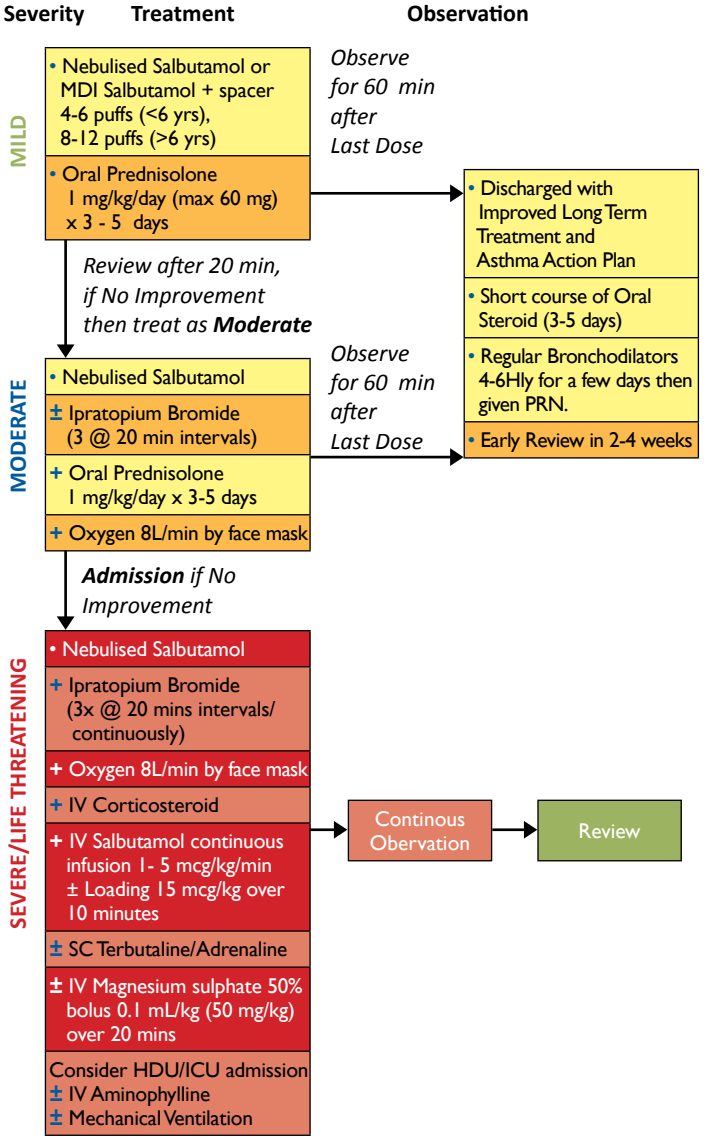
Management of acute asthma exacerbations

- Mild attacks can be usually treated at home if the patient is prepared and has a personal asthma action plan.
- Moderate and severe attacks require clinic or hospital attendance.
- Asthma attacks require prompt treatment.
- A patient who has brittle asthma, previous ICU admissions for asthma or with parents who are either uncomfortable or judged unable to care for the child with an acute exacerbation should be admitted to hospital.

Criteria for admission

- Failure to respond to standard home treatment.
- Failure of those with mild or moderate acute asthma to respond to nebulised β_2-agonists.
- Relapse within 4 hours of nebulised β_2- agonists.
- Severe acute asthma.

The Initial Assessment is the First Step in the Management of Acute Asthma				
Severity of Acute Asthma Exacerbations				
Parameters	*Mild*	*Moderate*	*Severe*	*Life Threatening*
Breathless	When walking	When talking *Infant:* Feeding difficulties	At rest *Infant:* Stops feeding	
Talks in	Sentences	Phrases	Words	Unable to speak
Alertness	Maybe agitated	Usually agitated	Usually agitated	Drowsy/ confused/ coma
Respiratory rate	Normal to Mildly Increased	Increased	Markedly Increased	Poor Respiratory Effort
Accessory Muscle usage / retractions	Absent	Present - Moderate	Present – Severe	Paradoxical thoraco-abdominal movement
Wheeze	Moderate, often only end expiratory	Loud	Usually loud	Silent chest
SpO_2 (on air)	>95%	92-95%	<92%	Cyanosis & <92%
Pulse /min	< 100	100-120	>120(>5yrs) >160 (infants)	Bradycardia
PEFR[1]	>80%	60-80%	<60%	Unable to perform
Footnote: *1, PEFR after initial bronchodilator, % predicted or of personal best*				


Severity
Treatment
Observation
MILD
• Nebulised Salbutamol or MDI Salbutamol + spacer 4-6 puffs (<6 yrs), 8-12 puffs (>6 yrs)
• Oral Prednisolone 1 mg/kg/day (max 60 mg) x 3 - 5 days
Observe for 60 min after Last Dose
• Discharged with Improved Long Term Treatment and Asthma Action Plan
• Short course of Oral Steroid (3-5 days)
• Regular Bronchodilators 4-6Hly for a few days then given PRN.
• Early Review in 2-4 weeks
Review after 20 min, if No Improvement then treat as Moderate
MODERATE
• Nebulised Salbutamol
± Ipratopium Bromide (3 @ 20 min intervals)
+ Oral Prednisolone 1 mg/kg/day x 3-5 days
+ Oxygen 8L/min by face mask
Observe for 60 min after Last Dose
Admission if No Improvement
SEVERE/LIFE THREATENING
• Nebulised Salbutamol
+ Ipratopium Bromide (3x @ 20 mins intervals/ continuously)
+ Oxygen 8L/min by face mask
+ IV Corticosteroid
+ IV Salbutamol continuous infusion 1- 5 mcg/kg/min ± Loading 15 mcg/kg over 10 minutes
± SC Terbutaline/Adrenaline
± IV Magnesium sulphate 50% bolus 0.1 mL/kg (50 mg/kg) over 20 mins
Consider HDU/ICU admission
± IV Aminophylline
± Mechanical Ventilation
Continous Obervation
Review

Footnotes on Management of Acute Exacerbation of Asthma:

1. Monitor pulse, colour, PEFR, ABG and O_2 Saturation.
   Close monitoring for at least 4 hours.
2. Hydration - give maintenance fluids.
3. Role of Aminophylline debated due to its potential toxicity.
   To be used with caution, in a controlled environment like ICU.
4. IV Magnesium Sulphate : Consider as an adjunct treatment in severe exacerbations unresponsive to the initial treatment. It is safe and beneficial in severe acute asthma.
5. Avoid Chest physiotherapy as it may increase patient discomfort.
6. Antibiotics indicated only if bacterial infection suspected.
7. Avoid sedatives and mucolytics.
8. Efficacy of prednisolone in the first year of life is poor.
9. On discharge, patients must be provided with an Action Plan to assist parents or patients to prevent/terminate asthma attacks.
   The plan must include:
   a. How to recognize worsening asthma.
   b. How to treat worsening asthma.
   c. How and when to seek medical attention.

- 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.

Drug Dosages for Medications used in Acute *Asthma*		
Drug	Formulation	Dosage
β_2-agonists		
• Salbutamol	Nebuliser solution 5 mg/ml or 2.5 mg/ml nebule Intravenous	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 Bolus: 5-10 mcg/kg over 10 min Infusion: Start 0.5-1.0 mcg/kg/min, increase by 1.0 mcg/kg/min every 15 min to a max of 20 mcg/kg/min
• Terbutaline	Nebuliser solution 10 mg/ml, 2.5 mg/ml or 5 mg/ml respule Parenteral	0.2-0.3 mg/kg/dose, or < 20 kg: 2.5 mg/dose > 20 kg: 5.0 mg/dose 5-10 mcg/kg/dose
• Fenoterol	Nebuliser solution	0.25-1.5 mg/dose
Corticosteroids		
• 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
Other agents		
Ipratropium bromide	Nebuliser solution (250 mcg/ml)	< 5 years old : 250 mcg 4-6 hourly > 5 years old : 500 mcg 4-6 hourly
Aminophylline	Intravenous	6 mg/kg slow bolus (if not previously on theophylline) followed by infusion 0.5-1.0 mg/kg/hr
Montelukast	Oral	4 mg granules 5mg/tablet on night chewable 10mg/tablet ON

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.

Guidelines 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
Crepitations 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 collapse/consolidation.
  - 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_2) 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_2 on inspired oxygen > 40%, or a rising pCO_2.
- Very young infants who are at risk of apnoea require greater vigilance.
- Blood gas analysis may have a role in the assessments of infants with severe respiratory distress or who are tiring and may be entering respiratory failure.
- Routine full blood count and bacteriological testing (of blood and urine) is not indicated in the assessment and management of infants with typical acute bronchiolitis .

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. Nasogastric feeding, although not universally practiced, may be useful in these children who refuse feeds and to empty the dilated stomach.
- *Intravenous fluids* for children with severe respiratory distress, cyanosis and apnoea. Fluid therapy should be restricted to maintenance requirement of 100 ml/kg/day for infants, in the absence of dehydration.

Pharmacotherapy

- The use of 3% saline solution via nebulizer has been shown to increase mucus clearance and significantly reduce hospital stay among non-severe acute bronchiolits. It improves clinical severity score in both outpatients and inpatients populations.
- *Inhaled β_2-agonists.* Pooled data have indicated a modest clinical improvement with the use of β_2-agonist. A trial of nebulised β_2-agonist, given in oxygen, may be considered in infants with viral bronchiolitis. Vigilant and regular assessment of the child should be carried out.
- *Inhaled steroids*. Randomised controlled trials of the use of inhaled or oral steroids for treatment of viral bronchiolitis show 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.
- Chest physiotherapy using vibration and percussion is not recommended in infants hospitalized with acute bronchiolitis who are not admitted into intensive care unit.

Aetiology and epidemiology

- A clinical syndrome characterised by barking cough, inspiratory stridor, hoarse voice and respiratory distress of varying severity.
- A 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 types A and B, Adenovirus, Enterovirus, Measles, Mumps and Rhinoviruses and rarely *Mycoplasma pneumoniae* and *Corynebacterium Diptheriae.*

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 epiglotitis, retropharyngeal abscess etc.
- **In severe croup, it is advisable to examine the pharynx under controlled conditions, i.e. in the ICU or Operation Theatre.**
- A 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

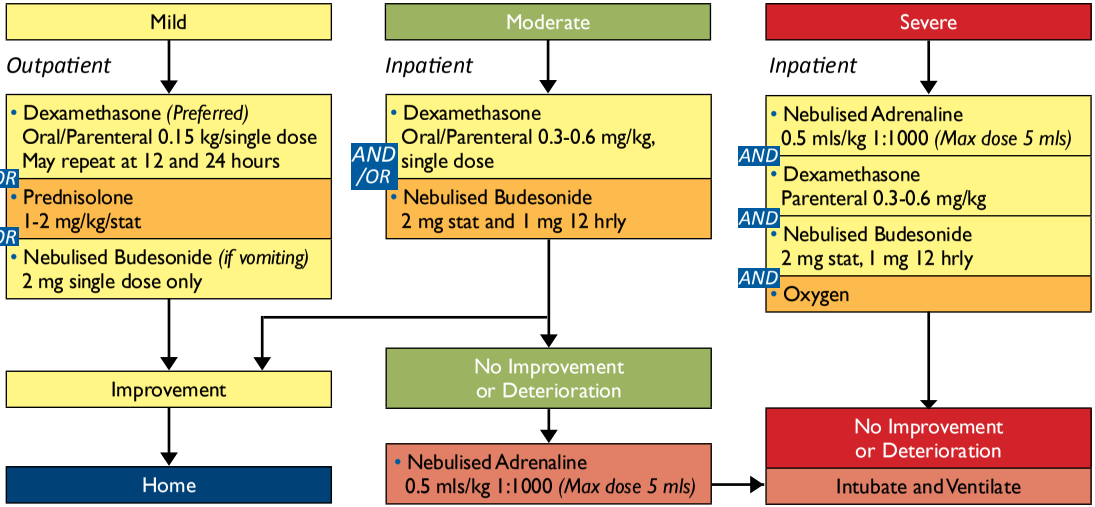
Indications for Hospital admission

- Moderate and severe viral croup.
- Age less than 6 months.
- Poor oral intake.
- Toxic, sick appearance.
- Family lives a long distance from hospital; lacks reliable transport.

Treatment (ref Algorithm on next page)

- The sustained action of steroids combined with the quick action of adrenaline may reduce the rate of intubation from 3% to nil.
- Antibiotics are not recommended unless bacterial super-infection is strongly suspected or the patient is very ill.
- IV fluids are not usually necessary except for those unable to drink.

Algorithm for the Management of Viral Croup



Footnote:

- The decision to intubate under controlled conditions (in Operation Theatre or Intensive Care Unit, with standby for tracheostomy) is based on clinical criteria, often from increasing respiratory distress.
- Indications for oxygen therapy include: 1. severe viral croup; 2. percutaneous SpO_2 < 93%
- With oxygen therapy, SpO_2 may be normal despite progressive respiratory failure and a high $PaCO_2$. Hence clinical assessment is important.

Definition

There are two clinical definitions of pneumonia:

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

Aetiology

- Specific aetiological agents are not identified in 40% to 60% of cases.
- It is often difficult to distinguish viral from bacterial disease.
- The majority of lower respiratory tract infections are viral in origin, e.g. Respiratory syncytial virus, Influenza A or B, Adenovirus, Parainfluenza virus.
- A helpful indicator in predicting aetiological agents is the age group. The predominant bacterial pathogens are shown in the table below:

Pathogens for Pneumonia	
Age	Bacterial Pathogens
Newborns	*Group B streptococcus, Escherichia coli, Klebsiella species, Enterobacteriaceae*
Infants 1- 3 months	*Chlamydia trachomatis*
Preschool age	*Streptococcus pneumoniae, Haemophilus influenzae type b, Staphylococcal aureus* Less common: Group A *Streptococcus, Moraxella catarrhalis, Pseudomonas aeruginosa*
School age	*Mycoplasma pneumoniae, Chlamydia pneumoniae*

Assessment of Severity in Pneumonia	
Age < 2 months	Age 2 months - 5 years
Severe Pneumonia	*Mild Pneumonia*
• Severe chest indrawing	• Tachypnoea
• Tachypnoea	*Severe Pneumonia*
	• Chest indrawing
Very Severe Pneumonia	*Very Severe Pneumonia*
• Not feeding	• Not able to drink
• Convulsions	• Convulsions
• Abnormally sleepy, difficult to wake	• Drowsiness
• Fever, or Hypothermia	• Malnutrition

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

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 suggest pneumonia.
  - Does not differentiate aetiological agents.
  - Not always necessary if facilities are not available or if pneumonia is mild.
- *White blood cell count*
  - Increased counts with predominance of polymorphonuclear cells suggests bacterial cause.
  - Leucopenia suggests either a viral cause or severe overwhelming infection.
- *Blood culture*
  - Non-invasive gold standard for determining the precise aetiology.
  - Sensitivity is low: Positive blood cultures only in 10%-30% of patients.
  - Do cultures in severe pneumonia or if poor response to first line antibiotics.
- *Pleural fluid analysis*
  - If there is significant pleural effusion, a diagnostic pleural tap will be helpful.
- *Serological tests*
  - Serology is performed in patients with suspected atypical pneumonia, i.e. *Mycoplasma pneumoniae, Chlamydia, Legionella, Moraxella catarrhalis*
  - Acute phase serum titre > 1:160 or paired samples taken 2-4 weeks apart with 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

- Objective measurement of hypoxia by pulse oximetry 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
- Identify indicators of severity in children who need admission, as pneumonia can be fatal. 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 ^{o}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, e.g. Immunodeficiency

Antibiotics

- When treating pneumonia, consider clinical, laboratory, radiographic findings, as well as age of the child, and the local epidemiology of respiratory pathogens and resistance/sensitivity patterns to microbial agents.
- Severity of the pneumonia and drug costs also impact on selection of therapy.
- Majority of infections are caused by viruses and do not require antibiotics.

Bacterial pathogens and Recommended antimicrobial agents.	
Pathogen	Antimicrobial agent
Beta-lactam susceptible	
• *Streptococcus pneumonia*	Penicillin, cephalosporins
• *Haemophilus influenzae* type b	Ampicillin, chloramphenicol, cephalosporins
• *Staphylococcus aureus*	Cloxacillin
• Group A *Streptococcus*	Penicillin, cephalosporin
Mycoplasma pneumoniae	Macrolides, e.g. erythromycin, azithromycin
Chlamydia pneumoniae	Macrolides, e.g. erythromycin, azithromycin
Bordetella pertussis	Macrolides, e.g. erythromycin, azithromycin

INPATIENT MANAGEMENT

Antibiotics

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

Suggested antimicrobial agents for inpatient treatment of pneumonia	
First line	*Beta-lactams*: Benzylpenicillin, moxycillin, ampicillin, amoxycillin-clavulanate
Second line	*Cephalosporins*: Cefotaxime, cefuroxime, ceftazidime
Third line	*Carbapenem*: Imipenam
Other agents	*Aminoglycosides*: 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 in pneumonia from *Mycoplasma* or *Chlamydia*.
- 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 chiefly occurs in infants with a significant risk of mortality.
- Radiological features include multilobar consolidation, cavitation, pneumatocoeles, spontaneous pneumothorax, empyema, pleural effusion.
- Treat with high dose Cloxacillin (200 mg/kg/day) for a longer duration
- Drainage of empyema often results in a good outcome.

Necrotising pneumonia and pneumatocoeles

- It is a result of localized bronchiolar and alveolar necrosis.
- Aetiological agents are bacteria, e.g. *Staphylococcal aureus, S. Pneumonia, H. Influenza, Klebsiella pneumonia* and *E. coli*.
- Give IV antibiotics until child shows signs of improvement.
- Total antibiotics course duration of 3 to 4 weeks.
- Most pneumatocoeles disappear, with radiological evidence resolving within the first two months but may take as long as 6 months.

Supportive treatment

- *Fluids*
  - Withhold oral intake when a child is in severe respiratory distress.
  - In severe pneumonia, secretion of anti-diuretic hormone is increased and as such dehydration is uncommon. Avoid overhydrating the child.
- *Oxygen*
  - Oxygen reduces mortality associated with severe pneumonia.
  - It should be given especially to children who are restless, and tachypnoeic with severe chest indrawing, cyanosis, or is not tolerating feeds.
  - Maintain the SpO_2 > 95%.
- *Cough medication*
  - Not recommended as it causes suppression of cough and may interfere with airway clearance. Adverse effects and overdosage have been reported.
- *Temperature control*
  - Reduces discomfort from symptoms, as paracetamol will not abolish fever.
- *Chest physiotherapy*
  - This assists in the removal of tracheobronchial secretions: removes airway obstruction, increase gas exchange and reduce the work of breathing.
  - No evidence that chest physiotherapy should be routinely done.

OUTPATIENT MANAGEMENT

- In children with mild pneumonia, their breathing is fast but there is no chest indrawing.
- Oral antibiotics can be prescribed.
- Educate parents/caregivers about management of fever, preventing dehydration and identifying signs of deterioration.
- The child should return in two days for reassessment, or earlier if the condition is getting worse.

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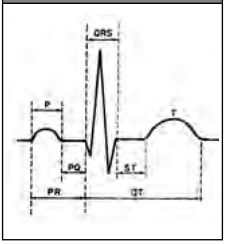
Age related changes in the anatomy and physiology of infants and children produce normal ranges for electrocardiographic features that differ from adults and vary with age. Awareness of these differences is the key to correct interpretation of paediatric ECG.

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)

The ECG cycle



Normal values for Heart rate 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

Normal values in 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)

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° to 180°) 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° to 120°). • RV remains dominant. • Negative T waves across right praecordial leads.
6 months to 3 years	• QRS axis < 90°. • R wave dominant in V6. • R/S ratio ≤ 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 seen in leads I, aVL, V5 and V6 provided amplitude < 5 mm.
- RSR' pattern of right praecordial leads: normal in 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); > 10mm (1 week - 6 mths); > 7mm (6 mths - 1 year); > 5mm (> 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 > 20mm in V6
- S (V1) + R (V6) > 40mm over 1 year of age; > 30mm if < 1year
- Q wave > 4 mm in V5-6
- T wave inversion in V5-6

Chapter 35: Congenital Heart Disease in the Newborn

Introduction

- Congenital heart disease (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 Gm/dL), confirmed by pulse oxymetry (SpO_2 < 85%) or ABG.

Causes of Cyanosis in the Newborn
Cyanotic Heart Disease
Obstructed pulmonary flow
Pulmonary atresia, Critical pulmonary stenosis, Tetralogy of Fallot
Discordant ventriculo-arterial connection
Transposition of great arteries.
Common mixing
Single ventricle, Truncus arteriosus, Tricuspid atresia, Total anomalous pulmonary venous drainage
Primary Pulmonary Disorders
Parenchymal disease
Meconium aspiration syndrome, Respiratory distress syndrome, Congenital pneumonia
Extraparenchymal disease
Pneumothorax, Congenital diaphragmatic hernia
Persistent pulmonary hypertension of newborn
Primary
Secondary
Meconium aspiration, Perinatal asphyxia, Congenital diaphragmatic hernia
Severe polycythaemia
Methaemoglobinuria

Heart Failure

Clinical presentation may mimic pulmonary disease or sepsis:

- Tachypnoea
- Tachycardia
- Hepatomegaly
- Weak pulses

Causes of Heart Faliure in the Newborn
Structural Heart Lesions
Obstructive Left Heart lesions
Hypoplastic left heart syndrome, critical aortic stenosis, severe coarctation of aorta
Severe Valvular Regurgitation
Truncal arteriosus with truncal valve regurgitation
Large Left to Right Shunts
Patent ductus arteriosus, ventricular septal defects, truncus arteriosus, aortopulmonary collaterals
Obstructed Pulmonary Venous Drainage
Total anomalous pulmonary venous drainage
Myocardial Diseases
Cardiomyopathy
Infant of diabetic mother, familial, idiopathic
Ischaemic
Anomalous origin of left coronary artery from pulmonary artery, perinatal asphyxia
Myocarditis
Arrhythmia
Atrial flutter, SVT, congenital heart block
Extracardiac
Severe anaemia
Neonatal thyrotoxicosis
Fulminant sepsis

Sudden Collapse

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

- Hypotension
- Extreme cyanosis
- Metabolic acidosis
- Oliguria

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.

Congenital heart lesions that may present with sudden collapse
Duct-dependent systemic circulation
Coarctation of aorta, Critical aortic stenosis, Hypoplastic left heart syndrome, Interrupted aortic arch
Duct-dependent pulmonary circulation
Pulmonary atresia with intact ventricular septum, Tricuspid atresia with pulmonary atresia, Single ventricle with pulmonary atresia, Critical pulmonary stenosis
Transposition of great arteries without septal defect
Obstructed total anomalous pulmonary drainage

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, 13; Turner syndrome, DiGeorge syndrome.
- Central cyanosis.
- Differential cyanosis (SpO_2 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_2 < 100 mmHg; rise in pO_2 is < 20 mmHg. (note: in severe lung diseases & PPHN, pO_2 can be < 100 mmHg).
- Echocardiography.

General principles of management

- Initial stabilization: secure airway, adequate ventilation, circulatory support
- Correct metabolic acidosis, electrolyte derangements, 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.
- If 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.

Summary of The Clinical Approach to Cyanotic Newborns					
Cause	History, Signs	Chest X-ray	ABG	Hyperoxia test	Echocardiography
Cyanotic Heart Disease	No/mild Respiratory distress. Heart murmur.	Abnormal heart size and pulmonary vasculature	Low PCO_2	No rise in PO_2	Usually diagnostic
Primary Lung Disease	Respiratory distress	Abnormal lungs	Low PO_2 Hgh PCO_2	PO_2 >100mmHg	Normal
Persistent Pulmonary Hypertension	Suggestive history (MAS, asphyxia, sepsis)	Maybe abnormal (lungs)	Differential cyanosis	Inconclusive	Right to left shunt across PFO or PDA
Methemoglbinemia	Normal	Normal	Normal	PO_2 >100mmHg	Normal
MAS, meconium aspiration syndrome; PFO, patent foramen ovale; PDA, patent ductus arteriosus					

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 (ASD primum):

- Elective surgical repair at 4 to 5 years old; earlier if symptomatic or severe AV valve regurgitation.

Complete AVSD:

- Primary surgical repair < 6 mths 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 (peak systolic gradient < 50 mmHg)

- No treatment.

Moderate-severe (gradient > 50 mmHg)

- Transcatheter balloon valvuloplasty is treatment of choice.

Neonatal critical PS:

- Characterized with cyanosis and RV dysfunction.
- Temporary stabilization with IV Prostaglandin E infusion.
- Early transcatheter balloon valvuloplasty.

Note: SBE prophylaxis is indicated in all cases

Coarctation of the aorta (CoA)

Neonatal severe CoA:

- Frequently associated with large malaligned VSD, intractable heart failure.
- Sick infants require temporary stabilization:
  - Mechanical ventilation.
  - Correction of metabolic acidosis, hypoglycaemia, electrolyte disorders.
  - 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.

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.

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.

Transposition of the great arteries (TGA)

Simple TGA (intact ventricular septum)

- 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:

- Does 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 < 3 months age.

TGA with VSD and PS:

- Blalock Taussig shunt during infancy followed by Rastelli repair at 4 to 6 years age.

Truncus arteriosus

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

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.

Chapter 36: 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, 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 the 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.

Definition

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

Causes of heart failure

- Congenital structural heart lesions: more common during infancy.
- Primary myocardial, acquired valvular diseases: more likely in older children.

Causes of Heart Failure	
Congenital heart disease	Acquired valvular disease
Left to right shunt lesions	• Chronic rheumatic valvular diseases
• VSD, PDA, AVSD, ASD	• Post infective endocarditis
Obstructive left heart lesions	Myocardial disease
• Hypoplastic left heart syndrome,	*Primary cardiomyopathy*
• Coarctation of aorta, aortic stenosis	• Idiopathic, familial
Common mixing unrestricted pulmonary flow	*Secondary cardiomyopathy*
• Truncus arteriosus, TAPVD, tricuspid atresia with	• Arrhythmia-induced: congenital heart block, atrial ectopic tachycardia
•TGA, single ventricle, pulmonary atresia with VSD,	• Infection: post viral myocarditis, Chagas disease
• Large aortopulmonary collateral	• Ischaemic: Kawasaki disease
Valvular regurgitation	• Myopathic: muscular dystrophy,
• AV valve regurgitation, Ebstein anomaly	• Pompe disease, mitochondrial dis.
• Semilunar valve regurgitation	• Metabolic: hypothyroidism
Myocardial ischaemia	• Drug-induced: anthracycline
• Anomalous origin of left coronary artery from pulmonary artery.	• Others: iron overload (thalassaemia)
	Acute myocarditis
	• Viral, rheumatic, Kawasaki disease

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, Poor peripheral pulses, poor peripheral perfusion.
  - Hyperactive praecordium, praecordial bulge.
  - Hepatomegaly.
  - 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.

Treatment

General measures

- Oxygen supplementation, propped up position
- Keep warm, gentle handling.
- Fluid restriction to ¾ 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
  - Use 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 ± steroid in acute rheumatic carditis.

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.

Diagnostic criteria for Acute Rheumatic Fever		
Major Criteria	**Minor Criteria**	**Investigations**
Carditis	Fever (Temp > 38 °C)	FBC: anaemia, leucocytosis
Polyarthritis, aseptic monoarthritis or polyarthralgia	ESR > 30 mm/h or CRP > 30 mg/L	Elevated ESR and CRP
		Throat swab, ASOT
		Blood culture
Chorea	Prolonged PR interval	CXR, ECG.
Erythema marginatum		Echocardiogram
Subcutaneous nodules		

Making the Diagnosis:

- Initial episode of ARF:
  2 major criteria or 1 major + 2 minor criteria,
  \+ *evidence of a preceding group A streptococcal infection*
- Recurrent attack of ARF: (known past ARF or RHD)
  2 major criteria or 1 major + 2 minor criteria or 3 minor criteria,
  \+ *evidence of a preceding group A streptococcal infection*

Note:

1. Evidence of carditis: cardiomegaly, cardiac failure, pericarditis, tachycardia out of proportion to fever, pathological or changing murmurs.

2. Abbrevations: ARF, Acute Rheumatic Fever; RHD, Rheumatic Heart Disease

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, tapering 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).

Important:

- ***Consider early referral to a 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.

Introduction

An uncommon condition 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.

Modified Duke Criteria for the Diagnosis of Infective Endocarditis	
Major Criteria	**Minor Criteria**
• Blood culture positive: *Typical microorganisms from two separate blood cultures:*	• Predisposing heart condition, prior heart surgery, indwelling catheter
	• Fever, temperature > 38°C
• *Viridans streptococci*	• Vascular phenomena:
• *Streptococcus bovis*	• Major arterial emboli
• *HACEK group*[1]	• Septic pulmonary infarcts
• *Staphylococcus aureus*	• Mycotic aneurysm
• *Community-acquired enterococci*	• Intracranial hemorrhage,
	• Conjunctival hemorrhages
• Evidence of endocardial involvement on echocardiogram	• Janeway's lesions
	• Immunologic phenomena:
	• Gomerulonephritis
Footnote: *1, Fastidious gram negative bacteria from Haemophilus spp, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens and Kingella kingae*	• Osler's nodes
	• Roth's spots
	• Positive Rheumatoid factor
	• Microbiological evidence:
	• Positive blood culture not meeting major criterion

Definition of Infective Endocarditis According to the Modified Duke Criteria		
Definite IE	**Possible IE**	**Rejected IE**

Pathological criteria
• Microorganisms by
  • Culture
  • Histological examination of vegetation or intra-cardiac abscess specimen.
• pathological lesions with active endocarditis.
Clinical criteria
• 2 major or
• 1 major + 3 minor or
• 5 minor
	• 1 major + 1 minor criteria
	OR
	• 3 minor
		• Firm alternative diagnosis
		• Resolution of symptoms with antibiotic therapy < 4 days.
		• No pathological evidence of IE at surgery or autopsy.
		• Not meet criteria for possible IE.

Footnote: 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 (see Table on facing page).

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/day in 4-6 div doses x 4wks AND IV/IM Gentamicin 3 mg/kg/day in 3 div doses x 2wks	IV Vancomycin 30 mg/kg/day in 2 div doses x 4–6wks AND IV/IM Gentamicin 3 mg/kg/day in 3 div doses x 2wks
Streptococcus viridans endocarditis	IV Vancomycin 30 mg/kg/day in 2 div doses x 4–6 wks AND IV/IM Gentamicin 3 mg/kg/day in 3 div doses x 2wks	IV Vancomycin 30 mg/kg/day in 2 div doses x 4–6wks AND IV/IM Gentamicin 3 mg/kg/day in 3 div doses x 2wks
Enterococcus endocarditis	IV Penicillin G 300,000 U/kg/day in 4-6 div doses x 4 - 6wks AND IV Gentamicin 3 mg/kg/day in 3 div doses x 4 - 6 wks	
Methicillin sensitive Staphylococcus endocarditis	IV Cloxacillin 200mg/kg/day in 4-6 div doses x 6wks +/- IV/IM Gentamicin 3mg/kg/day in 3 div doses x 3-5 days	
Penicillin allergy Methicillin Resistance	IV Cefazolin 100mg/kg/day in 3 div doses x 6 wks IV Vancomycin 40 mg/kg/day in 2-4 div doses x 6wks	IV Vancomycin 40 mg/kg/day in 2 div doses x 4–6wks
Culture- Negative Endocarditis	IV Ampicillin-Sulbactam 300mg/kg/day in 4-6 div doses x 4-6 wks AND IV Gentamicin 3mg/kg/day in 3 div doses x 4-6 wks	IV Vancomycin 40 mg/kg/day in 2 div doses x 4–6wks AND IV/IM Gentamicin 3 mg/kg/day in 3 div doses x 4-6wks AND IV Ciprofloxacin 20-30 mg/kg/day in 2 div doses x4-6wks
Fungal Endocarditis Candida spp or Aspergillosis	IV Amphotericin B > 6 weeks AND Valve replacement surgery AND Long-term (lifelong) therapy with Oral azole	

Guidelines on Infective Endocarditis (IE) prophylaxis

IE prophylaxis Recommended

High-risk category
- Prosthetic cardiac valves.
- Previous bacterial endocarditis.
- Complex cyanotic congenital heart disease.
- Surgical systemic pulmonary shunts or conduits.

Moderate-risk category
- Other congenital cardiac defects (other than high/low risk category)
- Acquired valvar dysfunction. (e.g. rheumatic heart disease)
- Hypertrophic cardiomyopathy.
- Mitral valve prolapse with regurgitation.

IE prophylaxis Not Recommended

Negligible-risk category
- Isolated secundum ASD.
- Repaired ASD, VSD, PDA (> 6 mths)
- Mitral valve prolapse without regurgitation.
- Functional, or innocent heart murmurs.
- Previous Kawasaki disease without valvar dysfunction.
- Previous rheumatic fever without valvar dysfunction.
- Cardiac pacemakers and implanted defibrillators.

Common procedures that require IE Prophylaxis

Oral, dental procedures
- Extractions, periodontal procedures.
- Placement of orthodontic bands (but not brackets).
- Intraligamentary local anaesthetic injections.
- Prophylactic cleaning of teeth.

Respiratory procedures
- Tonsillectomy or adenoidectomy.
- Surgical operations involving respiratory mucosa.
- Rigid bronchoscopy.
- Flexible bronchoscopy with biopsy.

Gastrointestinal procedures
- Sclerotherapy for esophageal varices.
- Oesophageal stricture dilatation.
- Endoscopic retrograde cholangiography biliary tract surgery.
- Surgical operations involving intestinal mucosa.

Genitourinary procedures
- Cystoscopy.
- Urethral dilation.

Antibiotic guidelines for IE prophylaxis

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

Standard general prophylaxis	Penicillin allergy (Either one of below):
• Oral Amoxicillin 50 mg/kg (max 2 Gm), one hour before procedure *OR* • IV/IM Ampicillin 50 mg/kg (max 2 Gm)	• Oral Clindamycin 20 mg/kg (max 600 mg) • Oral Cephalexin 50 mg/kg (max 2 Gm) • Oral Azithromycin/clarithromycin 50 mg/kg (max 500 mg) • Oral Erythromycin 20 mg/kg (max 3 Gm) • IV Clindamycin 20 mg/kg (max 600 mg)

Note: Give oral therapy 1 hour before procedure; IV therapy 30 mins before procedure.

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.

Diagnostic Criteria for Kawasaki Disease
• Fever lasting at least 5 days.
• At least 4 out of 5 of the following:
• Bilateral non-purulent conjunctivitis.
• Mucosal changes of the oropharynx (injected pharynx, red lips, dry fissured lips, strawberry tongue).
• Changes in extremities (oedema and/or erythema of the hands or feet, desquamation, beginning periungually).
• Rash (usually truncal), polymorphous but non vesicular.
• Cervical lymphadenopathy.
• Illness not explained by other disease process.

Clinical Pearls

Diagnosis is via table above. Other helpful signs in making the diagnosis:

- 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 are usually elevated.
- Serum albumin < 3g / dl; Raised alanine aminotransaminase
- Urine > 10 wbc / hpf
- Chest X-ray, ECG.
- Echocardiogram in the acute phase; Repeat at 6-8 wks/earlier if indicated.

Note:

- 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 or arrhythmia.

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 wks or until patient is afebrile for 2-3 days.

Maintainence:

- 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 ≥ 36hrs after completion of initial dose of IV Immunoglobulins.

Treatment

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

Vaccinations

- The use of Immunoglobulins may impair efficacy of live-attenuated virus vaccines. Delay these vaccinations for at least 11 months.

Prognosis

- Complete recovery in children without coronary artery involvement.
- Most (80%) 3-5 mm aneursyms 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.

Risk stratification and long term follow up after Kawasaki Disease				
Risk Level	**Treatment**	**Physical Activity**	**Follow up**	**Invasive Testing**
Level I No coronary artery changes	None beyond 6-8 weeks	No restrictions beyond 6-8 weeks	Cardiovascular risk assessment, counselling at 5yr intervals	None
Level II Transient coronary artery ectasia; none after 6-8 wks	None beyond 6-8 weeks	No restrictions beyond 6-8 weeks	Cardiovascular risk assessment, counselling at 3 - 5yr intervals	None
Level III 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
Level IV > 1 large or giant coronary artery aneurysm, or multiple or complex aneurysms in same coronary artery, without destruction.	Long term aspirin and 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
Level V Coronary artery obstruction.	Long term aspirin; Warfarin or LMWH if giant aneurysm persists. Also consider beta-blockers	Avoid contact sports	Biannual echocardiogram and ECG; Annual stress test	Angiography to address therapeutic options
LMWH, low molecular weight heparin				

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 prodromol 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.

Useful Investigations for Myocarditis
Electrocardiogram (ECG)
• Sinus tachycardia, Non-specific ST segment , Pathological Q wave, low QRS voltages (<5mm in any precordial lead), T wave inversion.
• 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
Need to exclude other structural abnormalities, especially coronary artery anomalies.
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 enhancement, regional wall motion abnormalities.
Endomyocardial biopsy

Management

- Depends on the severity of the illness. Patients with heart failure require intensive monitoring and haemodynamic support.
- Treatment of heart failure: see **Ch 37: Heart Failure.**
- Consider early respiratory support, 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.

BRADYARRHYTHMIA

Sinus node dysfunction

- Criteria for sinus bradycardia (Table below):

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
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
- Sepsis
- Acidosis
- Anorexia nervosa
- Electrolytes abnormalities i.e. hypokalaemia, hypocalcaemia

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: 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.

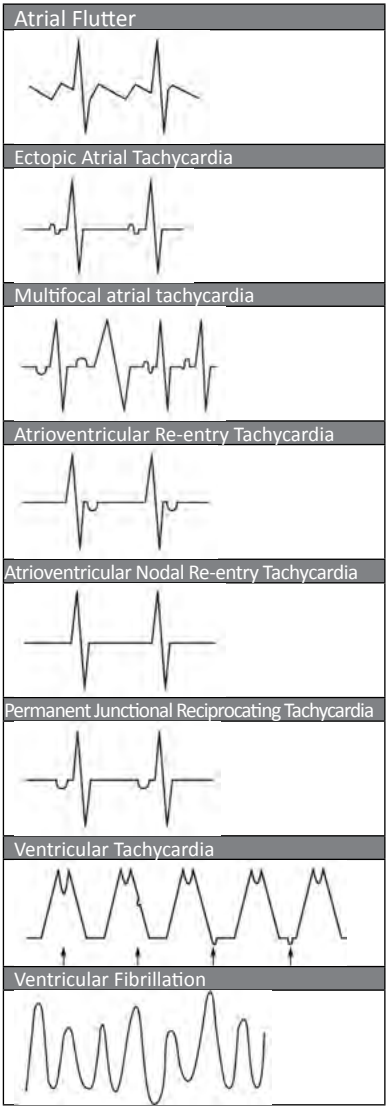
TACHYARRHYTHMIA

Classification

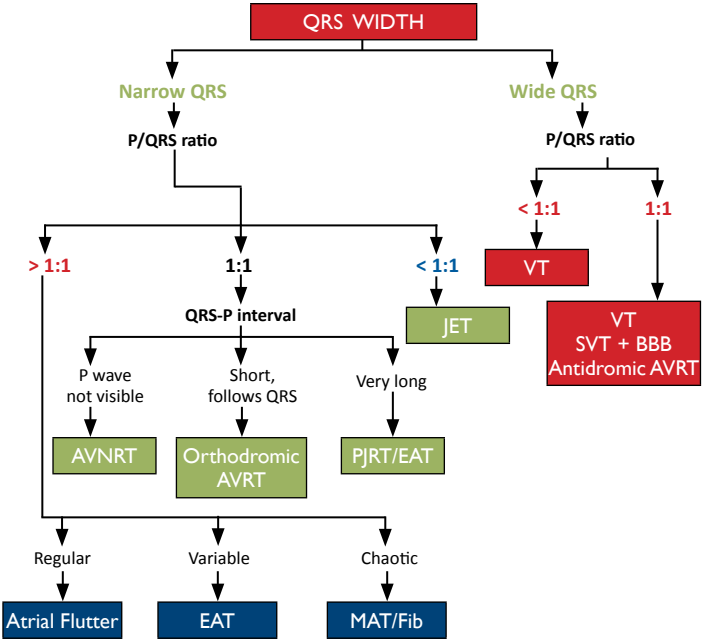
- Atrial tachycardia: AF, EAT, MAT
- Conduction system tachycardia or supraventricular tachycardia: AVRT, AVNRT, PJRT
- Ventricular tachycardia: VT, VF

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, chaotic.
  - No two RR intervals the same
- *Atrioventricular Re-entry Tachycardia (AVRT)*
  - P wave follows QRS.
- *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.

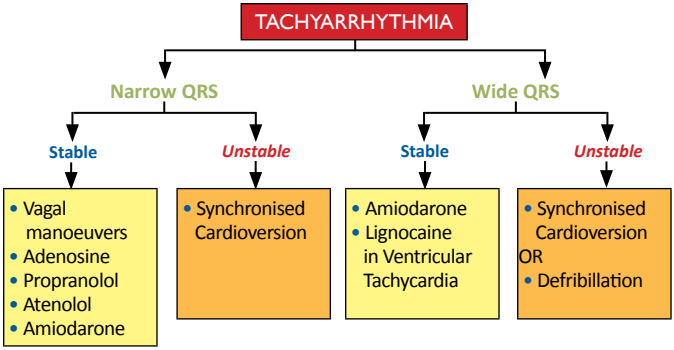


ALGORITHM FOR IDENTIFYING TACHYARRHYTHMIA



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

ALGORITHM FOR MANAGEMENT OF ACUTE TACHYARRHYTHMIA



Narrow QRS complex tachycardia

Haemodynamically stable

- Vagal manoeuvers:
  - Icepack/iced water for infants: apply to face for a max of 30 seconds .
  - Valsalva manoeuvers 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

- Consult a cardiologist if these acute measures fail to revert the tachycardia.
- In Wolff-Parkinson-White syndrome, digoxin is contraindicated because paroxysms 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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ALGORITHM FOR MANAGEMENT OF STATUS EPILEPTICUS

Child with SEIZURE

Seizure > 5 mins
Impending Status epilepticus

At Home, In Ambulance

PR Diazepam
0.2- 0.5 mg/kg (Max 10mg)
0.5mg/kg (2-5yrs); 0.3mg/kg (6-11yrs); 0.2mg/kg (12yrs +)

Ensure
- Ventilation
- Adequate Perfusion (ABC's)
- **Bedside Blood Sugar**

In Hospital

Obtain IV access
IV Diazepam 0.2mg/kg slow bolus (at 2 mg/min; maximum 10mg)

- If on maintainence Phenytoin, then give IV Phenobarbitone
- Monitor blood sugar, electrolytes, blood counts, liver function, blood gases.
- Consider blood culture, toxicology, neuroimaging, antiepileptic drug levels.
- If <2 yrs old, consider IV Pyridoxine 100 mg.

Seizure 5-30 mins
Established Status epilepticus

Consider:

IV Diazepam 0.2mg/kg slow bolus (if not already given)

IV Phenytoin 20 mg/kg
(Max Loading dose 1.25 Gm)
Dilute in 0.9% saline; Max. conc. at 10 mg/ml; Infuse over 20-30 mins, with cardiac monitoring.

CONSULT PAEDIATRICIAN !

Early Refractory Status epilepticus

Seizures continue > 10 mins after Phenytoin

Consider One of the following:

IV Midazolam 0.2 mg/kg bolus (at 2 mg/min; Max 10 mg), then infusion 3-5 mcg/kg/min up to a max of 15 mcg/kg/min)

IV Phenobarbitone 20 mg/kg
(Max Loading dose 1 Gm)
Infusion at 25- 50 mg/min),

IV Levetiracetam 40 mg/kg infused over 10 minutes, then 20 mg/kg 12 hourly

IV Sodium Valproate 20 mg/kg (Max Loading 1.25 Gm, given over 1-5 mins, at 20-50 mg/min), then infusion 1- 5 mg/kg/hour for 6 - 12 hours)

- Monitor BP, respiration
- Start inotropic support, esp. if given Midazolam or Phenobarbitone
- Arrange for ICU.
- Secure airway, prepare to use mechanical ventilation.
- Titrate Phenobarbitone to achieve burst-suppression pattern on EEG.
- Avoid Sodium Valproate in metabolic encephalopathy.

Seizure > 60 mins
Established Refractory Status epilepticus

Discuss with Paediatric Neurologist and Intensivist about inducing coma

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.

Salient Points

- Optimize vital functions throughout control of Status Epilepticus.
- Apart from terminating seizures, management of Status Epilepticus should include, identifying and treating underling cause.
- Presence of Status Epilepticus 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 are *underdosing* of anticonvulsants, *excessive time lag* between doses/steps of treatment and neglecting maintenance therapy after the initial bolus of anticonvulsants have been given. See **Drug Doses** for maintenance doses of anticonvulsants.

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.
- It is important to differentiate epileptic seizures from paroxysmal non-epileptic events such as neonatal sleep myoclonus, breath-holding spells, vasovagal syncope, long Q-T syndrome.

APPROACH TO A CHILD WITH A FIRST 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, gastroesophageal reflux.
- A thorough clinical examination is important to look for any possible underlying aetiology.
- There is a 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* seizures.
  - 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 the 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

APPROACH TO A CHILD WITH EPILEPSY

- Detailed history of the seizures. Video of the actual event is helpful. Also note birth history, developmental milestones and 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, hypocalcaemia.
  - Do an ECG 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.

ILAE Classification of seizure types
Generalised
Tonic-clonic
Absence (typical, atypical)
Myoclonic
Tonic
Clonic
Atonic
Focal seizures
Epileptic spasms

ILAE, International League Against Epilepsy

- Neuroimaging (preferably MRI) is indicated for any child with:
  - Epilepsy occurring in the first year of life, except febrile seizures.
  - Focal epilepsy except benign rolandic epilepsy.
  - Developmental delay or regression.
  - Intractable epilepsy.

Principles of antiepileptic drug therapy for Epilepsy

- Treatment recommended if ≥ 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.
- Drug level monitoring is not routinely done (except phenytoin), unless non-compliance, toxicity or drug interaction is suspected.
- When withdrawal of medication is planned (generally after 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.

Classification of epilepsies and epileptic syndromes (adapted from ILAE 2010)		
Neonatal period	Childhood	Adolescent - Adult
Benign familial neonatal epilepsy	Febrile seizure plus (FS+)	Juvenile absence epilepsy (JAE)
Early myoclonic encephalopathy	Epilepsy with myoclonic-atonic seizures	Juvenile myoclonic epilepsy (JME)
Ohtahara syndrome	Panayiotopoulos syndrome	Epilepsy with GTC seizures alone
	Benign rolandic epilepsy (BECTS)	Progressive myoclonic epilepsies (PME)
Infancy	Autosomal-dominant nocturnal FLE	Familial focal epilepsies
West syndrome	Late onset childhood occipital epilepsy	
Myoclonic epilepsy in infancy	Epilepsy with myoclonic absences	Others
Benign infantile epilepsy	Lennox-Gastaut syndrome	Mesial TLE with hippocampal sclerosis
Benign familial infantile epilepsy	Epilepsy with continuous spike-wave during sleep (CSWS)	Gelastic seizures with hypothalamic hamartoma
Dravet syndrome		Hemiconvulsion-hemiplegia-epilepsy
	Landau-Kleffner syndrome (LKS)	Rasmussen syndrome
	Childhood absence epilepsy (CAE)	Reflex epilepsies
* Epilepsies (generalized or focal), due to: (If unable to classify into the above) - Structural / metabolic causes - Genetic causes - Unknown cause.		

Selecting antiepileptic drugs according to seizure types		
Seizure type	**First line**	**Second line**
Focal Seizures		
	Carbamazepine Valproate	Lamotrigine, Topiramate, Levetiracetam, Clobazam, Phenytoin, Phenobarbitone
Generalized Seizures		
Tonic-clonic / clonic	Valproate	Lamotrigine, Topiramate, Clonazepam, Carbamazepine[1], Phenytoin[1], Phenobarbitone
Absence	Valproate	Lamotrigine, Levetiracetam
Atypical absences, Atonic, tonic	Valproate	Lamotrigine, Topiramate, Clonazepam, Phenytoin
Myoclonic	Valproate Clonazepam	Topiramate, Levetiracetam Clobazam, Lamotrigine[2], Phenobarbitone
Infantile Spasm	ACTH, Prednisolone, Vigabatrin[3]	Nitrazepam, Clonazepam, Valproate, Topiramate

Footnote:
1, May aggravate myoclonus/absence seizure in Idiopathic Generalised Epilepsy.
2, May cause seizure aggravation in Dravet syndrome and JME.
3, Especially for patients with Tuberous Sclerosis.

Antiepileptic drugs that aggravate selected seizure types	
Phenobarbitone	Absence seizures
Clonazepam	Causes Tonic status in Lennox-Gastaut syndrome
Carbamazepine	Absence, Myoclonic, Generalised tonic-clonic seizures
Lamotrigine	Dravet syndrome, Myoclonic seizures in Juvenile Myoclonic Epilepsy
Phenytoin	Absence, Myoclonic seizures
Vigabatrin	Myoclonic, Absence seizures

The patients with "Intractable Epilepsy"

Please re-evaluate for the following possibilities:-

- Is it a seizure or a non-epileptic event?
- Antiepileptic drug dose not optimised.
- Poor compliance to antiepileptic drug.
- Wrong classification of epilepsy syndrome, thus wrong choice of antiepileptic drug.
- Antiepileptic drug aggravating seizures.
- Lesional epilepsy, hence a potential epilepsy surgery candidate.
- Progressive epilepsy or neurodegenerative disorder.

When to refer to a Paediatric Neurologist?

Refer immediately (to contact paediatric neurologist)

- Behavioural or developmental regression.
- Infantile spasms.

Refer

- Poor seizure control despite monotherapy with 2 different antiepileptic medications.
- Difficult to control epilepsies beginning in the first two years of life.
- Structural lesion on neuroimaging.

Advice for Parents

- Educate and counsel on epilepsy.
- Emphasize compliance if on an antiepileptic drug.
- 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.

First Aid Measures during a Seizure (Advise for Parents/Teachers)
• Do not panic, remain calm. Note time of onset of the seizure.
• Loosen the child's clothing especially around the neck.
• Place the child in a 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 seizure is over and comfort the child as he/she is recovering.

Side effects and serious toxicity of Antiepileptic Drugs		
Antiepileptic Drug	**Common side effects**	**Serious toxicity**
Carbamazepine	Drowsiness, dizziness, ataxia, diplopia, rashes	Steven-Johnson syndrome[1], agranulocytosis
Clobazam[2] Clonazepam	Drowsiness, hypotonia, salivary and bronchial hypersecretion, hyperactivity and aggression	
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, sedation, hirsutism, gum hypertrophy megaloblastic anemia	
Sodium valproate	Nausea, epigastric pain, tremor, alopecia, weight gain, hair loss, thrombocytopaenia	Hepatic toxicity (< 2 yrs age), pancreatitis, encephalopathy
Topiramate	weight loss, somnolence, mental slowing, word finding difficulty, hypohidrosis, renal calculi	
Vigabatrin	drowsiness, dizziness, mood changes, weight gain	Peripheral visual field constriction (tunnel vision)

*Footnote: 1, Steven-Johnson syndrome occurs more frequently in Chinese and Malay children who carry the HLA-B*1502 allele.*
2, Clobazam is less sedative than clonazepam

Definition

- Seizures 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.
- No comprehensive local epidemiological data. Studies in Western Europe quote a figure of 3-4% of children < 5 years experiencing febrile seizures.

Classification of Febrile Seizures	
Simple Febrile Seizures	**Complex Febrile Seizures**
• Duration < 15 minutes	• Duration > 15 minutes
• Generalised seizure.	• Focal features
• Does not recur during the febrile episode	• > 1 seizure during the febrile episode
	• Residual neurological deficit post-ictally, such as Todd's paralysis

Management

- Not all children need hospital admission. The main reasons are: -
  - To exclude intracranial pathology especially infection.
  - Fear of recurrent seizures.
  - To investigate and treat the cause of fever besides meningitis/encephalitis.
  - To allay parental anxiety, especially if they are staying far from 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 **Ch 46: 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 seizures.
    - In district hospital without paediatrician.
    - Parents have difficulty bringing in child again if deteriorates at home.
  - Serum calcium and electrolytes are rarely necessary.
  - EEG is not indicated even if multiple recurrences or complex febrile seizures.
- Parents should be counselled on the benign nature of the condition

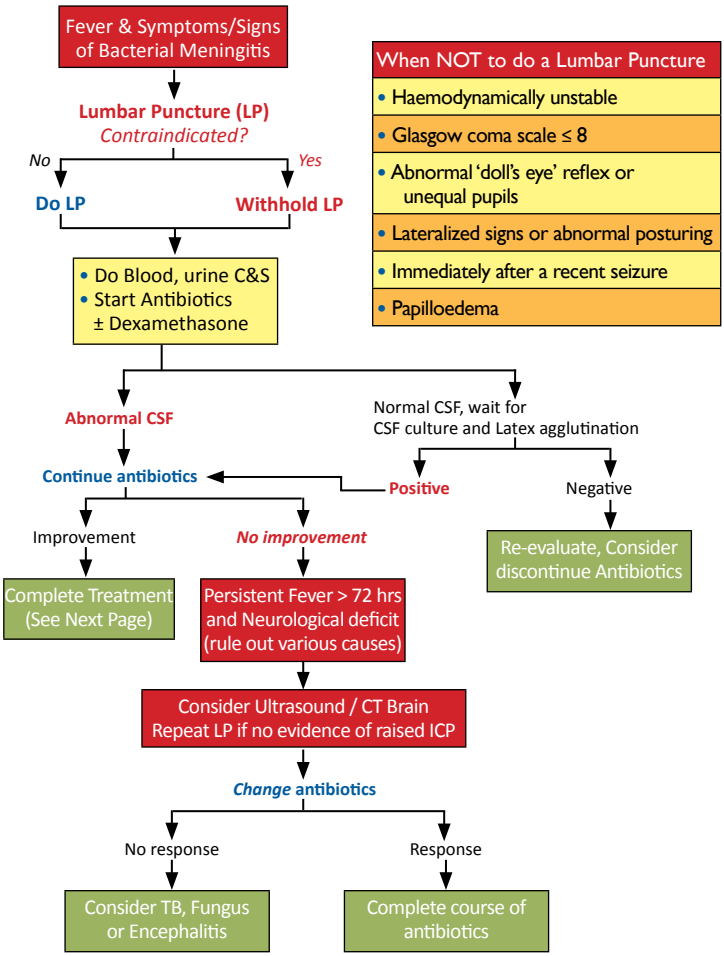
- Control fever
  - Avoid excessive clothing
  - Use antipyretic e.g. syrup or rectal Paracetamol 15 mg/kg 6 hourly for patient's comfort, though this may not reduce the recurrence of seizures.
- Parents should also be advised on **First Aid Measures during a Seizure.**
- Rectal Diazepam
  - Parents of children with high risk of recurrent febrile seizures should be supplied with Rectal Diazepam (dose : 0.5 mg/kg).
  - They should be advised on how to administer it if the seizures lasts more than 5 minutes.
- Prevention of *recurrent* febrile seizures.
  - Anticonvulsants are not recommended for prevention of recurrent febrile seizures 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 seizures have an excellent outcome with no neurological deficit nor any effect on intelligence.

Risk factors for Recurrent Febrile Seizures
• Family history of Febrile seizures
• Age < 18 months
• Low degree of fever (< 40 °C) during first Febrile seizure.
• Brief duration (< 1 hr) between onset of fever and seizure.
** No risk factor < 15 % recurrence* *≥ 2 risk factors > 30 % recurrence* *≥ 3 risk factors > 60 % recurrence*
Risk factors for subsequent Epilepsy
• Neurodevelopmental abnormality
• Complex febrile seizures
• Family history of epilepsy
Prognosis in Febrile Seizures
Febrile seizures are benign events with excellent prognosis
• 3 - 4 % of population have Febrile seizures.
• 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 seizures or even Febrile status epilepticus.

Introduction

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

APPROACH TO A CHIILD WITH FEVER AND SIGNS/SYMPTOMS OF MENINGITIS



Cerebrospinal fluid values in neurological disorders with fever				
Condition	Leukocytes (mm^3)	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 high PMN, but may have lymphocytes	> 1	Low	CSF may be sterile in Pneumococcal, Meningococcal meningitis
Tuberculous Meningitis	10 - 500 Early PMN, later high lymphocytes	1- 5	0 - 2.0	Smear for AFB, TB PCR + in CSF; High ESR
Fungal Meningitis	50 – 500 Lymphocytes	0.5 - 2	Normal or low	CSF for Cryptococcal Ag
Encephalitis	10 - 1,000	Normal / 0.5-1	Normal	CSF virology and HSV DNA PCR

Recommended antibiotic therapy according to likely pathogen			
Age Group	Initial Antibiotic	Likely Organism	Duration (if uncomplicated)
< 1 month	C Penicillin + Cefotaxime	*Grp B Streptococcus* *E. coli*	21 days
1 - 3 months	C Penicillin + Cefotaxime	*Group B Streptococcus* *E. coli* *H. influenzae* *Strep. pneumoniae*	10 – 21 days
> 3 months	C Penicillin + Cefotaxime, OR Ceftriaxone	*H. influenzae* *Strep. pneumoniae* *N. meningitides*	7 – 10 days 10 – 14 days 7 days

Note:

- Review antibiotic choice when infective organism has been identified.
- Ceftriaxone gives more rapid CSF sterilisation as compared to Cefotaxime or Cefuroxime.
- If Streptococcal meningitis, request for MIC values of antibiotics.

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. Extend duration of treatment if complications e.g. subdural empyema, brain abscess.

Use of Steroids to decrease the sequelae of bacterial meningitis

- Best effect achieved if 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 is turbid and patient has not received prior antibiotics.

Supportive measures

- Monitor temperature, pulse, BP and respiration 4 hourly and input/output.
- Nil by month if unconscious.
- Careful fluid balance required. Often, maintenance IV fluids is sufficient. However, if SIADH occurs, reduce to 2/3 maintenance for 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.
- Seizure chart.
- Daily Neurological 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 early formal hearing assessment in cases of proven meningitis.
- Until child shown to have normal development (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*, *S. pneumoniae.*
- Presence of focal signs.

Indications for Head 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

Indications for Subdural drainage
• Rapid increase in head circumference with no hydrocephalus
• Focal neurological signs
• Increased intracranial pressure
• Suspected subdural empyema

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
- MRI may show swelling and abnormal signal of the 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 - 21 days after symptom onset
- MRI may demonstrate swelling +/or abnormal signal in the spinal cord

Acute Disseminated Encephalomyelitis (ADEM)

- Acute encephalopathy (behavioural change or alteration of consciousness) with multifocal neurological deficits/signs,
  e.g. limb weakness, numbness, cerebellar ataxia, cranial nerve palsy, speech impairment, visual loss, seizures and spinal cord involvement.
- MRI shows multiple areas of abnormal signal in the white matter.
- No other aetiologies can explain the event.

ADEM: Common Differential Diagnoses
• CNS infection
• Bacterial, tuberculous meningitis, Herpes simplex encephalitis
• Clinically isolated syndrome (1st episode of Multiple sclerosis)
• Guillain Barré syndrome
• Acute stroke
• Mitochondrial disorders

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, divided into 8 hourly dosing, for 3 to 5 days
- Then oral Prednisolone 1 mg/kg/day (max 60 mg) daily to complete 2 wks.
- Give longer course of oral prednisolone, 4-8 weeks for ADEM and transverse myelitis with residual deficit.
- If no response, consider: IV Immunoglobulins 2 gm/kg over 2 - 5 days (or referral to a paediatric neurologist)

If Demyelinating episodes recur in the same patient, refer to a Paediatric Neurologist.

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.

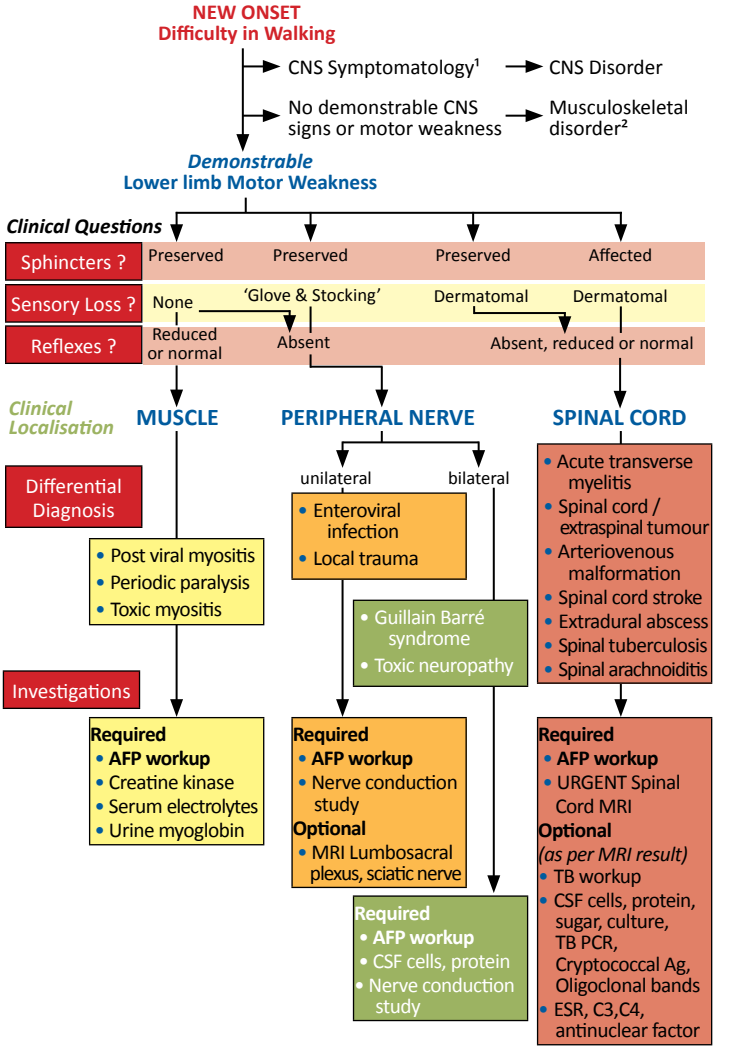
AFP is a ***medical emergency*** as unnecessary delays can result in death and disability. Children with AFP need to be assessed and managed carefully. A simple algorithm is provided on the next page.

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 all cases of AFP aged < 15 years, send stools for enterovirus isolation using a standardised protocol, and follow up children with AFP to determine the outcome.

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. Avoid rectal swabs. (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 frozen ice packs or dry ice. • Ensure stool specimens arrive at IMR within 72 hours of stool collection. • Caution: avoid desiccation, leakage; • Ensure adequate documentation and use AFP Case Laboratory Request Form
Follow up of patients	60 days from paralysis	• To determine whether there is residual paralysis on follow up

CLINICAL APPROACH TO A CHIILD WITH ACUTE FLACCID PARALYSIS



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.

Introduction

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

Clinical Pearls on GBS in Children
• Rapidly progressive, bilateral and relatively symmetric weakness of the limbs with decrease or absent reflexes. In atypical cases, weakness may begin in the face or upper limbs, or asymmetrical at onset.
• 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.
• GBS variants and overlapping syndrome: • Miller Fisher syndrome - cranial nerve variant characterised by opthalmoplegia, ataxia and areflexia. • Bickerstaff's brainstem encephalitis - acute encephalopathy with cranial and peripheral nerve involvement.

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, ascending weakness (< 4 wks) with areflexia, and an elevated CSF protein level and normal cell count ("protein-cellular dissociation").
- Nerve conduction study is ***Confirmatory.***

Initial measures

- Give oxygen, keep NBM if breathless. Monitor PEFR regularly
- Admit for PICU / PHDU care, if having:
  - Respiratory compromise (deteriorating PERF).
  - Rapidly progressive tetraparesis with loss of head control.
  - Bulbar palsy.
  - Autonomic and cardiovascular instability.
- Provide respiratory support early with BiPAP or mechanical ventilation

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

- IV Immunoglobulins (IVIG) 2 gm /kg total over 2 - 5 days in the first 2 wks of illness, with Hughes functional scale 3 and above or rapidly deteriorating.
- 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. These children, may 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.

consider:

1 INITIAL ASSESSMENT

Airway . . . . . secure airway, endotracheal intubation
Breathing . . . oxygen, artificial ventilation if required
Circulation . . IV bolus, ionotropes, chest compressions
Dextrostix . . correct hypoglycemia promptly

Once stable, monitor HR, BP, Resp rate, SpO_2, urine output

2 WHAT IS THE GCS?

If GCS ≥ 12 . . monitor GCS hourly

If GCS < 12 . . monitor GCS ½ hourly till improves

3 CONSIDER ENDOTRACHEAL INTUBATION IF:

- Airway obstructs if not supported.
- Airway compromised by vomiting.
- Respiratory rate too low for adequate ventilation.
- SpO_2 remains < 92 % despite high flow O_2 and airway opening manouevres.
- Signs of shock even after 40 ml/kg of fluid resuscitation.
- Signs of exhaustion.
- GCS < 8 and deteriorating.

Look for & treat:

SEPSIS **SHOCK** **SEIZURES**

4 RAISED INTACRANIAL PRESSURE

If Clinically has **Papilloedema**, or if *2 of the following:*

- GCS < 8
- Unreactive, unequal pupils
- Abnormal doll's eye reflex
- Decorticate, decerebrate posturing
- Abnormal breathing (Cheyne-Stokes, apneustic)

5 CONSIDER AETIOLOGY

- *CNS Infection*
  - Bacterial meningitis
  - Viral encephalitis
  - TB meningitis
  - Brain abscess
  - Cerebral malaria
- *Trauma*
- *Vasculitis*
- *Acute Poisoning*
- *Metabolic disease*
  - Diabetic ketoacidosis
  - Hypoglycaemia
  - Hyperammonemia
- *Non-accidental injury*
- *Post convulsive state*
- *Hypertensive crisis*
- *Acute Disseminated Encephalomyelitis*
- *Cerebral venous sinus thrombosis*

6 INVESTIGATIONS

Recommended

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

Delay Lumbar Puncture

Sample when ILL:

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

Optional:

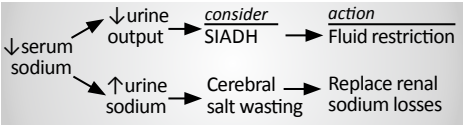
EEG, Vasculitis screen, Toxicology, IEM Screen, Blood film for malaria parasite

Neuroimaging: Consider CT Brain for all children with ↑ ICP, or if cause of coma is uncertain; MRI is more useful if a brain tumour or ADEM is suspected

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:



- Maintain cerebral blood flow
  - Keep CPP > 50 mmHg
  - If ↑ BP: do not lower unless hypertensive crisis, e.g. acute glomerulonephritis

Cerebral (CPP) Perfusion Pressure	=	Mean (MAP) Arterial Pressure	-	Intracranial Pressure (ICP)

- 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_2 , $PaCO_2$ level
  - Maintain good oxygenation, normocapnia. i.e. $PaCO_2$ 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 alternative cause of coma is evident
- *Acyclovir*: 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
- Metabolic causes may require long term dietary management.

Introduction

- The overall incidence of neonatal stroke is 1 in 4,000 live births, while for childhood stroke is 2.5-13 per 100,000 children / year.
- Ischaemic stroke, including arterial ischaemic stroke (AIS) and cerebral sinovenous thrombosis (CSVT) is increasingly diagnosed in children.

Arterial Ischaemic Stroke

- Incidence: 2-8 per 100,000 children / year.
- Recurrence occurs in 10-30% of childhood AIS.

Definition

1. Acute onset (may be evolving) of focal ± diffuse neurological disturbance and persistent for 24 hours or more, ***AND***
2. Neuro-imaging showing focal ischaemic infarct in an arterial territory and of maturity consistent with the clinical features.

Clinical features

- Typically sudden, maximal at onset (but may be evolving, waxing & waning).
- Focal deficits : commonest - motor deficits (hemiparesis), sensory deficits, speech / bulbar disturbance, visual disturbance, unsteadiness.
- Diffuse neurological disturbance : altered consciouness, headache
- Seizures.
- Other non-specific features in neonatal stroke including apnoea, feeding difficulty, abnormal tone.

Potential Risk Factors for Arterial Ischaemic Stroke

Cardiogenic
Congenital, acquired heart diseases; Cardiac procedure, Arrhythmia

Vasculopathy
- Non-vasculitis
  Dissection, Moyamoya, Post-varicella angiopathy
- Vasculitis
  Primary CNS vasculitis; Secondary vasculitis (Infective vasculitis, SLE, Takayasu)

Prothrombotic disorders
- Inherited thrombophilia
- Acquired thrombophilia:
  Nephrotic syndrome, malignancy, L-Asparaginase, anti-phospholipid syndrome

Acute disorders
- Head and neck disorder:
  Trauma, Infection - Meningitis, otitis media, mastoiditis, sinusitis.
- Systemic disorders:
  Sepsis, dehydration, asphyxia

Chronic disorders
- Iron deficiency anaemia
- Metabolic disorders
  Homocystinuria, Dyslipidaemia, Organic acidemia
  MELAS (Mitochondrial encephalomyopathy, lactic acidosis with stroke-like episodes)

Investigations

- Blood workup :
  - Basic tests: FBC / FBP, renal profile, LFT, RBS, lipid profile, iron assay (as indicated).
  - Thrombophilia screen: PT/PTT/INR, protein C, protein S, anti-thrombin III, factor V Leiden, lupus anti-coagulant, anti-cardiolipin, serum homocysteine level.
  - If perinatal / neonatal stroke: to do mother's lupus anti-coagulant and anti-cardiolipin level.
  - Further tests may include MTHFR (methylenetetrahydrofolate reductase), lipoprotein A, Prothrombin gene mutations.
  - Vasculitis workup (if indicated) : C3, C4, CRP, ESR, ANA
  - Further tests may include dsDNA, p-ANCA, c-ANCA
  - Others: Suspected metabolic aetiologies – lactate & VBG for MELAS.
- Cardiac assessment : ECG & Echocardiogram (ideally with bubble study)
- Neuro-imaging (consult radiologist)
  - Goals – to ascertain any infarction, haemorrhages, evidence of clots / vasculopathy and to exclude stroke-mimics.
  - If stroke is suspected, both brain parenchymal and cervico-cephalic vascular imaging should be considered.

Brain imaging	Cervico-cephalic Vascular Imaging
Cranial Ultrasound If fontanel is open.	*Carotid artery Ultrasound / Doppler* If suspected carotid dissection or stenosis.
CT scan Quick, sensitive for haemorrhages but may miss early, small and posterior fossa infarcts.	*MR Angiogram (MRA)* Intracranial vessels (with MRI) & to include neck vessels if suspected cervical vasculopathy.
MRI scan (with DWI+ADC) Better parenchymal details and sensitive for early infarct	*CT Angiogram / Formal cerebral angiogram* May be considered in certain cases.

Management

- General care
  - Resuscitation: A, B, C's.
  - Admit to ICU if indicated for close vital signs and GCS monitoring. (post-infarction cerebral oedema may worsen 2-4 days after acute stroke)
  - Workup for the possible underlying risk factor(s) and treat accordingly.
  - If cervical dissection is the likely aetiology (eg : history of head & neck trauma, Marfan syndrome, carotid bruit), apply soft cervical collar.
- Acute neuro-protective care :
  - General measures for cerebral protection.
  - Maintain normothermia, normoglycemia, normovolemia
  - Monitor fluid balance, acceptable BP, adequate oxygenation, treat seizures aggressively.
- Acute Anti-thrombotic therapy :
  - Consult paediatric neurologist (and haematology team if available) for the necessity, choice and monitoring of anti-thrombotic therapy.
  - If stroke due to cardiac disease/procedure, should also consult cardiologist/cardio-thoracic team.
  - If anti-thrombotic is needed, consider anti-coagulation therapy (unfractionated heparin / LMWH) or aspirin. Ensure no contraindications.
- Secondary preventive therapy:
  - If needed, consider Aspirin (3-5mg/kg/day, may be reduced to 1-3mg/kg/day if has side effects.)
  - Duration: generally for 3-5 years but may be indefinitely. Caution with long-term aspirin. (See below)
  - Alternatively, LMWH or warfarin may be used in extra-cranial dissection, intracardiac clots, major cardiac disease or severe prothrombotic disorders.

Contraindications of Anti-thrombotic therapy
Infarct associated with significant hemorrhage
Large infarct with the worry of secondary haemorrhagic transformation;
Uncontrolled hypertension
Other risks for bleeding
Caution with Aspirin
Reye's syndrome has been linked to use of aspirin during febrile illness.
Reduce aspirin by 50% during fever > 38°C.
Withhold for 3-5 days if suspected/confirmed varicella / influenza infection.

Childhood Cerebral Sino-venous Thrombosis (CSVT):

Introduction

- 20-30% of childhood stroke due to CSVT; 30-40 % of CSVT will lead to venous infarcts or stroke.
- More than 50% of venous infarcts are associated with haemorrhages.
- Consider CSVT if infarct corresponds to venous drainage territories or infarct with haemorrhage not due to vascular abnormality.

Clinical features *(Typically sub-acute)*

- Diffuse neurological disturbance:
  Headache, seizures, altered sensorium, features of increased intracranial pressure (papilloedema, 6th cranial nerves palsy).
- Focal deficits if venous infarct.

Risk factors

- Prothrombotic conditions (Inherited, L-asparaginase, nephrotic syndrome)
- Acute disorders (Head & neck trauma / infection, dehydration, sepsis)
- Chronic disorders (SLE, thyrotoxicosis, iron deficiency anaemia, malignancy)

Blood workup

- Thrombophilia screen and others depending on possible risk factor(s)

Neuro-imaging

- Brain imaging - as in Childhood AIS guidelines.
- Cerebral Venogram
  - MRV-TOF (time-of-flight) – flow dropout artefact may be a problem
  - CTV – better than MRV-TOF, but radiation exposure is an issue.

Management

- General care and acute neuro-protective care as in AIS.
- Consult Paediatric neurologist for anti-coagulation therapy (ensure no contraindications).
- Consult neuro-surgery if infarct associated with haemorrhage.

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, e.g. 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-pharygeal 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 the tympanic membrane is perforated.
- 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 a stable cardiovascular and respiratory state.
- Adjust ventilator to maintain $PaCO_2$ at or around 40 mmHg.
- Pre-oxygenate with 100% O_2 for 10 minutes.
- Disconnect from ventilator.
- Deliver 100% O_2 via tracheal catheter at 6 L/min
- Monitor O_2 saturation with pulse oximetry
- Measure $PaCO_2$ after 5 minutes and again after 8 minutes if $PaCO_2$ has not exceeded 60 mmHg.
- Re-connect to ventilator after the test.
- Disconnection of the ventilator shall not exceed 10 mins at any one time
- The apnoea test is ***positive*** when there is no respiratory effort with a $PaCO_2$ of ≥ 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 $PaCO_2$ < 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 $PaCO_2$ may already be above 40 mmHg. The apnoea test is then considered positive if there is no respiratory effort at a $PaCO_2$ of 20 mmHg above the baseline $PaCO_2$

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.

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.

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[1]	12 hours	Not needed

Footnote:
1. If hypoxic ischaemic encephalopathy is present, observation for at least 24 hr is recommended. This interval may be reduced if an EEG shows electrocerebral silence.

Pitfalls in Assessment / Certification

- Assessment may be difficult in patients with
  - Severe facial trauma.
  - Pre-existing pupillary abnormalities.
  - Sleep apnoea or severe pulmonary disease with chronic retention of CO_2
  - Toxic levels of 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.

Common CNS depressants and pharmacodynamics		
Drugs	Elimination T ½	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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Chapter 53: Approach to A Child 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

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 mths age).

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)

Measure serial heights to assess the growth pattern and height velocity.

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 a 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.

Differential diagnosis of short stature and growth failure	
Healthy but short children	Endocrinopathies
Familial short stature	Hypothyroidism
Constitutional growth delay	Hypopituitarism
Intrinsic short stature	• 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
Systemic diseases	• Haemosiderosis
Infectious: HIV, tuberculosis	GH insensitivity (Laron syndrome)
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	Non-organic aetiology
• Inflammatory bowel disease	Psychosocial deprivation
Central nervous system disease	Nutritional dwarfing
Chronic lung disease	
Malignancy	
Abbreviation: *GH, Growth Hormone*	

Clinical Approach to children with Short Stature	
History	
Antenatal	Nutrition
Complications of pregnancy	General well being
Pre-eclampsia, hypertension	Appetite, energy, sleep, bowel habits
Maternal smoking, alcohol	Pattern of growth from birth
Infections	Maternal and child relationship
Birth	Medical history
Gestational age	Underlying illness, medications, irradiation
Birth weight and length	Family History
Mode of delivery (breech, forceps)	Short stature (3 generations).
Apgar score	Age of onset of puberty in family members of the same sex
Neonatal complications	
Developmental milestones	Diseases in the family.
Physical Examination	
Anthropometry	General appearance and behaviour
Height, weight, head circumference	Dysmorphism
Height velocity	Pubertal staging
Arm span	
Upper: lower segment Ratio: 1.7 in neonates to slightly <1.0 in adults	
Family Measurements	
Measure height of parents for mid-parental heights (MPH)	
Boys : $\frac{\text{Father's height + (Mother's height +13)}}{2}$	
Girls: $\frac{\text{Mother's height + (Father's height -13)}}{2}$	

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
- 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-monthly 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.

Introduction

- Incidence of congenital hypothyroidism worldwide is 1:2500 - 4000 live births.
- In Malaysia, it is reported as 1:3666.
- It is the commonest preventable cause of mental retardation in children.
- Thyroid hormones are crucial for: -
  - Normal growth and development of brain and intellectual function, during the prenatal and early postnatal period.
  - Maturation of the foetal lungs and bones.

Causes of Congenital Hypothyroidism
Thyroid dysgenesis (85%)
Athyreosis (30%)
Hypoplasia (10%)
Ectopic thyroid (60%)
Other causes (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

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.
- Tablets should not be mixed with soy formulas or any preparation containing iron (formulas or vitamins), both of which reduce the absorption of T4.

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.
- Average dose in older children is 100 mcg/m^2/day.

Goals of therapy

- To restore the euthyroid state by maintaining a normal serum 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 FT4 level usually normalise within 1-2 weeks, and then TSH usually become normal after 1 month of treatment.
- Some infants continue to have high serum TSH concentration (10 - 20 mU/L) despite normal serum FT4 values due to resetting of the pituitary-thyroid feedback threshold. However, compliance to medication has to be reassessed and emphasised.

Goals of Therapy in the First Year of Life	
Adequate treatment	Inadequate treatment
FT4 1.4 – 2.3 ng/dL (18 - 30 pmol/L)	FT4 < 18 pmol/L
TSH < 5 mU/L	TSH >15 mU/L > once in first year

Follow-up

- Monitor growth parameters and developmental assessment.
- The recommended measurements of serum 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.

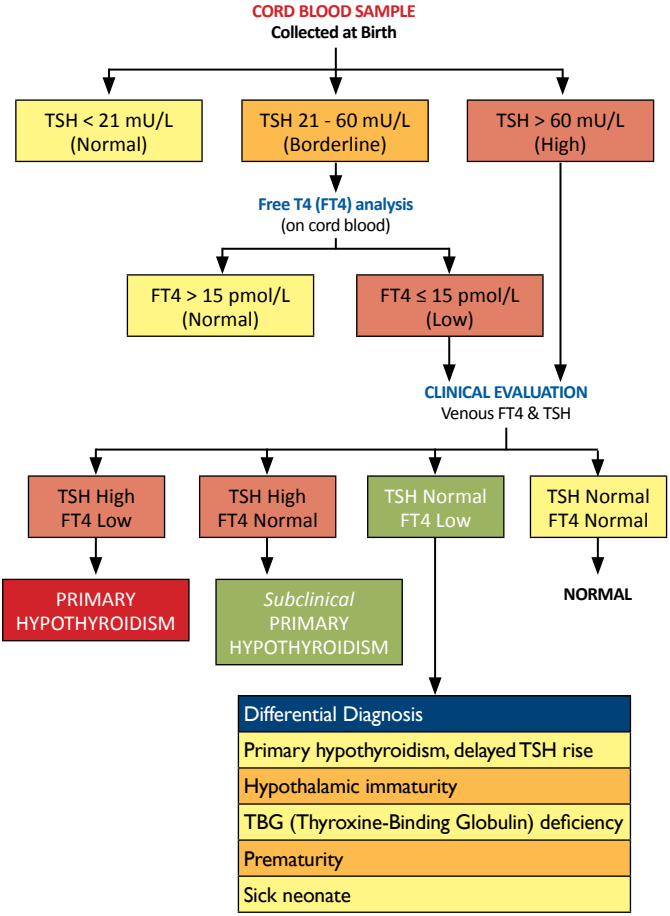
Re-evaluation of patients likely having transient hypothyroidism

- This is best done at age 3 years when thyroid dependent brain growth is completed at this age.
- Stop L-thyroxine for 4 weeks then repeat thyroid function test: 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 life-long L-thyroxine therapy is needed.

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.

SCREENING FOR CONGENITAL HYPOTHYROIDISM



Footnotes:

- *Interpretation of the results should take into account the physiological variations of the hormone levels during the neonatal period.*
- *Free thyroxine (FT4) level is preferable to total thyroxine level (T4).*

Introduction

- 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.

Symptoms and Signs of Diabetes Mellitus	
Early	Late
Polydipsia	Vomiting
Polyuria	Dehydration
Weight loss	Abdominal pain
Enuresis (secondary)	Hyperventilation due to acidosis
	Drowsiness, coma

Criteria for Diagnosis of Diabetes Mellitus

- Symptoms of diabetes

Plus

- Casual plasma glucose concentration ≥ 11.1 mmol/L (≥ 200 mg/dL).[1]

Casual is defined as any time of day without regard to time since the last meal.

OR

- Fasting plasma glucose ≥ 7.0 mmol/L (≥ 126 mg/dL).[2]

Fasting is defined as no caloric intake for at least 8 hours.

OR

- A 2-hour Postload Glucose ≥ 11.1 mmol/L (≥ 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).

Management

Principles of insulin therapy

- Daily insulin dosage
  - Daily insulin dosage varies 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), glycated hemoglobin (HbA1c) 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 to 1 - 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.

Types of Insulin

Type	Examples	Onset of Action	Peak	Duration
Rapid-acting insulin	NovoRapid, *Humalog*	5-15 mins	30-60 mins	3-5 hours
Short-acting insulin (regular)	Actrapid, *Humilin R*	30 mins	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 (*Determir*), Lantus (*Glargine*)	*Determir* 1-2 hours *Glargine* 1 hour	*Determir* 6-8 hours *Glargine* No peak	*Determir* 6-23 hours *Glargine* 24 hours

- Frequently used regimens:

Twice Daily Regimens

- 2 daily injections of a mixture of a short or rapid acting 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
- 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, 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

- Of the total daily insulin requirements, 40 - 60% should be basal insulin, the rest pre-prandial rapid-acting or regular insulin.
- If using regular insulin, inject 20 - 30 min before each main meal (breakfast, lunch; and the 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 given once daily at bedtime. However sometimes twice daily injections may be needed (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.
- Patient should learn about carbohydrate counting to adjust dose of pre-prandial insulin.

Choice of insulin regimen
• At least two injections of insulin per day are advisable in most children.
• The basal-bolus concept has the best possibility of imitating the physiological insulin profile.

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.
- 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.

Target Indicators of Glycaemic control		
Level of control	Ideal (non-diabetic)	Optimal (diabetic)
Clinical assessment		
Raised Blood Glucose (BG)	Not raised	No symptoms
Low BG	Not low	Few mild, no severe hypoglycaemias
Biochemical assessment		
• SBGM values, mmol/L		
AM fasting or preprandial	3.6 - 5.6	5.0 - 8.0
• Plasma Glucose (PG), 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 (%)	< 6.05	< 7.5

Monitoring of ketones should be done during:

- 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 Diabetic Ketoacidosis (DKA).
- Persistent polyuria with elevated blood or urine glucose.
- Episodes of drowsiness.
- Abdominal pain or rapid breathing.

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)
  - For any individual if 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 (SC) insulin depot.

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, especially in children < 6 years.

Diet

- A balance and healthy diet for age is required with dietician involvement.
- Carbohydrate counting should be taught to patients. Insulin dosage should match the carbohydrate intake.

Exercise

- Regular exercise and participation in sport should be encouraged.
- Plan the injection sites according to the activity e.g. inject insulin in the arm if one plans to go cycling.
- Approximately 1.0-1.5g carbohydrates /kg body weight/hour should be consumed during strenuous exercise if a reduction in insulin is not instituted.
- If pre-exercise blood glucose levels are high (>14 mmol/L) with ketonuria or ketonemia, exercise should be avoided. Give approximately 0.05 IU/kg or 5% of total daily dose and postpone exercise until ketones have cleared.
- Hypoglycemia may be anticipated during or shortly after exercise, but also possible up to 24 hours afterwards, due to increased insulin sensitivity.
- Risk of post exercise nocturnal hypoglycemia is high and particular care should be taken if bedtime blood glucose < 7.0 mmol/L.

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 DKA.
- 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.
- Obtain request forms for a medic alert 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.
- Blood pressure should be monitored at least annually. Blood pressure value should be maintained at the <95th percentile for age or 130/80 mmHg for young adults.
- Screening for fasting blood lipids should be performed when diabetes is stabilized in children over 12 years of age. If normal results are obtained, screening should be repeated every 5 years.
- 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 celiac 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.

Evaluation for complications

- Microalbuminuria: 2 of 3 urine collections should be used as evidence of microalbuminuria defined as :
  - Albumin excretion rate (AER) 20-200 mcg/min or AER 30-300 mg/day.
  - Albumin/creatinine ratio (ACR) 3.5-35 mg/mmol (males) and 4.0 -35 mg/mmol (females) on first morning urine specimen; Random ACR is higher.
  - Albumin concentration (AC) 30-300 mg/L (on early morning urine sample).

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
When to commence screening?			
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)
Screening methods			
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)
Risk factors			
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)
Potential intervention			
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

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 (DCCT)	≤ 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

Abbreviation: DCCT, Diabetes Control and Complication Trials Standard

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.

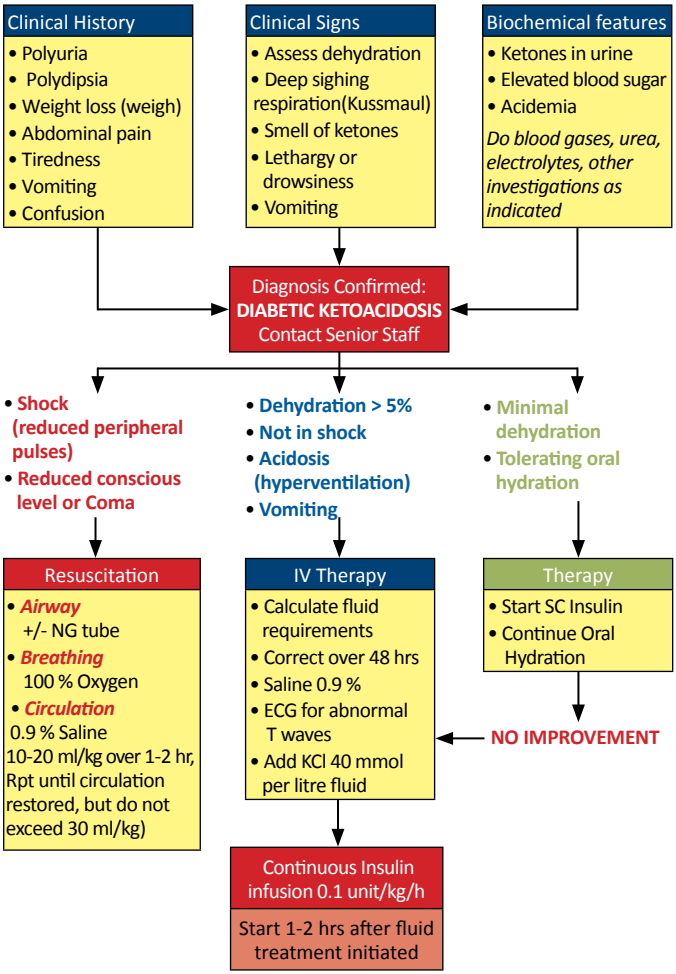
Emergency management

- 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 catherter (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)

Algorithm for Assessment and Management of Diabetic Ketoacidosis



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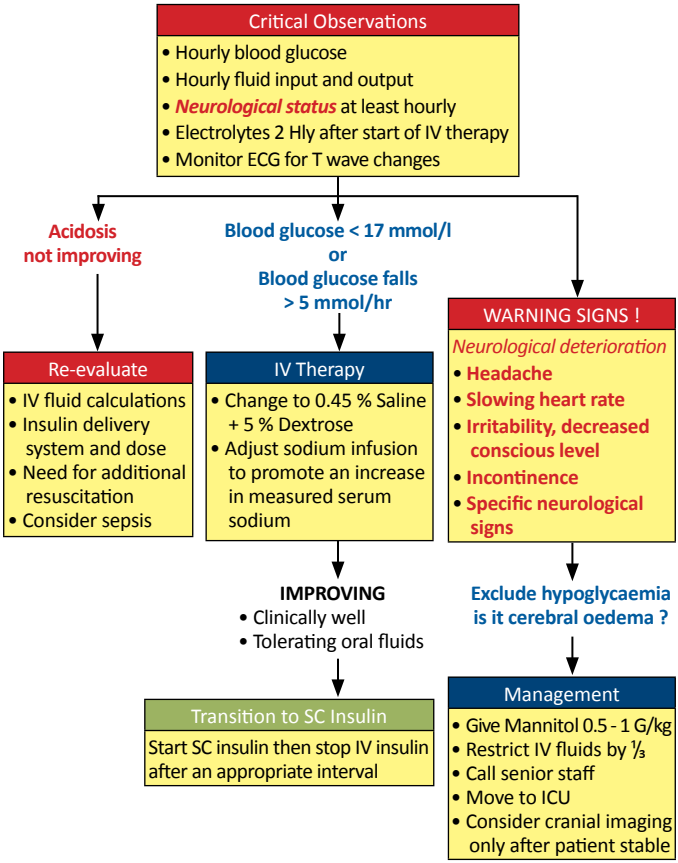

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Clinical and biochemical monitoring

- 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
• Anion gap = (Na + K) - (Cl + 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
• Corrected sodium (mmol/L) = measured Na + $\frac{2 \times (\text{plasma glucose} - 5.6)}{5.6}$
• Effective osmolality (mOsm/kg) = 2 x (Na + K) + plasma glucose + 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.

- ***Rehydrate the patient evenly over 48 hours:***
  - As a guide fluid infused each day usually < 1.5 - 2 times 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.
- 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.
  - The sodium content of the fluid may need to be increased if measured serum sodium is low and does not rise appropriately as the plasma glucose concentration falls.
- 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_3 > 15 mmol/L and/or closure of the anion gap), which takes longer than normalization of blood glucose concentrations.
- If patient has 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 IV fluid (e.g., 5% glucose in 0.45% saline) when plasma glucose falls to 14–17 mmol/L, or sooner if rate of fall is rapid.***
  - It may be necessary to use 10% - 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 hours.
  - 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 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
- 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.

Serum potassium level	Action
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).
Normokalemia	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)
Hyperkalaemia (K+ > 5.5 mmol/L)	Defer potassium replacement therapy until urine output is documented.

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 <6.9) 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; HCO3- > 15mmmol/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/kg before bedtime. Total insulin dose is about 1u/kg/day.
- To prevent rebound hyperglycemia, the first SC injection is given 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% - 25% of survivors of cerebral edema have significant residual morbidity.
- Other rare causes of morbidity and mortality include: sepsis; hypokalemia, hyperkalemia, severe hypophosphataemia; hypoglycaemia; 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.

Diagnostic Criteria for Cerebral Oedema	
• 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.	• Vomiting
	• Headache
• Sustained HR deceleration (decrease > 20 bpm), not attributable to improved intravascular volume or sleep state.	• Lethargy, not easily arousable
	• Diastolic blood pressure > 90 mmHg
• Age-inappropriate incontinence	• Age < 5 years

Treatment of cerebral oedema

- Initiate treatment as soon as the condition is suspected. (Mannitol and hypertonic saline should be available at the bedside)
- 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. ($PaCO_2$ 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.

Definition

- Individuals who have a genital appearance that does not permit gender declaration are said to have disorders of sexual development (DSD), formerly known as ambiguous genitalia.
- 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.

DSD 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 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 addressed.

Disorders of Sexual Development (DSD) - New Nomenclature				
Sex Chromosome DSD	46, XY DSD		46, XX DSD	
45, X Turner	Disorders of Testicular Development	Disorders of Androgen Synthesis/Action	Disorders of Ovarian Development	Fetal Androgen Excess
47, XXY Klinefelter and variants	Complete Gonadal Dysgenesis	Androgen Synthesis Defect	Ovotesticular DSD	CAH
45, X/46, XY MGD			Testicular DSD (SRY+, dup SOX9)	21-OH Deficiency
Chromosomal Ovotesticular DSD	Partial Gonadal Dysgenesis	LH-Receptor Defect		11-OH Deficiency
		Androgen Insensitivity	Gonadal Dysgenesis	Non-CAH
	Gonadal Regession	5 α-reductase Deficiency		Aromatase Deficiency
	Ovotesticular DSD			POR Gene Defect
		Disorders of AMH		Maternal
		Timing Defect		Luteoma
		Endocrine disrupters		Iatrogenic
		Cloacal exstrophy		

Abbreviations: MGD, Mixed gonadal dysgenesis; AMH, Anti-Mullerian hormone; CAH, Congenital adrenal hyperplasia; 21-OH, 21-Hydroxlylase; 11-OH, 11 Hydroxylase.

EVALUATION

Ideally, the baby or child and parents should be assessed by a competent multi-disciplinary 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

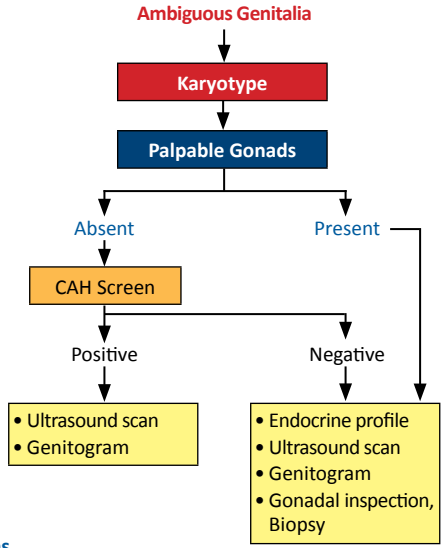
Physical examination

- 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 or appearance of scrotum
  - Presence or absence of palpable gonads
  - Presence or absence of cervix (per rectal examination)
  - Position and patency of anus

Criteria that suggests DSD include

- Overt genital ambiguity.
- Apparent female genitalia with enlarged clitoris, posterior labial fusion, or an inguinal labial mass.
- Apparent male genitalia with bilateral undescended testes, micropenis, isolated perineal hypospadias.
- Mild hypospadias with undescended testes.
- Family history of DSD, e.g. Complete androgen insensitivity syndrome (CAIS).
- Discordance between genital appearance and a prenatal karyotype.

Most of DSDs are recognized in the neonatal period. ***Others present as pubertal delay.***



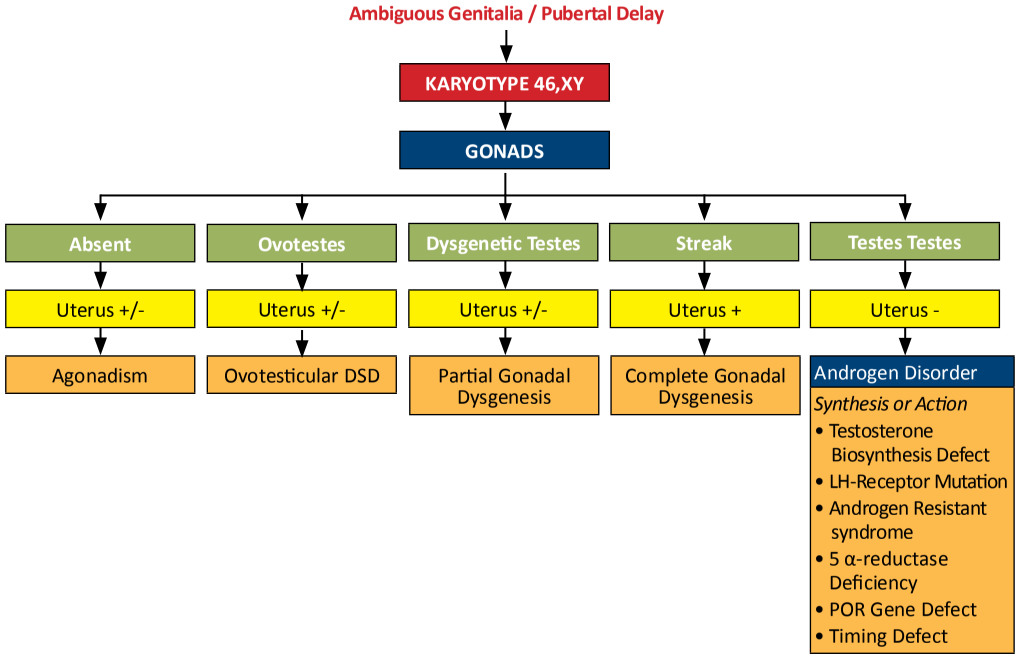
Investigations

- 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)

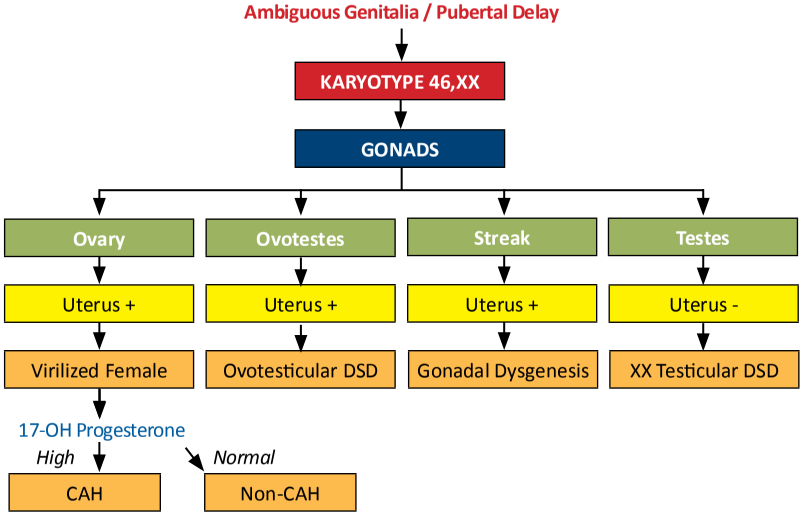
Additional investigations as indicated:

- 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.
- 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 DSD child as a male.

DIAGNOSTIC ALGORITHM OF 46, XY DSD



DIAGNOSTIC ALGORITHM OF 46, XX DSD



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. Otherwise 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 a Paediatric 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 (17-OHP) should be evaluated by a Pediatric Endocrinologist.
- The evaluation of an infant with DSD has 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.

Clinical presentation

Neonatal period

- Ambiguous genitalia.
- Salt loss (75%).
- Family history of previous unexplained neonatal death.
- Hyperpigmentation (90%) - both sexes.
- Virilisation of a girl.
- Hypertension.

Beyond the neonatal period

- Boy with gonadotrophin independent precocious puberty (prepubertal testicular size).

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 ml/kg of 10% glucose
- Correct hyperkalaemia with administration of glucose and insulin if necessary.
- Rehydrate using ½ 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/m²/d, but typical dosing is 10–15 mg/m²/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/m²/d).
- Dexamethasone dose is 0.25–0.375 mg/m²/d, given once daily.
- In children with advanced bone age and central precocious puberty, treatment with a GnRH agonist may be required.
- Therapy will reduce vasopressin, ACTH levels and lower dosage of glucocorticoid required.
- Assess the need for continuing mineralocorticoids 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 17-OHP, cortisol, and/or testosterone, and PRA or direct renin, every 3 months during infancy and every 4–12 months thereafter.
- 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 (> 38.5ºC), 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. A bolus dose is given as shown below followed by the same dose in four divided doses:
  - Below 3 years old: to give 25mg.
  - 3-12 years old: to give 50mg.
  - > 12 years old: to give 100mg.
- 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 DSD have been outlined in the preceding section on DSD.
- 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.

References

Section 6 Endocrinology

Chapter 53 Short Stature

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Introduction

Acute glomerulonephritis (AGN) is an abrupt onset of one or more features of an ***Acute Nephritic Syndrome***:

- Oedema e.g. facial puffiness.
- Microscopic /macroscopic haematuria. (urine: tea-coloured or smoky)
- Decreased urine output (oliguria).
- Hypertension.
- Azotemia.

- In children, the commonest cause of an acute nephritic syndrome is post-infectious AGN, mainly due to post-streptococcal infection of the pharynx or skin.
- Post streptococcal AGN is commonest at 6 – 10 years age.

Causes of Acute Nephritis
Post streptococcal AGN
Post-infectious acute glomerulonephritis (other than Grp A ß-Haemolytic *Streptococci*)
Subacute bacterial endocarditis
Henoch-Schoenlein purpura
IgA nephropathy
Hereditary nephritis
Systemic lupus erythematosus
Systemic vasculitidis

Presenting features of AGN
Acute nephritic syndrome (most common)
Nephrotic syndrome
Rapidly progressive glomerulonephritis
Hypertensive encephalopathy
Pulmonary oedema
Subclinical (detected on routine examination)

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 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 β - 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/m²/day. Do not administer intravenous or oral fluids if child has pulmonary oedema.
  - Day 2 : till patient diureses – 400 mls/m²/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 autoregulatory 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.

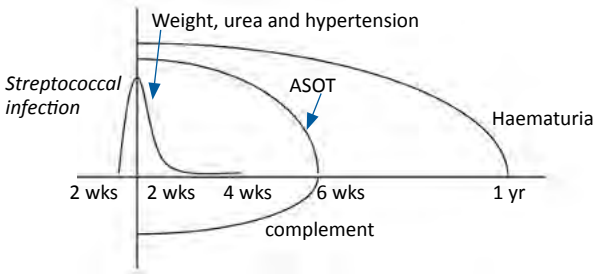
Pulmonary oedema

- 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 kidney injury

- Mild renal impairment is common.
- ***Severe persistent oliguria or anuria with azotaemia is uncommon.***
- Management of severe acute renal failure, ***see Ch 60 Acute Kidney Injury.***

Natural History of Acute Post-Streptococcal Glomerulonephritis



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

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 the time of discharge.

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.

Diagnosis

Nephrotic syndrome is a clinical syndrome of massive proteinuria defined by

- Oedema
- Proteinuria > 40 mg/m²/hour (> 1g/m²/day) or an early morning urine protein creatinine index of >200 mg/mmol (> 3.5 mg/mg).
- Hypoalbuminaemia of < 25g/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
- Serum cholesterol
- Liver function tests
  - Particularly serum albumin
- Urinalysis, urine culture
- Quantitative urinary protein excretion
  (spot urine protein: creatinine ratio or 24 hour urine protein)

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) levels to exclude SLE, post-infectious glomerulonephritis.
- ASOT titres to exclude Post-streptococcal glomerulonephritis.
- Other tests as indicated.

Renal biopsy

- A renal biopsy is not needed prior to corticosteroid or cyclophosphamide therapy. This is because 80% of children with idiopathic nephrotic syndrome have minimal change steroid responsive disease.
- 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 may 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 dipstix 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 dipstix 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.
  - Give live vaccines 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***
  - May be seen in children who have been on long term corticosteroid therapy (equivalent to 18 mg/m² of cortisone daily) when they undergo situations of stress.
  - Give Hydrocortisone 2-4 mg/kg/dose TDS or Prednisolone 1 mg/kg/day.

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 a Paediatric Nephrologist.

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/ m²/day (maximum 80 mg / day) for 4 weeks followed by
  - 40 mg/m²/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 at 60 mg/m²/ day, should be referred to a Paediatric Nephrologist for further management, which usually includes a renal biopsy.

Treatment of relapses

- The majority of children with nephrotic syndrome will relapse. A relapse is defined by *urine albumin excretion > 40 mg/m²/hour or urine dipstix of ≥ 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/m²/day (maximum 80 mg / day) *until remission* followed by
  - 40 mg/m²/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 ***≥ 2 relapses within 6 months of initial diagnosis or ≥ 4 relapses within any 12 month period.***

Treatment

- Induction of relapse is with oral Prednisolone as follows:
  - 60 mg/m²/day (maximum 80 mg/day) ***until remission*** followed by
  - 40 mg/m²/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 ***≥ 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.*

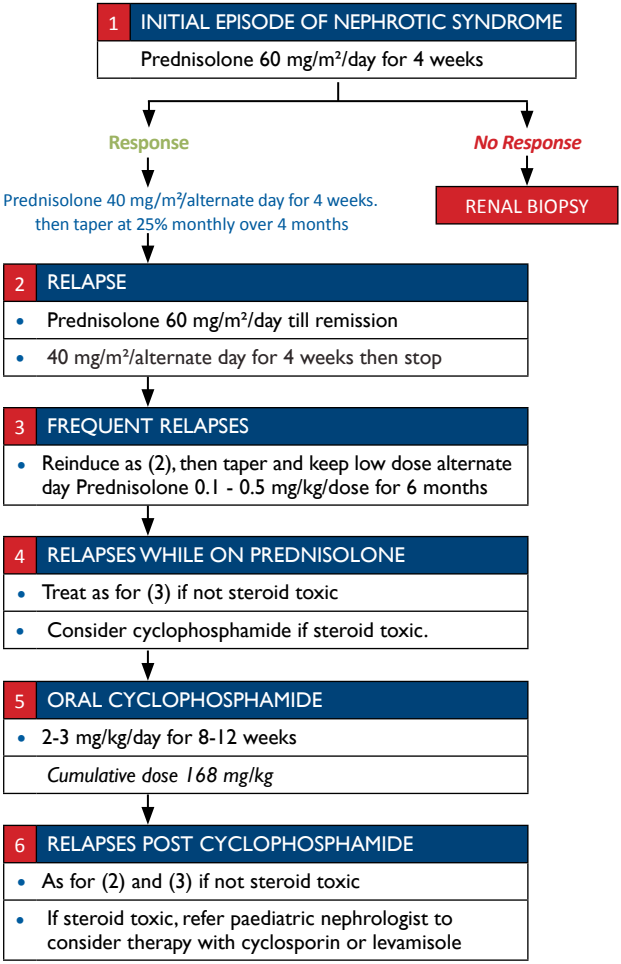
Cyclophosphamide therapy

- 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.

Algorithm for the Management of Nephrotic Syndrome



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 (AIIRB).
  e.g. Losartan, Irbesartan, to reduce proteinuria.
  - ***Monitor BP and renal profile 1-2 weeks after initiation of ACE inhibitor or AIIRB.***
- Control of hypertension: antihypertensive of choice - ACE inhibitor/AIIRB.
- Penicillin prophylaxis.
- Monitor renal function.
- Nutrition: normal dietary protein content, salt-restricted diet.
- Evaluate calcium and phosphate metabolism.

Definition

- Acute kidney injury (AKI) was previously called acute renal failure.
- Abrupt rise in serum creatinine level and decreased glomerular filtration rate resulting in inability of the kidneys to regulate fluid and electrolyte balance.

Clinical features

- Of underlying cause.
- Oliguria (< 300 ml/m²/day in children; < 1 ml/kg/hour in neonates)
- Non-oliguria.
- Clinical features arising from complications of AKI
  e.g. seizures, acute pulmonary oedema

Common causes of Acute Kidney Injury	
Pre-renal	**Renal, or intrinsic**
Hypovolaemia	Glomerular
• Dehydration, bleeding	Infection related
Third space loss	Systemic lupus erythematosus
• Nephrotic syndrome, burns	Acute glomerulonephritis
Distributive shock	Tubulointerstitial
• Dengue shock, sepsis syndrome	Acute tubular necrosis
Cardiac	• Hypoxic-ischaemic injury
• Congestive heart failure	• Aminoglycosides, chemotherapy
• Cardiac tamponade	Toxins, e.g.
Post-renal	• Myoglobin, haemoglobin
Posterior urethral valves	Venom
Acute bilateral ureteric obstruction	• Bee sting
Acute obstruction in solitary kidney	Tumour lysis, Uric acid nephropathy
	Infection, pyelonephritis
	Vascular
	ACE-inhibitors
	Vascular lesions
	• Haemolytic uremic syndrome
	• Renal vein thrombosis

- 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.

Investigations

- Blood:
  - Full blood count.
  - Blood urea, electrolytes, creatinine.
  - Blood gas.
  - Serum albumin, calcium, phosphate.
- Urine: biochemistry and microscopy.
- Imaging: renal ultrasound scan (urgent if cause unknown).
- Other investigations as determined by cause.

MANAGEMENT

Prevention

- Identify patients at risk of AKI. They include patients with the following:
  - Prematurity, asphyxia, trauma, burns, post-surgical states, other organ failures (eg heart, liver), pre-existing renal disease, malignancy (leukaemia, B-cell lymphoma).
- Monitor patients-at-risk actively with regards to renal function and urine output.
- Try to ensure effective non-dialytic measures, which include:
  - Restoring adequate renal blood flow.
  - Avoiding nephrotoxic agents if possible.
  - Maximizing renal perfusion before exposure to nephrotoxic agents.

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.

See Chapter 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 ml/m²/day or 30ml/kg in neonates depending on ambient conditions)
- IV Frusemide 2 mg/kg/dose (over 10-15 minutes), maximum of 5 mg/kg/dose *or* IV Frusemide infusion 0.5 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.

Metabolic acidosis

- Treat if pH < 7.2 or symptomatic or contributing to hyperkalaemia
- ***Bicarbonate deficit = 0.3 x body weight (kg) x base excess (BE)***
- Ensure that patient's serum calcium is > 1.8 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 K^+ > 6.0 mmol/l (neonates) and > 5.5 mmol/l (children).
- Cardiac toxicity generally develops when plasma potassium > 7 mmol/l
- Regardless of degree of hyperkalaemia, treatment should be initiated in patients with ECG abnormalities from hyperkalaemia.

ECG changes in Hypokalemia
Tall, tented T waves
Prolonged PR interval
Widened QRS complex
Flattened P wave,
Sine wave (QRS complex merges with peaked T waves)
VF or asystole

Treatment of Hyperkalemia in AKI patients	
• Do 12-lead ECG and look for hyperkalaemic changes	
• If ECG is abnormal or plasma K^+ > 7 mmol/l, connect patient to a cardiac monitor and give the following in sequence:	
1	IV 10% Calcium gluconate 0.5 - 1.0 ml/kg (1:1 dilution) over 5 -15 mins (Immediate onset of action)
2	IV Dextrose 0.5 g/kg (2 ml/kg of 25%) over 15 – 30 mins.
3	± IV Insulin 0.1 unit/kg (onset of action 30 mins).
4	IV 8.4% sodium bicarbonate 1 ml/kg (1:1 dilution) over 10 - 30 mins (Onset of action 15 - 30 mins)
5	Nebulized 0.5% salbutamol 2.5 - 5 mg (0.5 - 1 ml : 3 ml 0.9% Saline) (Onset of action 30 mins)
6	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	
6	Sodium polystyrene sulphonate 1g/kg oral or rectally 4 times/day (Max15g/dose) (Resonium)
• In patients with serum potassium between 5.5 - 7 mmol/L *without* ECG changes, give calcium or sodium polystyrene sulphonate	
• If insulin is given after dextrose, monitor RBS / Dextrostix for hypoglycaemia.	
• 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 AKI 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

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

Medications

- Avoid nephrotoxic drugs if possible; if still needed, monitor drug levels and potential adverse effects.
- Check dosage adjustment for all drugs used.
- Concentrate drugs to the lowest volume of dilution if patient is oliguric.

Dosage adjustment in renal failure for some common antimicrobials

Drug	Cr Clearance[1]	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-hly	
	< 10	Normal dose initially then half-dose 24-hly	
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

Dosage adjustment in renal failure for some common antimicrobials (cont).

Drug	Cr Clearance[1]	Dose	Dose Interval
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.		

Footnote:
1, Creatinine Clearance:
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.

$$\text{Calculated creatinine clearance } (\text{ml/min/1.73m}^2) = \frac{\text{Height (cm)} \times 40}{\text{Serum creatinine (micromol/l)}}$$

Assume creatinine clearance of < 10ml/min/1.73m² if patient is on dialysis or anuric.

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

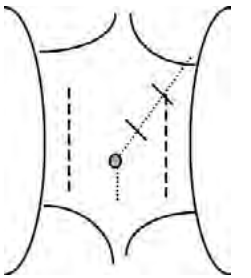
- A *soft PD catheter* implanted percutaneously or surgically (preferred).
- A *straight rigid catheter* if a soft PD catheter is not available.

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

Sites 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.

Site of Insertion and Direction of Catheter Introduction



Procedure of PD catheter insertion

1. Consent for 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 tables below*.
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. cover the site with dry gauze and secure with plaster.

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 Gm 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).

Technique of insertion of different PD catheters	
Acute stiff PD catheter	
1	Check catheter for any breakages (by withdrawing the stilette) 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 cather with the stillete perpendicular to the abdominal wall while controlling the length with the dominant hand, until the peritoneum is pierced.
4	The stilette 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.

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^2 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 availabe)
  - Bicarbonate dialysate[1], 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.

[1]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 listed in the next page.

Pharmacy constituted PD-Bicarbonate solution 1.5% dextrose 3000ml / bag	
Content	Quantitiy (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

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.
- Peritonitis

  Diagnostic criteria :
  - Abdominal pain, fever, cloudy PD effluent, PD effluent cell count > 100 WBC/mm^2.

  Treatment:
  - Intraperitoneal antibiotics (empirical Cloxacillin + Ceftazidime) for 7 - 14 days.
  - Adjust antibiotics once culture results known (dosage as given below).
- 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.***

Paediatric Antibiotic Dosing Recommendations Administration should be via intraperitoneal route unless specified otherwise			
	Continuous therapy		Intermittent therapy
	Loading dose	Maintenance dose	
Glycopeptides			
Vancomycin	500 mg/L	30 mg/L	30 mg/kg q 5-7 days
Cephalosporins			
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
Antifungals			
Amphotericin B	1 mg/kg IV	1 mg/kg/day IV	---
Fluconazole	---	---	3-6 mg/kg IP, IV, or PO q24-48 hrs (max 200 mg)
Aminoglycosides			
Amikacin	25 mg/L	12 mg/L	
Gentamicin	8 mg/L	4 mg/L	
Netilmycin	8 mg/L	4 mg/L	
Penicillins			
Amoxicillin	250-500 mg/L	50 mg/L	
Combinations			
Ampicillin/ Sulbactam	1000 mg/L	100 mg/L	
Imipenem/ Cilastin	500 mg/L	200 mg/L	

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 the table below 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.

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 a lumbosacral myelomeningocoele.
- At birth, the majority of patients with lumbosacral myelomeningocoele have normal upper urinary tracts, but 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 catheterisation (CIC):

- Aim is to create a low-pressure reservoir and ensuring complete and safe bladder emptying with clean intermittent catheterisation.
- CIC should be started once the myelomeningocoele 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.
- Hydronephrosis.
- Incontinence despite CIC.
- Thickened bladder wall.
- Raised serum creatinine. In infants with lumbosacral myelomeningocoele with any of the above conditions and who have been started on CIC.

Anti-cholinergics 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 years of age, have learnt to do self-catheterisation.
- 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

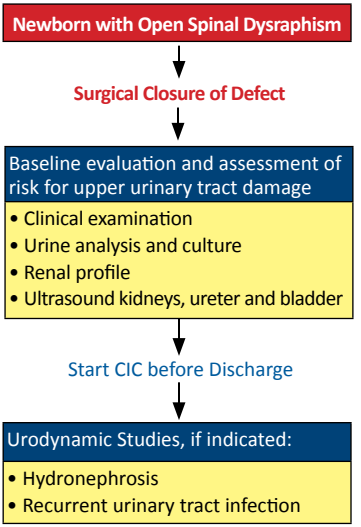
- Urethral trauma with creation of false passages, urethral strictures and bacteriuria.

Notes on CIC:

- In infants with myelomeningocoele, management is directed at creating a low-pressure reservoir and ensuring complete and safe bladder emptying with clean intermittent catheterisation.
- CIC should be started once the myelomeningocoele 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.

Technique of Clean Intermittent Catheterisation (CIC)	
Procedure	
1	Assemble all equipment: catheter, ± 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)/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 catheterisation.
5	Catheterise at the prescribed time with the best available measures.
Size of Catheters Small babies: 6F Children: 8-10F Adolescents: 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.

Algorithm for the Management of Neurogenic Bladder



Refer to Combined Urology/Nephrology Care

- Deteriorating upper tract
- Abnormal serum creatinine
- Recurrent urinary tract infection
- Urinary Incontinence

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.

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 > 10^5 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 diagnosis is best made with a combination of culture and urinalysis
- ***The quality of the urine sample is of crucial importance.***

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.

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 but have higher success rates and the procedure is less painful compared to SPA.
Suprapubic aspiration (SPA)
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.

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.

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)

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

- Antibiotic prophylaxis should not be routinely recommended in infants and children following first time UTI as antimicrobial prophylaxis does not seem to reduce significantly the rates of recurrence of pyelonephritis, regardless of age or degree of reflux.

However, 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.

Antibiotic Treatment for UTI		
Type of Infection	**Preferred Treatment**	**Alternative Treatment**
UTI (Acute cystitis)		
E.coli. *Proteus spp.*	PO Trimethoprim 4mg/kg/dose bd (max 300mg daily) for 1 week	PO Trimethoprim/ Sulphamethazole 4mg/kg/dose (TMP) bd for1 week
• Cephalexin, cefuroxime can also be used especially in children who had prior antibiotics. • Single dose of antibiotic therapy not recommended.		
Upper Tract UTI (Acute pyelonephritis)		
E.coli. *Proteus spp.*	IV Cefotaxime 100mg/kg/day q8h for 10-14 days	IV Cefuroxime 100mg/kg/day q8h *OR* IV Gentamicin 5-7mg/kg/day daily
• Repeat culture within 48hours if poor response. • Antibiotic may need to be changed according to sensitivity. Suggest to continue intravenous antibiotic until child is afebrile for 2-3 days and then switch to appropriate oral therapy after culture results e.g. Cefuroxime, for total of 10-14 days.		
Asymptomatic bacteriuria		
No treatment recommended		

Antibiotic Prophylaxis for UTI		
Indication	**Preferred Treatment**	**Alternative Treatment**
UTI Prophylaxis	PO Trimethoprim 1-2mg/kg ON	PO Nitrofurantoin 1-2mg/kg ON or PO Cephalexin 5mg/kg ON
• Antibiotic prophylaxis is not be routinely recommended in children with UTI. • Prophylactic antibiotics should be given for 3 days with MCUG done on the second day. • 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.		

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 cystourethogram (MCUG)

Since meta-analyses of data from recent, randomized controlled trials do not support antimicrobial prophylaxis to prevent febrile UTI; routine MCUG after the first UTI should not be routinely recommended after the first UTI.

MCUG may 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 VESICOURETERIC REFLUX 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

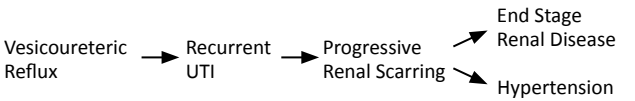
Definition

- Vesicoureteric 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).

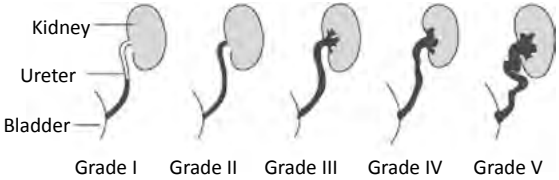
Significance of VUR

- 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 (reflux nephropathy).

NATURAL HISTORY OF VESICOURETERIC REFLUX



CLASSIFICATION OF VESICOURETERIC REFLUX ACCORDING TO THE INTERNATIONAL REFLUX STUDY COMMITTEE.



Management

- ***Antibiotic prophylaxis*** – refer to antibiotic prophylaxis section above
- ***Surgical management or endoscopic treatment*** is considered if the child has recurrent breakthrough febrile UTI.

POSTERIOR URETHRAL VALVE

- Refer to a 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 and expensive radiological studies
- Antibiotic prophylaxis should not be routinely recommended following first-time UTI.

Definition

- No consensus statement to date.
- Most studied parameter is the measurement of antero -posterior diameter (APD) of renal pelvis as visualized on transverse plane.
- Most agree that APD of renal pelvis of at least 5 mm on antenatal ultrasound of the fetus is abnormal.
- APD > 15mm represents severe or significant hydronephrosis.
- Fetal Hydronephrosis Index(HI): APD of renal pelvis divided by urinary bladder volume has been proposed as studied parameter but not uniformly accepted yet.

Advantages of prenatal detection

- May potentially be used for prenatal counseling and has allowed identification of conditions that require immediate treatment and which otherwise would go unrecognized until symptoms arose postnatally.
- Meta-analysis of 17 studies revealed that calculated risk of any postnatal pathology per degree of antenatal hydronephrosis was 11.9% for mild , 45.1% for moderate and 88.3% for severe.

Goals in evaluation of patients with antenatal hydronephrosis

- Prevent potential complications.
- Preserve renal function.
- Distinguish children who require follow up and intervention from those who do not.

Timing of detection

- 90% after eighteen weeks of gestation.
- 95% by 22 weeks.

Grading

The Society of Fetal Urology (SFU) Hydronephrosis Grading System	
Grades	Pattern of renal sinus splitting
SFU Grade 0	No splitting (renal pelvis)
SFU Grade I	Urine in pelvis barely splits sinus
SFU Grade II	Urine fills intrarenal pelvis
SFU Grade II	Urine fills extrarenal pelvis. Major calyces dilated
SFU Grade III	SFU Grade 2 and minor calyces uniformly dilated but renal parenchyma preserved.
SFU Grade IV	SFU Grade 3 and renal parenchyma thin

- Marked hydronephrosis is frequently seen in pelvic ureteric junction obstruction whereas the mild hydronephrosis is associated with vesicoureteric reflux.

Epidemiology

- 1-5% of all pregnancies
- 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 %.

Aetiology in Antenatal Hydronephrosis	
Abnormality	Frequency (%)
Transient	48
Physiologic	15
Pelvic ureteric junction obstruction	11
Vesicoureteric reflux	4
Megaureter,obstructed or non-obstructed	4
Multicystic kidneys	2
Ureterocoeles	2
Posterior urethral valves	1

Transient and physiologic hydronephrosis

- 60% of antenatal hydronephrosis is physiological. This will resolve before end of pregnancy or within 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.

Timing of postnatal evaluation

- Within first week of life: Neonates with unilateral hydronephrosis and normal contralateral kidney.
- Immediate evaluation before discharge: Bilateral hydronephrosis, hydronephrosis in solitary kidneys and bladder outlet obstruction.

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 shows 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 MCUG.

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.

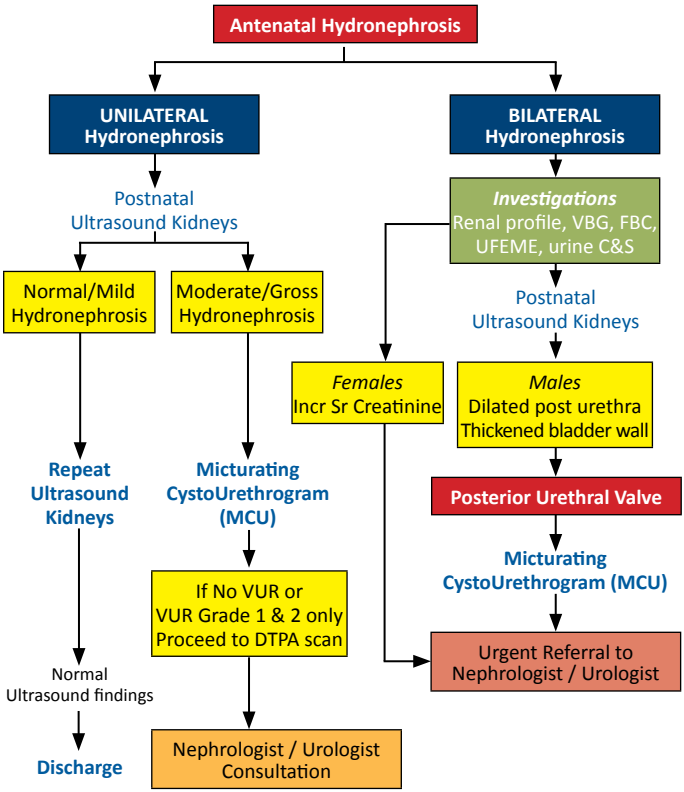
Antibiotics

Efficacy of antibiotic prophylaxis has not been proven. Consider antibiotic prophylaxis in high risk population such as those with gross hydronephrosis and hydroureters.

Commonly used Antibiotic Prophylaxis	
Trimethoprim	1-2mg/kg at night
Cephalexin	5mg/kg at night

Follow up Care

All children with significant hydronephrosis should be referred to paediatric nephrologists / urologist after relevant radiological investigations have been completed.


Antenatal Hydronephrosis
UNILATERAL Hydronephrosis
BILATERAL Hydronephrosis
Postnatal Ultrasound Kidneys
Investigations
Renal profile, VBG, FBC, UFEME, urine C&S
Normal/Mild Hydronephrosis
Moderate/Gross Hydronephrosis
Postnatal Ultrasound Kidneys
Females
Incr Sr Creatinine
Males
Dilated post urethra
Thickened bladder wall
Repeat Ultrasound Kidneys
Micturating CystoUrethrogram (MCU)
Posterior Urethral Valve
Micturating CystoUrethrogram (MCU)
If No VUR or VUR Grade 1 & 2 only Proceed to DTPA scan
Urgent Referral to Nephrologist / Urologist
Normal Ultrasound findings
Discharge
Nephrologist / Urologist Consultation

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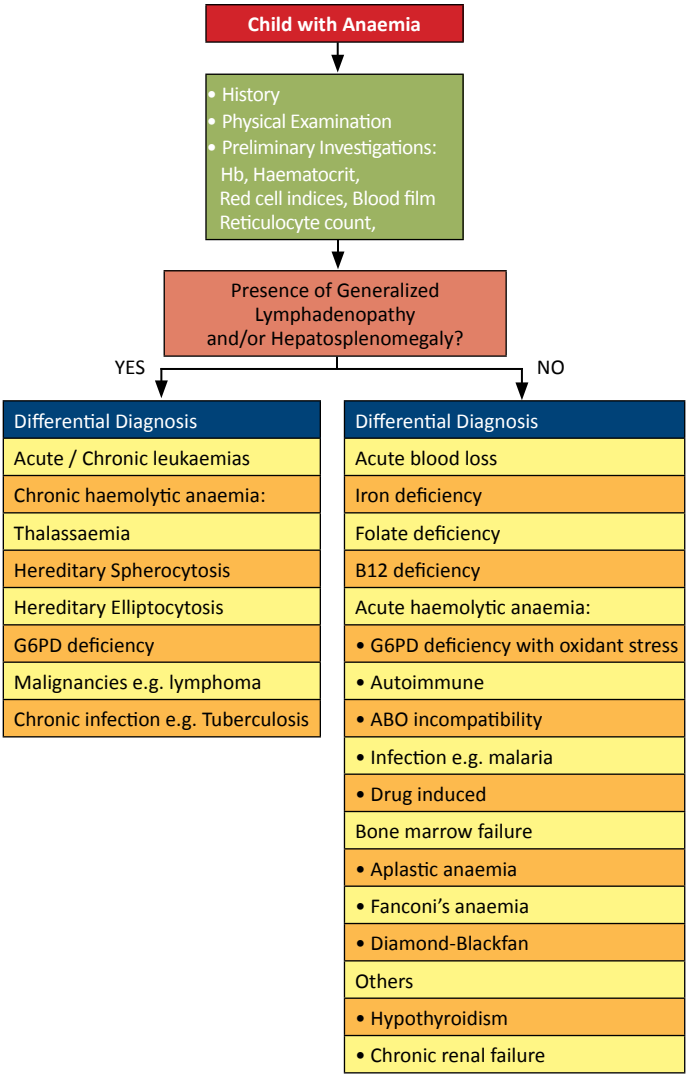
APPROACH TO CHILDREN WITH ANAEMIA



Variation in Red Blood Cell Indices with Age			
Age	Hb (g/dl)	RBC (x10 /l)	MCV (fl)
Birth	14.9 – 23.7	3.7-6.5	100-135
2 months	9.4-13.0	3.1-4.3	84-105
12 months	11.3-14.1	4.1-5.3	71-85
2-6 year	11.5-13.5	3.9-5.3	75-87
6-12 year	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			

IRON DEFICIENCY ANAEMIA

Laboratory findings

- Red cell indices : Low MCV, Low MCH values
- Low serum ferritin

Causes of Iron Deficiency Anemia
Chronic blood loss
Increase demand
• Prematurity
• Growth
Malabsorption
• Worm infestation
Poor diet

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): the content of elemental iron per ml depends on the preparation available.
- Tab. Ferrous fumarate 200 mg has 66 mg of elemental iron per tablet.

Consider the following if failure to response to oral iron:

- Non-compliance.
- Inadequate iron dosage.
- Unrecognized blood loss.
- Impaired GI absorption.
- Incorrect diagnosis.

Blood transfusion

- No transfusion required in chronic anaemia 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 IV Frusemide (1mg/kg) midway.

Pathogenesis

- A defective structural protein (spectrin) in the RBC membrane producing spheroidal shaped and osmotically fragile RBCs that are trapped and 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 and severe

- Anaemia
- Intermittent jaundice plenomegaly
- Splenomegaly
- Haemolytic crises
- Pigmented gallstones in adolescents and young adults
- Aplastic crises with Parvovirus B19 infections
- Megaloblastic crises
  - All patients should receive folate supplement

Rare manifestations

- Leg ulcers, spinocerebellar ataxia, myopathy
- Extramedullary haematopoietic tumours,

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.
- Splenectomy is avoided for patients < 5 years age because of the increased risk of postsplenectomy sepsis.
- Give pneumococcal, haemophilus and meningococcal vaccination 4-6 weeks prior to splenectomy and prophylactic oral penicillin to be given post-splenectomy.

Introduction

- β-Thalassaemia major is an inherited blood disorder presenting with anaemia at 4 - 6 months of age.
- Common presenting symptoms are pallor, lethargy, failure to thrive and hepatosplenomegaly.
- In Malaysia, the β-thalassaemia carrier rate is estimated at 3-5%, most of whom are unaware of their carrier / thalassaemia minor status.
- The carrier rates of α-thalassaemia and Haemoglobin E (HbE) are 1.8-7.5% and 5-46% respectively. HbE are found more in the northern peninsular states.
- Interaction between a β-thalassaemia carrier with a HbE carrier may result in the birth of a patient with HbE/β-thalassaemia or thalassaemia intermedia with variable clinical severity.
- The moderate to severe forms behave like β-thalassaemia major patients while the milder forms are asymptomatic.

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 findings for β-thalassaemia major: HbA decreased or absent, HbF increased, HbA2 variable.
- Serum ferritin.
- Red cell phenotyping (ideal) before first transfusion.
- DNA analysis (ideal)
  - For the detection of α-carrier and confirmation of difficult cases.
  - Mandatory in prenatal diagnosis.
  - Available upon request at tertiary centre laboratories in IMR, HKL, 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 siblings)
- All nuclear family members must be investigated by Hb Analysis for genetic counselling.
- 1st degree and 2nd degree relatives should also be encouraged to be screened & counselled (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 in β+-thalassaemia major/severe forms of HbE-β-thalassaemia if impaired growth, para-spinal masses, severe 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.
  - Keep mean Hb 12 - 12.5 g/dl.
  - The above targets allow for normal physical activity and growth, abolishes chronic hypoxaemia, reduce compensatory marrow hyperplasia which causes irreversible facial bone changes and para-spinal masses.
- 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).
- Transfusion volume?
  - Volume: 15 - 20mls/kg (maximum) packed red cells (PRBC).
  - 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 minimizes 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 lower volume PRBC (< 5ml/kg) at slow infusion rate over > 4 hours with IV Frusemide 1 mg/kg (20 mg maximum dose).
- It is recommended for patients to use leucodepleted (pre-storage, post storage or bedside leucocyte filters) PRBC < 2 weeks old.
- Leucodepletion would minimize non-haemolytic febrile reactions and alloimmunization by removing white cells contaminating PRBC.

Thalassaemia intermedia

- A *clinical diagnosis* where patients present later with less severe anaemia at > 2 years of age usually with Hb 8g/dl or more.
- Severity varies from being symptomatic at presentation to being asymptomatic until later adult life.
- Assessment and decision to start regular transfusion is best left to the specialist.

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 in transfusion dependent thalassaemia.
- Compliance to optimal treatment is directly related to superior survival outcome, now possible beyond the 6th decade.
- Currently 3 approved iron chelators are available: Desferrioxamine (DFO), Deferiprone (DFP) and Deferasirox (DFX).

Desferrioxamine (Desferal®)

- When to start?
  - Usually when the child is > 2 - 3 years old.
  - When serum ferritin reaches 1000 µg/L.
  - Usually after 10 – 20 blood transfusions.
- Dosage and route
  - Average daily dose is 20 – 40mg/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 µg/L.
- Vitamin C augments iron excretion with Desferal®.
- Severely iron loaded patients require longer or continuous SC or IV infusion (via Portacath) of Desferal®.

Complications of Desferal®

- Local skin reactions usually due to inadequately diluted Desferal® or infection
- Yersinia infection: presents with fever, abdominal pain & diarrhoea.
  - Stop Desferal® and treat with cotrimoxazole, aminoglycoside or 3rd generation cephalosporin.
- Desferal® toxicity (if using high doses > 50mg/kg/day in the presence of low serum ferritin in children):
  - Ocular toxicity: reduced vision, visual fields, night blindness; reversible
  - Auditory toxicity: high tone deafness. Not usually reversible
- Skeletal lesions: pseudo rickets, metaphyseal changes, vertebral growth retardation.

Complications of chronic iron overload in Thalassaemics over 10 years

- Endocrine: growth retardation, impaired glucose tolerance, pubertal delay, hypothyroidism, hypoparathyroidism and diabetes mellitus.
- Cardiac: arrhythmias, pericarditis, cardiac failure.
- Hepatic: liver cirrhosis (especially if with Hepatitis B/C infection).

Oral iron chelator

- **Deferiprone / L1 (Ferriprox®/Kelfer®)** 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 are risks of GI disturbance, arthritis and rare occurrence of idiopathic agranulocytosis.
- Weekly full blood count monitoring is recommended. Stop if neutropenic (<1,500/mm³).
- **Deferasirox (Exjade®)** can also be used for transfusional iron overload in patients 2 years or older but is expensive.
- The dose is 20-30 mg/kg/day in liquid dispersible tablet, taken once daily.
- There are risks of transient skin rash, GI disturbance and a reversible rise in serum creatinine.
- 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, any adverse side effects of chelation therapy.
- Pre-transfusion Hb, platelet count and WBC (if on Deferiprone).
- Post transfusion Hb – ½ hour post transfusion.
- Calculate the volume of pure RBC transfused based on the haematocrit (HCT) of packed red blood cells (PRBC) given (usually HCT of PRBC from blood bank is > 50 - 55%).
  - Volume of pure RBC transfused = volume of blood given x HCT of PRBC given (e.g. 600 mls x 0.55 = 330 mls).
  - Annual volume of pure RBC transfused per kg body weight.
  - Iron balance assessment.
- Review of current 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 – modified GTT, 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 hormone levels.
- Infection screen (6 monthly) – Hepatitis B and C, HIV, VDRL.
- Annual volume of pure red blood cell transfused/median body weight.
- Evaluate iron balance and overload status.
- Bone: osteoporosis & skeletal abnormalities.

Cardiac assessment at variable intervals and especially after 10 years of age

- Yearly ECG or Holter monitoring for arrhythmias.
- Annual cardiac echocardiography.
- Cardiac T2* MRI.

Liver iron assessment

- Liver T2* MRI for non-invasive assessment of liver iron.
- Liver biopsy for liver iron concentration and the assessment of hepatitis, fibrosis or cirrhosis in selected cases and prior to bone marrow transplantation.

Splenectomy

Indications

- Blood consumption volume of pure RBC > 1.5X normal or >200-220 mls/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^3 after splenectomy.

Diet and supplements

- Oral folate at minimum 1 mg daily may benefit most patients.
- Low dose Vitamin C at 3 mg/kg augments iron excretion for those on Desferral only.
  - Dose: <10 yrs, 50mg daily; >10yrs, 100mg daily given only on deferral days
- 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.
- Calcium and zinc.

Bone marrow transplantation (BMT)

- Potential curative option when there is an HLA-compatible sibling donor.
- Results from matched unrelated donor or unrelated cord blood transplant are still inferior with higher morbidity, mortality and rejection rates.
- Classification of patients into Pesaro risk groups based on the presence of 3 risk factors: hepatomegaly > 2cm, irregular iron chelation and presence of liver fibrosis.
- Best results if performed at the earliest age possible in Class 1 patients.

Pesaro Risk Groups and Outcome following BMT				
Class	No. of risk factors	Event Free Survival %	Mortality %	Rejection %
1	0	91	7	2
2	1-2	83	13	3
3	3	58	21	28
Adults	-	62	34	-

Note: In newly diagnosed transfusion dependent thalassaemics, the family should be informed of this option and referred early to a Paediatrician for counselling and 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.

Patient and parents support groups

- Various states and local Thalassaemia Societies are available nationwide.
- Provide support and education for families.
- Organises fund raising activities and awareness campaigns.
- Health professionals are welcomed to participate.
- More information in *www.moh.gov.my* or *www.mytalasemia.net.my.*

Definition

- Isolated thrombocytopenia with otherwise normal blood counts in a patient with no clinically apparent alternate cause of 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 Manifestations

- Onset is usually acute.
- Majority will give a history of a viral infection in the preceding 2-4 weeks
- Spectrum of bleeding severity ranges from cutaneous bleeding i.e. petechiae, to mucosal bleeds i.e. gum bleeds and epistaxis, to life threatening bleeds i.e. intracranial haemorrhage.

Diagnosis and Investigations

- Diagnosis is based on history, physical examination, blood counts, and examination of the peripheral blood smear.
  - Physical examination: absence of hepatosplenomegaly or lymphadenopathy.
  - Blood counts: isolated thrombocytopenia, with normal haemoglobin and white cell count.
  - Peripheral blood picture: normal apart from reduced, larger platelets, no abnormal cells.
- Threshold for performing a bone marrow aspiration is low and is indicated:
  - Before starting steroid therapy (to avoid partially inducing an undiagnosed acute leukaemia).
  - If there is failure to respond to Immunoglobulin therapy.
  - When there is persistent thrombocytopenia > 6 months.
  - Thrombocytopenia recurs after initial response to treatment.
- Other tests that may be indicated when there is atypical presentation are:
  - Antinuclear factor and DNA antibodies.
  - Coomb's test.
  - CMV serology for those less than a year old.
  - Coagulation profile for those suspected non-accidental injury and inherited bleeding disorder.
  - HIV testing for those at risk i.e. parents who are HIV positive or intravenous drug users.
  - Immunoglobulin levels for those with recurrent infections.

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

Management

- Not all children with diagnosis of acute ITP need hospitalization.
- Hospitalization is indicated if:
  - There is severe life-threatening bleeding (e.g. ICH) regardless of platelet count.
  - Platelet count < 20 x 10^9/L with evidence of bleeding.
  - Platelet count < 20 x 10^9/L without bleeding but inaccessible to health care.
  - Parents request due to lack of confidence in homecare.
- Most children remit spontaneously: 70% achieve a platelet count > 50 x 10^9/L by the end of the 3rd week. Treatment should be individualised.
- Precautions with physical activities, avoidance of contact sports and seeking immediate medical attention if bleeding occurs should be advised.
- Careful observation and monitoring of platelet count, without specific treatment, is appropriate for patients with:
  - Platelet count > 20 x 10^9/L without bleeding.
  - Platelet count > 30 x 10^9/L with only cutaneous purpura.
- A repeat blood count should be performed within the first 7-10 days to ensure that there is no evidence of serious evolving marrow condition.
- Treatment is indicated if there is:
  - Life threatening bleeding episode (e.g. ICH) regardless of platelet count.
  - Platelet count < 20 x 10^9/L with mucosal bleeding.
  - Platelet count < 10 x 10^9/L with any bleeding.

- Choice of treatment includes:
  - Oral Prednisolone 2 mg/kg/day for 14 days then taper off.
  - Oral Prednisolone 4 mg/kg/day for 4 days.
  - IV Immunoglobulin (IVIG) 0.8 g/kg/dose for a single dose.

Notes regarding treatment:

- All above are effective in raising platelet count much quicker compared to no treatment. However there is no evidence that these treatment regimens 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 (treat the child and not the platelet count).

Intracranial Haemorrhage (ICH)

- The most feared complication of ITP.
- Incidence of ICH in a child with ITP is very low between 0.1 - 0.5%.
- The risk of ICH highest with platelet count < 20 x 10^9/L, 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

Emergency treatment of ITP with severe bleeding i.e. severe epistaxis or GIT bleed causing drop in Hb or ICH (alone or in combination) includes:

- High dose IV Methylprednisolone 30 mg/kg/day for 3 days.
- IVIG 0.8g - 1g/kg as a single dose.
- Combination of IVIG and methylprednisolone in life threatening conditions.
- Platelet transfusion in life threatening haemorrhage: 8 - 12 units/m^2 body surface area (2 to 3 folds larger than usual units) as the platelets will be consumed by the haemorrhage to form blood clots and will reduce further circulating platelets.
- Consider emergency splenectomy if other modalities fail.
- Neurosurgical intervention in ICH, if indicated and to perform with splenectomy if necessary.

CHRONIC ITP

Definition

- 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

Counselling and education of patient and caretakers regarding natural history of disease and how to detect problems and possible complications early are important. Parents should be comfortable of taking care of patients with persistent low platelet counts at home. At the same time they must be made aware of when and how to seek early medical attention when the need arises.

- 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, collagen disorders, HIV infection).
- Asymptomatic children can be left without therapy and kept under observation with continued precautions during physical activity.
- Symptomatic children may need short course of treatments as for acute ITP to tide them over the "relapse" period or during surgical procedures.

For those with Persistent bleeding, Second line therapies includes:

- Pulses of steroids: oral Dexamethasone 1 mg/kg given on 4 consecutive days every 4 weeks for 4 months.
- Intermittent anti-Rh(D) Immunoglobulin treatment for those who are Rhesus D positive: 45 - 50 ug/kg. May cause drop in Hb levels.
- ***Second line therapy should only be started after discussion with a Paediatric haematologist.***

Note:

- Care must be taken with any pulse steroid strategy to avoid treatment-related steroid side effects.
- Family and patient must be aware of immunosuppressive complications e.g. risk of severe varicella.
- There is no justification for long-term continuous steroids.

If first and second-line therapies fail, the patient should be managed by a paediatric haematologist.
Other useful agents are Rituximab and Cyclosporine.

Splenectomy

- Rarely indicated in children as spontaneous remissions continue to occur up to 15 years from diagnosis.
- The risk of dying from ITP is very low - 0.002% whilst the mortality associated with post-splenectomy sepsis is higher at 1.4 - 2.7 %.
- *Justified when there is:*
  - Life-threatening bleeding event
  - Severe life-style restriction with no or transient success with intermittent IVIG, pulsed steroids or anti-D immunoglobulin.
- *Laparoscopic method* preferred if expertise is available.
- Pre-splenectomy preparation of the child with immunization against pneumococcus, haemophilus and meningocccus must be done and post-splenectomy life-long penicillin prophylaxis must be ensured.
  - Pneumococcal booster should be given every 5 years.
- Up to 70% of patients achieve complete remission post-splenectomy.

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 presents 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.
- Intracranial haemorrhages can be life threatening.
- Bleeding may also occur spontaneously or after trauma, operation or dental procedures.

Diagnostic Investigations

- Full blood count
- Coagulation screen: PT, APTT
- Specific factor assay: FVIII level (low in Haemophilia A).
- Specific factor assay: FIX level (low in Haemophilia B).
- Bleeding time if applicable.
- Von Willebrand screen even if APTT normal.

In haemophilia, the activated partial thromboplastin time (APTT) is prolonged in moderate and severe haemophilia but may not show prolongation in mild haemophilia. The platelet count and prothrombin time (PT) are normal. When the APTT is prolonged, then the lab will proceed to do the factor VIII antigen level. If this is normal, only then will they proceed to assay the Factor IX level. Once the level has been measured, then the haemophilia can be classified as below.

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 trauma, surgery or dental procedures
5-25 %	Mild	

Further Investigations

- Hepatitis B surface antigen, anti HBS antibody
- Hepatitis C antibody
- HIV serology
- Renal profile and Liver function test.
- Platelet aggregation if high suspicion of platelet defect.
- 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

- Ideally, treatment of severe haemophilia should be prophylactic to prevent arthropathy and ensure the best quality of life possible.The dosage of prophylaxis is usually 25-35 U/kg of Factor VIII concentrate, given every other day or 3 times a week. For Factor IX, the dosage is 40-60 U/kg, given every 2-3 days. However, this form of management is costly and requires central venous access.
- On demand treatment is another treatment option when clotting factors are inadequate. It consists of replacing the missing factor: Factor VIII concentrates are used in haemophilia A, Factor IX concentrates in Haemophilia B. Fresh frozen plasma and cryoprecipitate ideally SHOULD NOT be used as there is a high risk of viral transmission.
- The dose of factor replacement depends on the type and severity of bleed.

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	100 U/kg

- Dose of factor required can also be calculated using the formulas below
  - Units of Factor VIII: (% rise required) x (weight in kg) x 0.5.
  - Units of Factor IX: (% rise required) x (weight in kg) x 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%.
- Infuse Factor VIII by slow IV push at a rate not exceeding 100 units per minute in young children.

- 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.
- Veins must be handled with care. Never perform cut-down unless in an emergency as it destroys the vein.

Complications

Joint destruction:

- Recurrent haemarthroses into the same joint will eventually 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 recommended.

Inhibitors:

- These are antibodies directed against the exogenous factor VIII or IX neutralizing the clotting activity.
- Overall incidence is 15-25% in haemophilia A and 1-3% in haemophilia B.
- Can develop at any age but usually after 10 – 20 exposure days. It is suspected when there is lack of response to replacement therapy despite high doses.
- Treatment requires “bypassing” the deficient clotting factor. Currently 2 agents are available - Recombinant activated Factor VII (rfVIIa or Novoseven) and FEIBA. Immune tolerance induction is also another option.
- Management of inhibitors are difficult and requires consultation with the haematologist in specialized centres.

Supportive Treatment

Analgesia

- There is rapid pain relief in haemarthroses once missing factor concentrate is infused.
- If analgesia is required, avoid intramuscular injections.
- Do not use aspirin or the non-steroidal anti-inflammatory drugs (NSAIDS) as they will affect platelet function.
- Acetaminophen with or without opioids can provide adequate pain control.

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

- This is important and must be given: The subcutaneous route is preferred.
- Give under factor cover if haematomas are a problem.

Haemophilia Society

- All haemophiliacs should be registered with a patient support group e.g. Haemophilia Society.
- They should have a medic-alert bracelet/chain which identifies them as haemophiliacs and carry a book in which the diagnosis, classification of severity, types of bleeds and admissions can be recorded

SPECIFIC GUIDELINES FOR MANAGEMENT

Intracranial haemorrhage (ICH)

- Give factor replacement before suspected bleed is confirmed by CT scan
- Aim to increase Factor VIII level to 100%.
- For haemophilia B if monoclonal factor IX is used a level of 80% is adequate and if prothrombin complex concentrate (PCC) is used 50% level is recommended.
- Urgent CT scan:
  - If CT scan confirms ICH : maintain factor level 80%–100% for 1–7 days and 50% for 8–21 days.
  - If CT scan show no evidence of ICH, admit 1 day for observation.
- Follow up for long term sequelae.
- Lab investigations:
  - 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.
- Maintain adequate factor levels -
  - Days 1-3 60-80%
    4-7 40-60%
    8-14 30-50%
- Repeat factor assay and check inhibitor level on day 3 to ensure adequate. levels. Post operatively a minimum of 10 to 14 days replacement therapy is recommended.

Iliopsoas bleed

- *Symptoms*: Pain/discomfort in the lower abdomen/upper thighs
- *Signs*: Hip flexed, internally-rotated, unable to extend
- *Danger*: Hypovolaemia, large volumes of blood may be lost in the retroperitoneal space.

Management:

- Factor replacement: 50U/kg stat, followed by 25U/kg bd till asymptomatic, then 20U /kg every other day for 10-14 days.
- Ultrasound / CTscan to diagnose.
- Physiotherapy - when pain subsides.
- Repeat U/S to assess progress.

Haematuria

Management

- Bed rest.
- Hydration (1.5 x 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)

- 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.
- Severe haemarthroses
  - Splint in position of comfort.
  - Rest.
  - Early physiotherapy.

I. METABOLIC EMERGENCIES

Tumour Lysis Syndrome

Tumour lysis syndrome
Characterised by:
Hyperuricemia
Hyperkalemia
Hyperphosphatemia with associated Hypocalcemia

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)

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 $CaPO_4$ precipitation. Occurs when Ca X PO_4 > 60 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

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

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 mg/dl.

- Increased phosphorus excretion causing calcium phosphate precipitation (in vivo solubility dependant on Ca X 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).

Management (Prevention):
To be instituted in every case of acute leukaemia or lymphoma prior to induction chemotherapy.

- *Hydration*: Double hydration - 125ml/m²/hr or 3000ml/m²/day.
  No added potassium.
- *Alkalization of urine:* Adding $NaHCO_3$ at 150 - 200 mmol/m²/day (3 mls/kg/day $NaHCO_3$ 8.4%) into IV fluids to keep urine pH 7.0 - 7.5. Avoid over alkalinization as this may aggravate hypocalcemia 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 $NaHCO_3$ infusion. This can only be done if HCO_3 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^{2+}, PO_4, 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 hypokalaemia 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 / 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/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 / m^2 should increase platelets by 50,000 / mm^3.
- Fresh frozen plasma (FFP) or cryoprecipitate.
- Vitamin K.
- +/- Heparin therapy (10u/kg/hr) - controversial

Other haematological energencies

- 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 and chemotherapy if pathology due to Non-Hodkin 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 neutorphil count (ANC) <500 /mm³. Risk increases maximally if ANC < 100 /mm³ and greatly reduced if the ANC > 1000 /mm³.

Management (Follow Algorithm on next page)

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 cisplatinum - nephrotoxic and ototoxic. If required, monitor renal function closely.

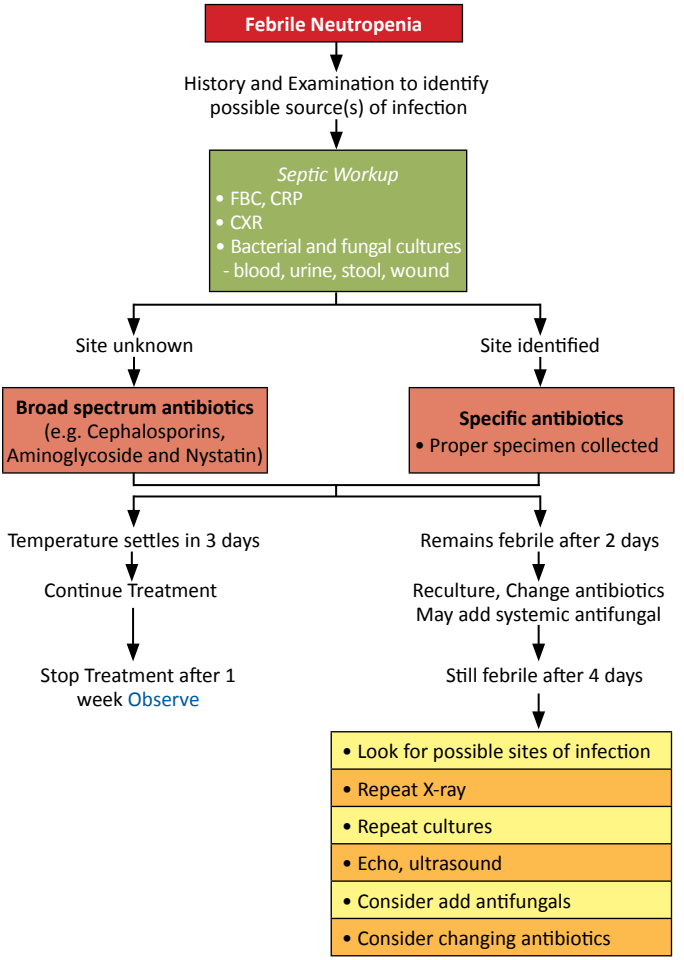
Typhlitis

- A necrotizing colitis localised to the caecum occuring 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).

APPROACH TO CHILD WITH FEBRILE NEUTROPENIA



Abbrevations. FBC, full blood count; CRP, C-reactive protein; CXR, chest X-ray; CVL, central venous line.

Common causes of Shock in Children with Cancer		
Distributive	**Hypovolaemic**	**Cardiogenic**
Sepsis	Haemorrhage • Haemorrhagic cystitis • Gastrointestinal bleeding - Ulcers - Typhlitis • Massive haemoptysis	Myopathy • Anthracycline • High dose cyclophosphamide • Radiation therapy
Anaphylaxis • Etoposide • L-asparaginase • Anti-thymocyte globulin • Cytosine • Carboplatin • Blood products • Amphotericin B	Pancreatitis	Cardiac tamponade • Intracardiac tumour • Intracardiac thrombus • Pericardial effusion • Constrictive pericarditis
	Addisonian crisis	
	Intractable vomiting	
Veno occlusive disease	Diabetes mellitus	Metabolic • Hyperkalaemia, hypokalaemia • Hypocalcaemia
	Diabetes insipidus	
	Hypercalcaemia	
		Myocarditis • 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: craniopharyngima , 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 DIVC and CVA, due to the release of procoagulants.

Management

- Supportive.
- Use of anticoagulant potentially detrimental.
- In L-Asparaginase induced, recommended FFP bd.

VI. MISCELLANOUS 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.

Definition

- Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy, representing nearly one third of all paediatric cancers.

Peak age

- 2 – 5 years old. Male: Female ratio of 1.2:1.

Pathophysiology

- Genetically altered lymphoid progenitor cells which undergo dysregulated proliferation and clonal expansion.

Presentation

- Signs and symptoms which reflect bone marrow infiltration causing anaemia, neutropenia, thrombocytopenia and extra-medullary disease.
  - Pallor and easy bleeding – common
  - Non remitting fever.
  - Lymphadenopathy.
  - Hepatosplenomegaly.
  - Bone pains - not to be misdiagnosed as Juvenile Idiopathic Arthritis (JIA).
- Uncommon at presentation:
  - CNS involvement e.g. headache, nausea and vomiting, lethargy, irritability, seizures or spinal mass causing signs and symptoms of spinal cord compression.
  - Testicular involvement, usually as a unilateral painless testicular enlargement.
  - Skin manifestations e.g. skin nodules.

Initial investigations

Diagnosis

- Full Blood Count (FBC) and Peripheral Blood Film (PBF).
  - Anaemia and thrombocytopenia.
  - Total White Count (TWC) can be normal, low or high.
  - Occasionally PBF may not show presence of blast cells.
- Bone marrow aspirate (BMA) and trephine biopsy.
- Bone marrow for flowcytometry analysis (immunophenotyping).
- Bone marrow cytogenetics.
- Bone marrow/Blood for molecular studies wherever possible.
  - Option to send to Hospital Kuala Lumpur (HKL) Pathology Laboratory (Haematology unit)/Haematology Laboratory in IMR (3mls in EDTA bottle) or other University/Private laboratories for molecular characterisation (Prior appointments must be made before sending samples).
- Cerebral Spinal Fluid (CSF) examination for blast cells.
- CXR to evaluate for mediastinal masses.

For assessment and monitoring:

- Blood Urea and Serum Electrolytes (BUSE) especially serum Potassium.
- Serum Creatinine, Uric Acid, Phosphate, Calcium, Bicarbonate levels.
- Lactate dehydrogenase (LDH) – to assess degree of leukaemic cell burden and risk of tumour lysis.
- Coagulation studies in APML (acute promyelocytic leukemia) or if the child is toxic or bleeding.
- Blood cultures and septic workup if febrile.
- Hepatitis B/C, HIV and VZ IgG screen pre transfusion and pre treatment.
- Repeat BMA and CSF examinations.

Prognosis

Overall cure rates for childhood ALL are now over 80% but it depends among others on the prognostic groups, clinical and laboratory features, treatment in centres with paediatric oncologist and special diagnostics, use of standard treatment protocols and also the level of supportive care available.

Unfavourable if:

- Clinical features indicating high risk
  - Age > 10 years old and infants.
  - WBC count at diagnosis > 50000/mL.
- Molecular characteristics of the leukaemic blasts, e.g. Presence of abnormal cytogenetics with oncogenes producing abnormal fusion proteins e.g. Philadelphia chromosome t(9;22)(q34;q11); BCR-ABL;P185BCR-ABL tyrosine kinase.
- Poor response to the induction chemotherapy
  - Day 8 peripheral blast cell count > 1000 x 10^9/L.
  - Day 33 BMA not in remission

Treatment

The regimes or treatment protocols used vary according to originator groups/institutions from the various countries (BFM – Germany, MRC – UK, CCG/COG – USA) but generally consists of induction, central nervous system treatment/prophylaxis, consolidation/intensification and maintenance therapy.

Complications considered as oncologic emergencies can be seen before, during and after treatment (see **Ch 69 Oncologic Emergencies**). These include:

- Hyperleucocytosis at presentation.
- Superior vena caval obstruction.
- Tumor lysis syndrome leading on to renal failure.
- Sepsis.
- Bleeding.
- Thrombosis.
- Typhlitis.
- CNS manifestations: Cord compression, neuropathy, encephalopathy and seizures.

Once discharged, care givers must be able to recognise signs and symptoms that require urgent medical attention, especially infections as they can be life threatening. Even on maintenance therapy, infections must be taken seriously as patients are still immunocompromised up to 3 months after discontinuing chemotherapy.

General guidelines for children with Acute Lymphoblastic Leukaemia on maintenance chemotherapy for a total of 2 - 2.5 years:

- Check height, weight and calculate surface area (m2) every 3 months and adjust drug dosages accordingly.
  To calculate body surface area = √ [Height (cm) x Weight (kg) / 3600]
- Check full blood count every 2 weeks for the first 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. Majority of relapse (>2/3) would occur within the first year of stopping treatment.
- CNS disease would present itself usually with headache, vomiting, abnormal sensorium or hypothalamic symptoms (e.g. Hyperphagia and abnormal weight gain).
- Testicular relapse present as a painless unilateral swelling
- Cotrimoxazole is routinely used as prophylaxis against *Pneumocystis carinii* pneumonia (PCP) and continued until the end of therapy. In the event of chronic cough or unexplained tachypnoea, CXR is required.

  If there is evidence of interstitial pneumonitis, send nasopharyngeal secretions for PCP Antigen detection e.g. Immunoflorescent test (IFT) or PCP PCR detection and treat empirically with high dose Cotrimoxazole 20 mg/kg/day in divided doses for a total of 2 weeks.
- Different institutions and protocols will have different regimes for maintenance chemotherapy.
  Check the TWC and Absolute Neutrophil Count (ANC) threshold levels of the various protocols:

  As a general rule, chemotherapy is adjusted to maintain TWC at 2 - 3 $X10^9$/L and ANC at or more than 0.75 X 10^9/L.
  - If TWC drop to levels of 1-2 $X10^9$/L and ANC to levels of 0.5 -0.75 x 10^9 /L or platelet level at 50-100 x 10^9/L, reduce tablet 6-Mercaptopurine (6MP) and oral methotrexate (MTX) normal dose by 50%.
  - Once counts are above those levels, increase 6MP and MTX back to 75% of normal dose.
  - Review the patient in 1 week and if counts can be maintained, increase back to 100% of normal dose.
  - If TWC is < 1 X 10^9/L and ANC < 0.5 x 10^9/L or platelets < 50 x 10^9/L, stop both drugs.
  - Restart drugs at 50% dose once neutrophil count have recovered > 0.75 x 10^9/L and then increase back to 75% and 100% as above.

- Normally Haemoglobin would remain stable but repeated falls in haemoglobin alone may be due to 6MP intolerance.
  - Transfuse if anaemia occurs early in the course of maintenance therapy and the standard doses of 6MP and MTX are to be maintained as much as possible.
  - If there is persistent anaemia (i.e. Hb< 8 gm/dl), reduce 6MP dose first and maintain the MTX dose.
  - If anaemia persists despite reducing the dose of 6MP, reduce the MTX dose appropriately.
- If counts are persistently low and doses of 6MP/MTX are already suboptimal, consider withholding Cotrimoxazole.
  - Re-introduce Cotrimoxazole once 6MP or MTX are at > 75% of standard protocol dosage.
  - If neutropaenia recurs or if child cannot tolerate at least 75% drug of dosages, Cotrimoxazole should be stopped
  - ***Maintenance of adequate drug dose should take priority over continuing Cotrimoxazole.***
  - If Cotrimoxazole is stopped, keep in mind that the child is at increased risk of *Pneumocystis* pneumonia and there should be a relatively low threshold for treatment of any suspected interstitial pneumonitis.
- If counts take longer to recover, consider performing bone marrow aspiration after 2-3 weeks to rule out sub-clinical relapse.
- If the diagnostic test is available, consider to also send blood for Thiopurine Methyltransferase (TPMT) enzyme deficiency screening. Children who are homozygous TPMT deficient can become profoundly myelosuppressed with 6MP administration.
- In severe diarrhoea and vomiting, stop both drugs. Restart at 50% dose 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 and antifungal treatment.
- In clinically significant liver dysfunction; 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:
  - If there is significant fever (T° ≥ 38.5 °C x 1 or ≤ 38 °C x 2 one hour apart) and neutropenia, stop all chemotherapy drugs and admit for IV antibiotics.
  - Take appropriate cultures and CXR if indicated and give bolus IV antibiotics immediately without waiting for specific bacteriological confirmation.
  - Use a combination of aminoglycoside and cephalosporins to cover both gram negative and gram positive organisms. If nosocomial infection is suspected, use the appropriate antibiotics according to your hospital's cultures sensitivity pattern.
  - Any fever developing within 24 hours of central venous line access should be treated as catheter related blood stream infection. Common organisms are the gram positive cocci. Consider adding cloxacillin to the antibiotic regime.
  - Assume multiresistant bacterial sepsis when dealing with patients presenting with septic shock especially if recently discharged from hospital.
  - Vancomycin may be indicated if there is a long line (Hickman) or chemoport in situ or if MRSA or coagulase negative Staphylococcus infections are suspected.
  - Antifungal therapy may be indicated in prolonged neutropenia or if there is no response to antibiotics or if fungal infection is suspected.
  - Early and aggressive empirical therapy without waiting for blood culture results will save lives.
- Chicken Pox/Measles
  - 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

For exposed patients:
(VZ IgG –ve at diagnosis, on treatment or within 6 months of stopping treatment); give:

- VZIG if available (should be given within 7 days of contact) < 5yrs: 250mg, 5 – 7 yrs: 500mg, 7 – 12 yrs: 750mg.
- If VZIG not available - Oral acyclovir 200mg 5x/day if < 6 years old; 400 mg 5x/day if > 6 years old for 5 days.
- Monitor for signs of infections.

Patient with chickenpox

- Admit, isolate and treat immediately with IV acyclovir 500 mg/m^2/dose 8 hourly or 10mg/kg 8 hourly until no new lesions are noted.
- Switch to oral acyclovir 400mg 5x daily if <6 years old; 800mg 5x daily if >6 years until the lesions are healed, usually in about 10 days.
- Chemotherapy must be stopped on suspicion of exposure. If infected and treated, it should only be recommenced 2 weeks after the last vesicle has dried up.

Vaccinations

- Children on chemotherapy should not receive any vaccinations until 6 months after cessation of chemotherapy.
- Recommence their immunisation programme continuing from where they left off.

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Introduction

The following is based on Integrated Management of Childhood Illness (IMCI) and the College of Paediatrics, Academy of Medicine of Malaysia guidelines on the management of Acute Diarrhoea in Children 2011 and modifications have been made to Treatment Plan C in keeping with Advanced Paediatric Life Support (APLS) principles.

- Acute gastroenteritis is a leading cause of childhood morbidity and mortality and an important cause of malnutrition.
- Many diarrhoeal deaths are caused by dehydration and electrolytes loss.
- Mild and moderate dehydration is safely and effectively treated with ORS solution but severe dehydration requires intravenous fluid therapy.

If you have gone through the PALS or APLS course, First assess the state of perfusion of the child.

Is the child in shock?

- Signs of shock include tachycardia, weak peripheral pulses, delayed capillary refill time > 2 seconds, cold peripheries, depressed mental state with or without hypotension.

Any child with shock 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.

Assess:			
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 secs)
Classify:			
	Mild Dehydration <5% Dehydrated* *IMCI: No signs of Dehydration*	≥ 2 above signs: **Moderate Dehydration** 5-10% Dehydrated *IMCI: Some signs of Dehydration*	≥ 2 above signs: **Severe Dehydration** > 10% Dehydrated
Treat:			
	Plan A Give fluid and food to treat diarrhoea at home	**Plan B** Give fluid and food for some dehydration	**Plan C** Give fluid for severe dehydration

**% of body weight (in g) loss in fluid (Fluid Deficit) e.g. a 10 kg child with 5% dehydration has loss 5/100 x 10000g = 500 mls of fluid deficit.*

PLAN C: TREAT SEVERE DEHYDRATION QUICKLY

- Start intravenous (IV) or intraosseous (IO) fluid immediately.
  If patient can drink, give ORS by mouth while the drip is being set up.
  - Initial fluids for resuscitation of shock: 20 ml/kg of NaCl 0.9% or Hartmann solution as a rapid IV bolus.
  - Repeated if necessary until patient is out of shock or if fluid overload is suspected. Review patient after each bolus.
  - Calculate the fluid needed over the next 24 hours:
    Fluid for Rehydration (also called fluid deficit)
    + Maintenance (minus the fluids given for resuscitation).
  - Fluid for Rehydration: percentage dehydration X body weight in grams
  - Maintenance fluid (NaCl 0.45 / D5%)
    (See **Ch 3 Fluid And Electrolyte Guidelines**)
    1st 10 kg = 100 ml/kg;
    10-20 kg = 1000 ml/day + 50 ml/kg for each kg above 10 kg
    >20 kg = 1500 ml/day + 20 ml/kg for each kg above 20 kg.

Example:
A 6-kg child is clinically shocked and 10% dehydrated as a result of gastroenteritis.
Initial therapy:

- 20 ml/kg for shock = 6 × 20 = 120 ml of 0.9% saline given as a rapid intravenous bolus.
- Estimated fluid therapy over next 24 hours:
- Fluid for Rehydration: 10/100 x 6000 = 600 ml
- 100ml/kg for daily maintenance fluid = 100 × 6 = 600 ml
- Rehydration + maintenance = 600 + 600 =1200 ml
- Start with infusion of 1200/24 = 50 ml/h

- ***The cornerstone of management is to reassess the hydration status frequently (e.g. at 1-2 hourly), and adjust the infusion as necessary.***
- Start giving more of the maintenance fluid as oral feeds
  e.g. 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. This fluid should be administered frequently in small volumes (cup and spoon works very well for this process).
- Generally normal feeds should be administered in addition to the rehydration fluid, particularly if the infant is breastfed.
- Once a child is able to feed and not vomiting, oral rehydration according to Plan A or B can be used and the IV drip reduced gradually and taken off.

- 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 nasogastric or 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.
- ***If there is an outbreak of cholera in your area, give an appropriate oral antibiotic after the patient is alert.***

Other indications for intravenous therapy

- Unconscious child.
- Continuing rapid stool loss (> 15-20ml/kg/hour).
- Frequent, severe vomiting, drinking poorly.
- Abdominal distension with paralytic ileus, usually caused by some antidiarrhoeal 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).

IV regime as for Plan C but the replacement fluid volume is calculated according to the degree of dehydration. (5% for mild, 5-10% for moderate dehydration).

Indications for admission to Hospital

- Moderate to severe dehydration.
- 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.

* *Lower threshold for children with obesity due to possibility of underestimating degree of dehydration.*

Other problems associated with diarrhoea

- 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.
- Seizures
  - Consider:
    - Febrile convulsion (assess for possible meningitis)
    - Hypoglycaemia
    - Hyper/hyponatraemia
- 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 (sensitivity of the test can be greatly increased by sending the liquid portion of the stool for analysis simply by inverting the diaper).
  - 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.
- Cow's Milk Protein Allergy
  - A known potentially serious complication following acute gastroenteritis.
  - To be suspected when trial of lactose free formula fails in patients with protracted course of diarrhoea.
  - Children suspected with this condition should be referred to a paediatric gastroenterologist for further assessment.

Non pharmacological / Nutritional strategies

- Undiluted vs diluted formula
  - No dilution of formula is needed for children taking milk formula.
- Soy based or cow milk-based lactose free formula
  - Not recommended routinely. Indicated only in children with suspected lactose intolerance.

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 medications
  - The locally available diosmectite (Smecta®) has been shown to be safe and effective in reducing stool output and duration of diarrhoea. It acts by restoring integrity of damaged intestinal epithelium, also capable to bind to selected bacterial pathogens and rotavirus.
    Other anti diarrhoeal agents like kaolin (silicates), loperamide (anti-motility) and diphenoxylate (anti motility) are not recommended.
- Antiemetic medication
  - Not recommended, potentially harmful.
- Probiotics
  - Probiotics has been shown to reduce duration of diarrhoea in several randomized controlled trials. However, the effectiveness is very strain and dose specific. Therefore, only probiotic strain or strains with proven efficacy in appropriate doses can be used as an adjunct to standard therapy.
- 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.

Introduction

WHO defines persistent or chronic diarrhea as an episode of diarrhea that begins acutely and lasts for 14 days or more. It is a complex condition with multitude aetiologies. Locally, commonest aetiology is believed to be infection related where as autoimmune enteropathy is an important aetiology in developed countries.

Mechanisms of diarrhea

- Osmotic e.g. Lactose intolerance
- Secretory e.g. Cholera
- Mixed secretory-osmotic e.g. Rotavirus
- Mucosal inflammation e.g. Invasive bacteria, Inflammatory Bowel Disease
- Motility disturbance

Differentiation of Osmotic from Secretory Diarrhoea

Parameter	Osmotic diarrhoea	Secretory diarrhoea
Stool volume	Small (generally <200ml/24 hours)	Large (>200ml/24 hours)
Response to fasting	Diarrhoea stops	Diarrhoea continues
Stool Osmolality	> (Stool Na + K) x 2	= (Stool Na + K) x 2
Osmotic Gap	> 135 mOsm/l	< 50 mOsm/l
Stool Sodium	< 70 mmol/l	> 70 mmol/l
Stool Potassium	< 30 mmol/l	> 40 mmol/l
Stool Chloride	< 35 mmol/l	> 40 mmol/l
Stool pH	<5.5	> 6.0
Stool reducing substance	Positive (>0.5%)	Negative

Adapted from M Ravikumara. Investigation of chronic diarrhea. Paediatrics and Child Health 2008; 18: 441-47

Causes of chronic diarrhea in children
Functional diarrhea (chronic nonspecific diarrhea)
Excessive intake of juice/osmotically active carbohydrates
Inadequate dietary fat
Idiopathic
Enteric infection
Postenteritis syndrome
Parasites Giardia lamblia; Cryptosporidia parvum; Cyclospora cayetanensis; Isospora belli; Microsporidia; Entamoeba histolytica; Strongyloides, Ascaris, Tricuris spesies
Bacteria Enteroaggregative E. coli (EAggEC); Enteropathogenic E. coli (EPEC); Enterotoxigenic E. coli (ETEC); Enteroadherent E. coli (EAEC); Mycobacterium avium complex; Mycobacterium tuberculosis; Salmonella, Shigella, Yersinia, Campylobacter
Viruses Cytomegalovirus; Rotavirus; Enteric adenovirus; Astrovirus; Torovirus; Human Immunodeficiency Virus (HIV)
Syndromic persistent diarrhea (common in developing countries)
Associated with malnutrition
Immune deficiency
Primary immune deficiencies
Secondary immune deficiencies (HIV)
Abnormal immune response
Celiac disease
Food allergic enteropathy (dietary protein-induced enteropathy)
Autoimmune disorders
Autoimmune enteropathy (including IPEX)
Graft vs Host disease
Inflammatory bowel disease (more common in developed countries)
Ulcerative Colitis
Crohn's disease
Protein losing gastroenteropathy
Lymphangiectasia (primary or secondary)
Other diseases affecting the gastrointestinal mucosa

Causes of chronic diarrhea in children (continued)
Congenital persistent diarrhea (rare)
Microvillus inclusion disease (Microvillus atrophy)
Intestinal epithelial dysplasia (Tufting enteropathy)
Congenital chloride diarrhea
Congenital sodium diarrhea
Congenital disaccharidase (sucrase-isomaltase, etc.) deficiencies
Congenital bile acid malabsorption
Neuroendocrine tumors
Gastrinoma (Zollinger-Ellison syndrome)
VIPoma (Verner-Morrison syndrome)
Mastocytosis
Factitious diarrhea
Laxative abuse
Manipulation of stool samples

Common causes of chronic diarrhea classified by typical stool characteristics, irrespective of age
Watery diarrhea
Osmotic diarrhea
• Functional diarrhea (sometimes)
• Magnesium, phosphate, sulfate ingestion
• Carbohydrate malabsorption (lactose intolerance, mucosal disease, congenital disaccharidase deficiencies)
Secretory diarrhea
• Laxative abuse (nonosmotic laxatives)
• Bacterial toxins
• Bile acid malabsorption (post cholecystecomy ileal)
• Inflammatory bowel disease
• Autoimmune enteropathy (isolated or IPEX syndrome)
• Vasculitis
• Drugs and poisons
• Disordered motility (Hirshsprung's disease, pseudoobstruction)
• Neuroendocrine tumors (gastrin, VIP, carcinoid, mastocytosis)
• Neoplasia
• Addison's disease
• Epidemic secretory diarrhea (brainerd diarrhea)
• Idiopathic secretory diarrhea
• Congenital secretory diarrheas
Inflammatory diarrhea
• Inflammatory bowel disease (ulcerative colitis, Crohn's disease, microscopic [lymphocytic and collagenous] colitis, diverticulitis)
• Infectious diseases (ulcerating viral infections, enteric bacterial pathogens, parasites)
• Ischemic colitis
• Radiation colitis
• Neoplasia (colon cancer, Lymphoma)
Fatty diarrhea
• Malabsorption syndromes (mucosal diseases [eg, celiac], short-bowel syndrome, post-resection diarrhea, mesenteric ischemia)
• Maldigestion (pancreatic insufficiency [eg, cystic fibrosis], bile acid deficiency)

Implications of some aspects of the medical history in children with chronic diarrhea	
Line of Questioning	**Clinical Implication**
Onset	
• Congenital	Chloridorrhea, Na+ malabsorption
• Abrupt	Infections
• Gradual	Everything else
• With introduction of wheat cereals	Celiac disease
Stool Characteristics	
• Daytime only	Functional diarrhea (chronic nonspecific diarrhea of childhood)
• Nocturnal	Organic etiology
• Blood	Dietary protein intolerance (eg, milk), inflammatory bowel disease
• White/light tan color	Absence of bile; Celiac disease
• Family history	Congenital absorptive defects, inflammatory bowel disease, celiac disease, multiple endocrine neoplasia
Dietary History	
• "Sugar-free" foods	Fructose, sorbitol, or mannitol ingestion
• Excessive juice	Osmotic diarrhea/chronic nonspecific diarrhea
• Raw milk	Brainerd diarrhea
• Exposure to potentially impure water source	Chronic bacterial infections (eg, aeromonas), giardiasis, cryptosporidiosis, Brainerd diarrhea
Travel history	Infectious diarrhea, chronic idiopathic secretory diarrhea
Failure to thrive/weight loss	Malabsorption, pancreatic exocrine insufficiency, anorexia nervosa
Previous therapeutic interventions (drugs, radiation, surgery, antibiotics)	Drug side effects, radiation enteritis, postsurgical status, pseudomembranous colitis (C. difficile), post-cholecystectomy diarrhea
Secondary gain from illness	Laxative abuse
Systemic illness symptoms	Hyperthyroidism, diabetes, inflammatory bowel disease, tuberculosis, mastocytosis
Intravenous drug abuse, sexual promiscuity (in adolescent/child's parent)	HIV disease
Immune problems	HIV disease, immunoglobulin deficiencies
Abdominal pain	Obstruction, irritable bowel syndrome
Excessive flatus	Carbohydrate malabsorption
Leakage of stool	Fecal incontinence (consider occult constipation)

Investigations in Chronic Diarrhoea
Baseline investigations
Stool microscopy ova, cysts, parasites, fat globules
Stool microbiology
Stool pH, reducing substances, electrolytes
Full blood count and differential
Urea and electrolytes, CRP and ESR
Liver function tests including albumin
Coeliac serology
Subsequent investigations
Stool elastase-I
Stool alfa-1-antitrypsin
Vitamins A, D, E, coagulation, B12, folate levels, Ca, Mg, phosphate, ferritin
Endoscopy, colonoscopy and biopsies for histology, disaccharidases, bacterial culture, Electron microscopy
Imaging studies x-ray, ultrasound, barium, MRI
Sweat test
Immunoglobulins, subclass, lymphocyte and neutrophil function test, complements
Zinc level
Cholesterol, triglycerides, low-density lipoproteins
Autoantibodies including anti-enterocyte antibodies
Isoelectric focussing of transferrin
Gastrin, secretin, calcitonin, VIP
Manometric studies
Urinary laxatives
Breath hydrogen tests
Plasma and urinary bile acids and salts
Response to dietary modifications
Adapted from M Ravikumara. Investigation of chronic diarrhea. Paediatrics and Child Health 2008; 18: 441-47

Specific diagnostic consideration on routine blood examination results	
Parameter	**Diagnostic considerations**
Anaemia	Iron, folate and B12 deficiency due to malabsorption
Neutropenia	Shwachman–Diamond syndrome
Lymphopenia	Intestinal lymphangiectasia, immunodeficiency
Eosinophilia	Food allergies, eosinophilic gastroenteritis
Elevated platelets	Acute infections, IBD (especially Crohn's disease)
Acanthocytes in blood film	Abetalipoproteinemia
Elevated ESR, CRP	IBD, infections
Low albumin	Protein losing enteropathies
Positive coeliac serology	Coeliac disease
Metabolic alkalosis	Congenital chloride diarrhoea
Adapted from M Ravikumara. Investigation of chronic diarrhea. Paediatrics and Child Health 2008; 18: 441-47	

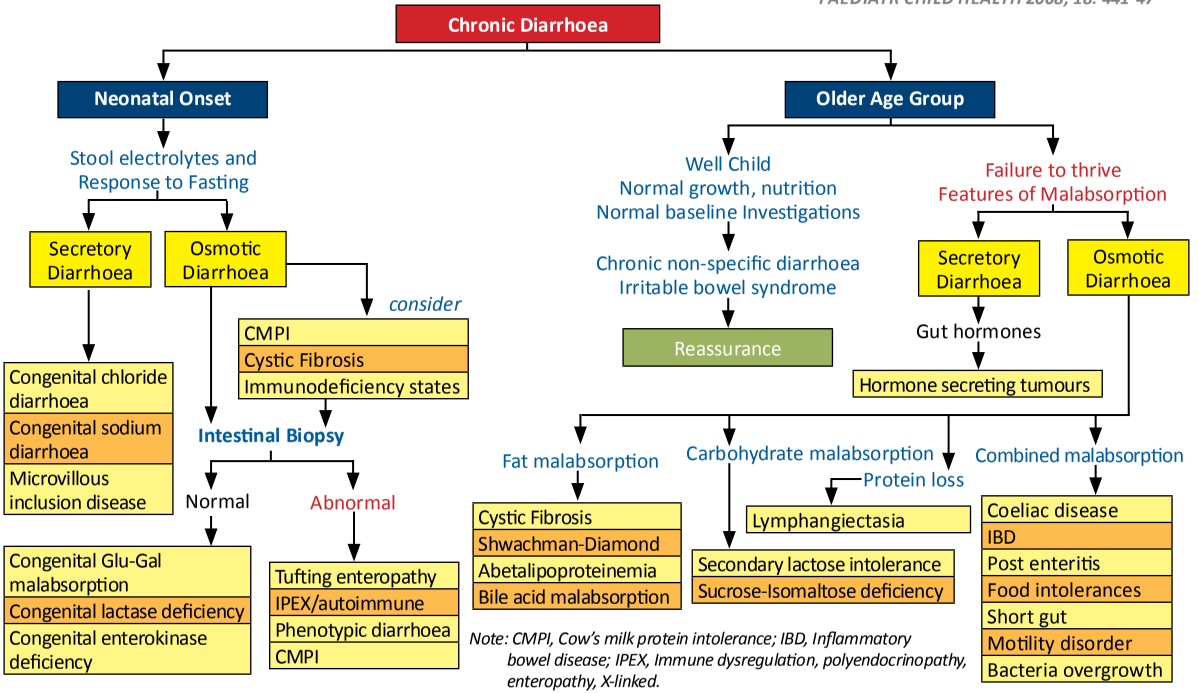
- **Collection of stool** with the help of a bag placed around the anus, using an inverted diaper or insertion of a rectal tube to collect stool sample are practical ways to confirm the watery nature of stool and also to obtain samples for investigations.
- Collecting the liquid portion of the stool increases the sensitivity of stool for reducing sugar testing.

Conclusion

- Despite being a complex condition which frequently requires tertiary gastroenterology unit input, a complete history, physical examination and logical stepwise investigations would usually yield significant clues on the diagnosis.
- The type of diarrhea ie. secretory vs osmotic type should be determined early in the course of investigations.
- It helps to narrow down the differential diagnosis and assists in planning the therapeutic strategies.
- The nutritional status should not be ignored. It should be ascertained on initial assessment and appropriate nutritional rehabilitation strategies (parenteral or enteral nutrition) should be employed whilst investigating the aetiology.

ALGORITHM FOR APPROACH TO CHRONIC DIARRHOEA

ADAPTED FROM RAVIKUMARA, PAEDIATR CHILD HEALTH 2008; 18: 441-47



Note: CMPI, Cow's milk protein intolerance; IBD, Inflammatory bowel disease; IPEX, Immune dysregulation, polyendocrinopathy, enteropathy, X-linked.

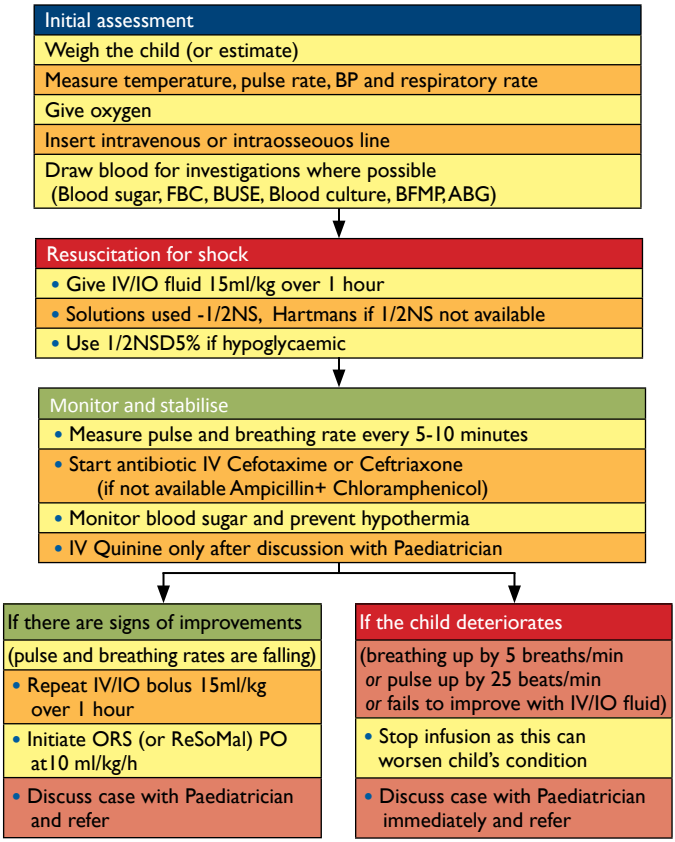
RESUSCITATION PROTOCOL FOR CHILDREN WITH SEVERE MALNUTRITION

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 only recommended for those who fulfill the following criteria:

- Orang asli or other indigenous ethnic group
- Severe malnutrition
- Ill
- Lethargic or has lost consciousness
- Shock



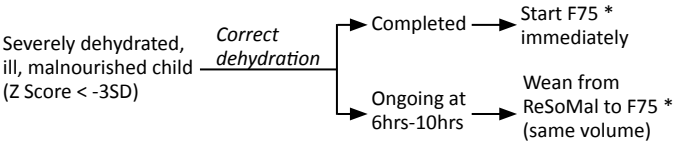
Reference

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.

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, gains 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.
- Gaining weight well.
- Afebrile.
- Has completed antibiotics.
- Aged ≥ 12 mths (caution < 12 mths: A Specialist opinion is required before discharge).

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.

WHO electrolyte/mineral solution recipe		
Item	Quantity (gm)	Molar content (in 20 ml)
Potassium chloride, KCl	224	20 mmol
Tripotassium citrate: C6H5K3O7.H2O	81	2 mmol
Magnesium chloride: MgCl2.6H2O	76	3 mmol
Zinc acetate: Zn(CH3COO)2.2H20	8.2	300 µmol
Copper sulphate: CuSO4.5H2O	1.4	45 µmol
Water	to make up 2500 ml	
Note: if available, add Selenium (Sodium Selenate 0.028 g), and Iodine (Potassium Iodide 0.012g) per 2500ml		

Recipes for starter and catch-up formulas			
	F-75	F-100	F-135
	(starter)	(catch-up)	(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 100ml			
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.

Chapter 74: Gastro-oesophageal Reflux

Introduction

- Gastro-oesophageal reflux (GER) is the passage of gastric contents into the oesophagus with/without regurgitation and vomiting. This is a normal physiological process occurring several times per day in healthy children.
- Gastro-oesophageal reflux disease (GERD) in paediatric patients is present when reflux of gastric contents is the cause of troublesome symptoms and/or complications.

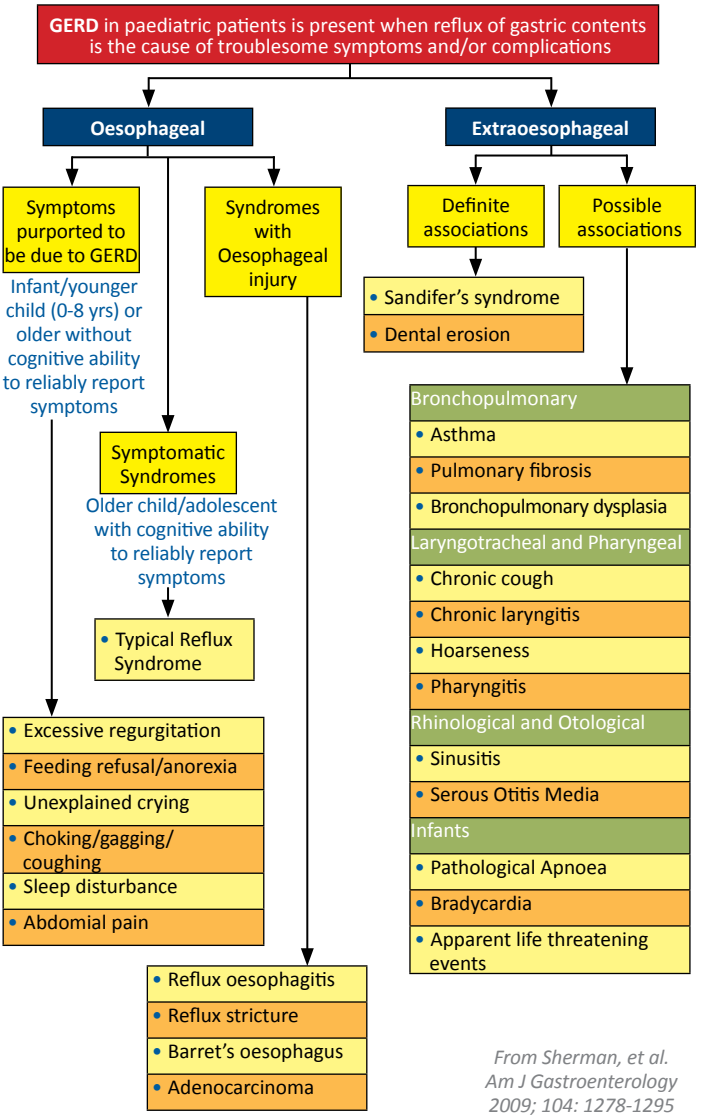
Symptoms and Signs:

- Symptoms and signs associated with reflux vary by age and are nonspecific.

Warning signals requiring investigation in infants with recurrent regurgitation or vomiting:

- Symptoms of gastrointestinal obstruction or disease
  - Bilious vomiting.
  - GI bleeding: hematemesis, hematochezia.
  - Consistently forceful vomiting.
  - Onset of vomiting after six months of life.
  - Constipation.
  - Diarrhea.
  - Abdominal tenderness, distension.
- Symptoms suggesting systemic or neurologic disease
  - Hepatosplenomegaly.
  - Bulging fontanelle.
  - Macro/microcephaly.
  - Seizures.
  - Genetic disorders (e.g., Trisomy 21).
  - Other chronic disorders (e.g., HIV).
- Nonspecific symptoms
  - Fever.
  - Lethargy.
  - Failure to thrive.

GLOBAL DEFINITION OF GERD IN THE PAEDIATRIC POPULATION



From Sherman, et al. Am J Gastroenterology 2009; 104: 1278-1295

Investigations

GERD is often diagnosed clinically and does not require investigations

- Indicated:
  - If its information is helpful to define difficult or unusual cases.
  - If of value in making treatment decisions.
  - When secondary causes of GERD need to be excluded especially in severely affected patients.
- Oesophageal pH Monitoring
  - The severity of pathologic acid reflux does not correlate consistently with symptom severity or demonstrable complications
  - For evaluation of the efficacy of antisecretory therapy
  - To correlate symptoms (e.g., cough, chest pain) with acid reflux episodes, and to select those infants and children with wheezing or respiratory symptoms in whom GER is an aggravating factor.
  - Sensitivity, specificity, and clinical utility of pH monitoring for diagnosis and management of extraesophageal complications of GER is uncertain.
- Barium Contrast Radiography
  - Not useful for the diagnosis of GERD as it has poor sensitivity and specificity but is useful to confirm or rule out anatomic abnormalities of the upper gastrointestinal (GI) tract.
- Nuclear Scintigraphy
  - May have a role in the diagnosis of pulmonary aspiration in patients with chronic and refractory respiratory symptoms. A negative test does not rule out possible pulmonary aspiration of refluxed material.
  - Not recommended for the routine evaluation of GERD in children.
- Oesophageal manometry
  - Not sufficiently sensitive or specific to diagnose GERD.
  - To diagnose motility disorder e.g. achalasia or other motor disorders of the esophagus that may mimic GERD.
- Endoscopy and Biopsy
  - Endoscopically visible breaks in the distal esophageal mucosa are the most reliable evidence of reflux oesophagitis.
  - To identify or rule out other causes of oesophagitis including eosinophilic oesophagitis which do not respond to conventional anti reflux therapy.
  - To diagnose and monitor Barrett's oesophagus and its complications.
- Empiric Trial of Acid Suppression as a Diagnostic Test
  - Expert opinion suggests that in an older child or adolescent with typical symptoms of GERD, an empiric trial of PPI is justified for up to 4 weeks.
  - However, improvement of heartburn, following treatment, does not confirm a diagnosis of GERD because symptoms may improve spontaneously or respond by a placebo effect
  - No evidence to support an empiric trial of acid suppression as a diagnostic test in infants/young children where symptoms of GERD are less specific.
  - Exposing them to the potential adverse events of PPI is not the best practice. Look for causes other than GERD before making such a move.

Treatment

- Physiologic GER does not need medical treatment.
- Symptoms are often non specific esp. during infancy; many are exposed to anti-reflux treatment without any sufficient evidence.
- Should always be balance between intended improvement of symptoms with risk of side-effects.

Suggested Schematic Therapeutic Approach

- Parental reassurance & observe. Avoid overeating
- Lifestyle changes.
  - Dietary treatment
    - Use of a thickened formula (or commercial anti regurgitation formulae) may decrease visible regurgitation but does not reduce in the frequency of oesophageal reflux episodes.
    - There may be association between cow's milk protein allergy and GERD.
    - Therefore infants with GERD that are refractory to conventional anti reflux therapy may benefit from a 2- to 4-week trial of elimination of cow's milk in diet with an extensively hydrolyzed protein formula that has been evaluated in controlled trials. Locally available formulas are Alimentum, Pepti and Pregestimil. Usually there will be strong family history of atopy in these patients.
    - No evidence to support the routine elimination of any specific food in older children with GERD.
  - Position during sleep
    - Prone positioning decreases the amount of acid oesophageal exposure measured by pH probe compared with that measured in the supine position. However, prone and lateral positions are associated with an increased incidence of sudden infant death syndrome (SIDS). Therefore, in most infants from birth to 12months of age, supine positioning during sleep is recommended.
    - Prone or left-side sleeping position and/or elevation of the head of the bed for adolescents with GERD may be of benefit in select cases.
- Buffering agents (some efficacy in moderate GERD, relatively safe). Antacids only in older children.
  - Buffering agents e.g. alginate and sucralfate are useful on demand for occasional heartburn.
  - Chronic use of buffering agents is not recommended for GERD because some have absorbable components that may have adverse effects with long-term use.
- Prokinetics .
  - Treat pathophysiologic mechanism of GERD.
  - There is insufficient evidence of clinical efficacy to justify the routine use of metoclopramide, erythromycin, or domperidone for GERD.

- Proton Pump Inhibitors (PPI) (drug of choice in severe GERD). Histamine-2 receptor antagonists less effective than PPI.
  - Histamine-2 Receptor Antagonists (H2RAs).
    - Exhibit tachyphylaxis or tolerance (but PPIs do not)
    - Useful for on-demand treatment
  - Proton Pump Inhibitors
    - Administration of long-term acid suppression without a diagnosis is inadvisable.
    - When acid suppression is required, the smallest effective dose should be used.
    - Most patients require only once-daily PPI; routine use of twice-daily dose is not indicated.
    - No PPI has been officially approved for use in infants <1 year of age.
    - The potential adverse effects of acid suppression, including increased risk of community-acquired pneumonias and GI infections, need to be balanced against the benefits of therapy.
  - Antireflux surgery (either open or laparoscopic surgery).
    - May be of benefit in selected children with chronic-relapsing GERD.
    - Indications include: failure of optimized medical therapy, dependence on long-term medical therapy, significant non adherence with medical therapy, or pulmonary aspiration of refluxate.
    - Children with underlying disorders predisposing to the most severe GERD e.g. neurological impairment are at the highest risk for operative morbidity and postoperative failure.
    - It is essential therefore to rule out all non-GERD causes of the child's symptoms, confirm the diagnosis of chronic relapsing GERD, discuss with the parents the pros and cons of surgery and to assure that the caregivers understand the potential complications, symptom recurrence and sometimes the need to be back on medical therapy.

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).

Grading of Hepatic Encephalopathy - Coma Level
Grade 1
Irritable, lethargic
Grade 2
Mood swings, aggression, photophobia,
Not recognising parents, presence of flap
Grade 3
Sleepy but rousable, incoherent, sluggish
Pupils, hypertonia ± clonus, extensor spasm
Grade 4
Comatose; decerebrate, decorticate
or no response to pain

Causes of Hepatic Failure
Infection
Hepatitis A, B, non A- non B, CMV
Leptospirosis, Dengue
Herpes simplex virus (particularly in small infants)
Drugs
Carbamazepine, valproate
Paracetamol, halothane
Ingested toxins
Mushrooms, Amanita phalloides
Metabolic
Fructosaemia, galactosaemia, tyrosaemia,
Wilson's disease
Neonatal haemochromatosis
Ischaemic shock
Gram negative septicaemia,
Budd Chiari syndrome
Autoimmune
Autoimmune Hepatitis
Tumour
Histiocytosis, lymphoproliferative disorder

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 capillary blood sugar every 2 - 4 hourly.
- Strict monitoring of urine output and fluid balance. Catheterise if necessary.
- Check urinary electrolytes, serum urea, creatinine, electrolytes, osmolarity.
- Frequent neurological observations (1-4 hourly).
- Maintain oxygenation with facial oxygen.
- Give Vitamin K to correct prolonged PT. If frank bleeding (GIT/oral) occurs, consider prudent use of FFP or IV Cryoprecipitate at 10 ml/kg.
- Prophylactic Ranitidine + 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 > 0.5 ml/kg/hour.
- Consider N-Acetylcysteine. (discuss with hepatologist). The dose is a continuous infusion at 10mg/kg/hr for at least 48-72 hours with regular serial monitoring of liver biochemical and synthetic function parameters. Small risk of anaphylaxis is present.
- Antibiotics : Combination that provides a good cover against gram negative organisms and anaerobes eg. cefotaxime and metronidazole if no specific infective agent suspected (eg. leptospira, mycoplasma)
- Antiviral : Acyclovir is recommended in neonates and small infants with Acute Liver Failure due to possibility of Herpes simplex virus infection
- Renal dysfunction
  - Possible causes : Hepato-renal syndrome, Dehydration and Low CVP/ low cardiac output. Consider haemofiltration (to discuss with Paediatric nephrologist) if supportive measures like fluid challenge, renal dose dopamine and frusemide infusion fail.

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.

Indication for Liver Transplantation
Paracetamol-induced disease
• Arterial pH < 7.3 (independent of the grade of encephalopathy)
OR
• Grade III or IV encephalopathy and
• Prothrombin time > 100 s and
• Serum creatinine > 3.4 mg/dL (301 µmol/l)
All other causes of fulminant hepatic failure
• Prothrombin time > 100 s (independent of grade of encephalopathy)
OR
• Any 3 of the following variables (independent of grade of encephalopathy)
• Age < 10 years or > 40 years
• Aetiology: non-A, non-B hepatitis, halothane hepatitis, idiosyncratic drug reactions
• Duration of jaundice before onset of encephalopathy > 7 days
• Prothrombin time > 50 s
• Serum bilirubin > 18 mg/dl (308 µmol/l)
Adapted from the King's College Hospital Criteria

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 Destrostix readings)
Potassium	1 - 3.5 mmol/kg/day	NIL WHILE ANURIC
Sodium	1.5 - 3.5 mmol/kg/day	No added sodium to existing maintenance fluid (Adjust to keep serum Na normal)
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		

Definitions

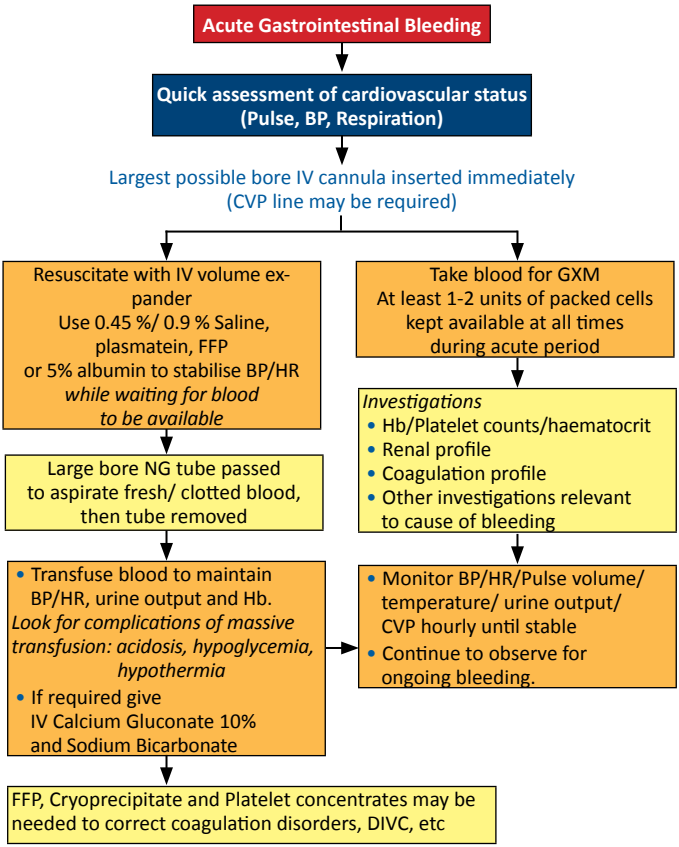
- ***Haemetemesis*** - vomiting out blood whether fresh or stale
- ***Malaena*** - passing out tarry black stools per rectum

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.

ACUTE RESUSCITATION IN A CHILD WITH GASTROINTESTINAL BLEEDING



Decision making after acute resuscitation

Reassessment of patients

When patient's condition is stable and resuscitative measures have been instituted,
Assess patient for cause of bleeding and the need for surgery.

History is reviewed.
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, antibiotics treatment (pseudomembranous colitis).

Physical examination should be directed towards looking for signs of chronic liver disease (spider angiomata, palmar erythema, portal hypertension or splenomegaly) or telengiectasia / angiomata in mouth, trunk, etc.)

Diagnostic measures to localise source of bleeding

- ***Oesophagogastro-duodenoscopy (OGDS)*** or colonoscopy can be performed when patient's condition is stable.
- Double contrast barium study less useful than endoscopy but may be indicated in patients when endoscopy cannot precisely locate the source of bleeding (e.g. in intussusception).
- Visceral angiography can precisely locate the source of bleeding. But is only reserved for patients with a difficult bleeding problem.

Definitive measures to management of gastrointestinal bleeding
Medical Cause
Bleeding peptic ulcer • Start H2 receptor antagonist (e.g. cimetidine or ranitidine). Proton pump inhibitor (omeprazole) should be considered when available as it has higher acid suppressant activity. Pantoprazole infusion has been increasingly used "off label" (discuss with Paediatric Gastroenterologist). • If biopsy shows presence of *Helicobacter pylori* infection, treat accordingly. • Stop all incriminating drugs e.g. aspirin, steroids and anticoagulant drugs if possible.
Bleeding oesophageal varices or ulcer • 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. • Aim to maintain Hb at 10 g/dL. • Refer Paediatric Surgeon and Paediatric Gastroenterologist to consider use of octreotide.
Pseudomembranous colitis • Stop all antibiotics • Start oral metronidazole or oral vancomycin immediately.
Surgical Cause
When surgical cause is suspected, early referral to the surgeon is important so that a team approach to the problem can be adopted. • Intussusception requires immediate surgical referral and intervention. • Meckel's diverticulum • Malrotation

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Section 9 Gastroenterology

Chapter 72 Chronic Diarrhoea

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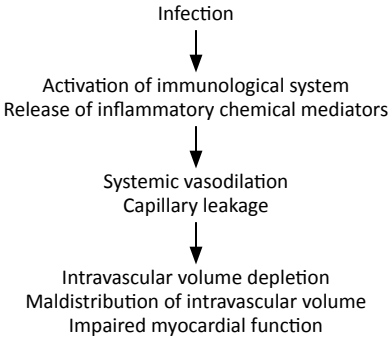
Definitions of Sepsis and Shock	
SIRS (Systemic Inflammatory Response Syndrome)	• Non-specific systemic inflammatory response to infection, trauma, burns, surgery etc. • Characterized by abnormalities in ≥ 2 of the following (one of which must be abnormal temperature or leukocyte count): • Body temperature. • Heart rate. • Respiratory function. • Peripheral leucocyte count.
Sepsis	• SIRS in the presence of or as a result of suspected or proven infection.
Severe sepsis	• Sepsis plus one of the following: • Cardiovascular organ dysfunction. • Acute respiratory distress syndrome. • Two or more other organ dysfunction.
Septic shock	• Severe sepsis with cardiovascular organ dysfunction i.e. Hypotension (systolic Blood Pressure < 5th centile for age).
Early septic shock (WARM shock)	• Compensated warm phase of shock. • Prompt response to fluids, pharmacologic treatment.
Refractory septic shock (COLD shock)	• Late decompensated phase. • Shock lasting >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 healthcare associated sepsis.

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°C) or hypothermia, often in neonate (< 36°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:

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: urine output < 0.5ml/kg per hour

- When SEPTIC SHOCK sets in, look for features of ***Warm*** or ***Cold*** shock:

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:

Localising Signs
Central nervous system
meningism , encephalopathy
Respiratory
localised crepitations, evidence of consolidation
Cardiovascular
changing murmurs
Gastrointestinal
focal or rebound tenderness, guarding
Bone and soft tissue
focal erythema, tenderness and oedema
Head and neck
cervical lymphadenopathy, sinus tenderness,
inflamed tympanic membrane, stridor,
exudative pharyngotonsillitis
Skin
pustular lesions

Complications

Multiorgan Failure:

- Acute respiratory distress syndrome.
- Acute renal failure.
- Disseminated intravascular coagulopathy.
- Central nervous system dysfunction.
- Hepatic failure.

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	
- 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, SpO_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_2 to keep SaO_2 > 90%, PaO_2 > 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/L.
  - Platelet concentrate transfusion if platelet count < 20 000/mm^3.
  - 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_2).
  - Aim to maintain normal electrolytes and blood sugar.
- Monitoring
  - Frequent serial re-evaluation is essential to guide therapy and gauge response, as below:

Monitoring in Children with Sepsis
Clinical
• *Vital signs*
• Heart rate via cardiac monitor
• Capillary return
• Skin temperature
• Pulse volume
• Blood pressure
• Non invasive
• Invasive - ideal if available
• SpO_2 via pulse oximeter
• Central venous pressure (CVP)
Urine output via continuous bladder drainage
Head chart (GCS)
Laboratory
See *previous Table on Investigations*

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 /underage).
  - Sexually abused children and children with sexually transmitted disease.
  - Children receiving regular blood transfusions or blood products e.g. Thalassemics.

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 leak proof 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
  - Give IPV (killed polio vaccine) as recommended in current schedule.
  - 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.
- Blood and blood products should be used judiciously even though the risk of transmission of HIV infection from blood transfusion is very small.

Several interventions have proven effective in reducing vertical transmission:

- Total substitution of breastfeeding with infant formula.
- Elective Caesarean section.
- Antiretroviral (ARV) prophylaxis.

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

Management of Babies Born to HIV Infected Mothers

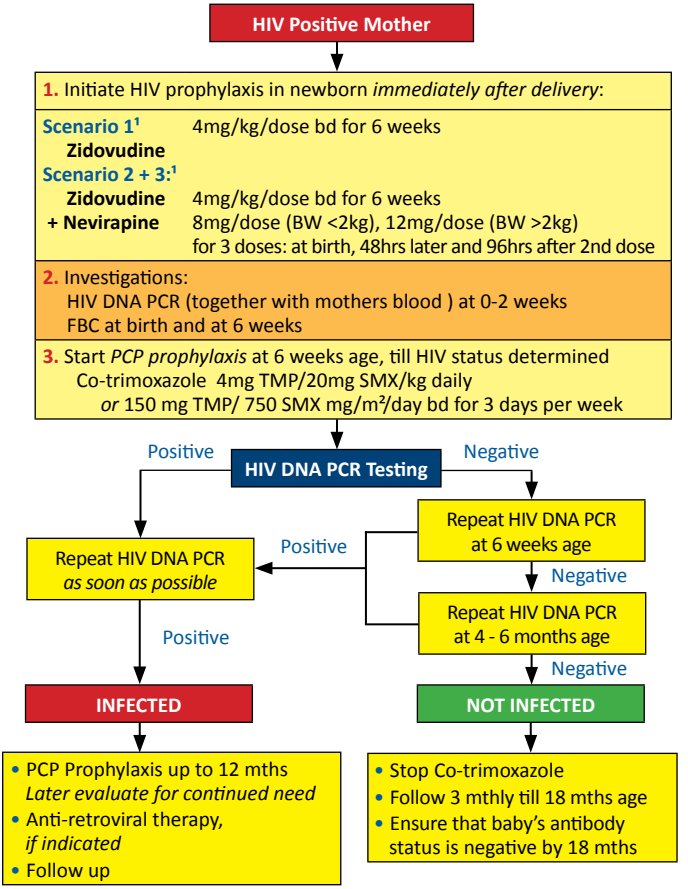
Children born to HIV positive mothers are usually asymptomatic at birth. However, all will have acquired maternal antibodies. In uninfected children, antibody testing becomes negative by 10 - 18 months age.

During pregnancy

- Counsel mother regarding:
  - Transmission rate (without intervention) –25 to 30%.
  - ARV prophylaxis + elective LSCS reduces transmission to ~3%.
- 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 is helpful).
- Most babies are asymptomatic and only require routine perinatal care
- Start on prophylaxis ARV as soon as possible.
- 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.



[1] Footnote:

Scenario 1: HIV infected pregnant mother who is on HAART

Scenario 2: HIV infected mother at delivery who has not received adequate ARV

Scenario 3: Infant born to HIV infected mother who has not received any ARV

- ARV should be served as soon as possible (preferably within 6-12 hrs of life) and certainly no later than 48 hours.
- Dose of Syr ZDV for premature baby >30 wks: 2mg/kg 12hrly for 2 wks, then 2mg/kg 8hrly). If oral feeding is contraindicated, use IV ZDV 1.5mg/kg/dose.

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
- Hepatosplenomegaly
- Failure to thrive
- Developmental delay, regression
- Recurrent infections (respiratory, skin, gastrointestinal)

Diagnosis of HIV infection

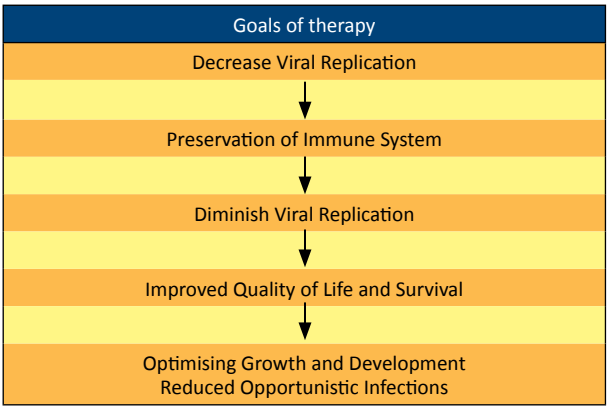
- In children > 18 months age: 2 consecutive positive HIV antibody tests.
- In children ≤ 18 months age: 2 positive HIV DNA PCR tests.

Monitoring

- Monitor disease progression through clinical, immunological (CD4+ count or %) and viral load status.
- 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?

- Starting ART is very rarely an emergency. 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.
- Please consult a specialist/consultant before starting treatment.

WHO classification of HIV-associated immunodeficiency using CD4 count

Classification of HIV-associated Immunodeficiency	Age related CD4 values			
	< 11 mths (CD4 %)	12-35 mths (CD4 %)	36-59 mths (CD4 %)	≥5 years (cells/mm³ 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 i.e CDC's 1994 Revised Paediatric Classification and the more recently updated WHO Clinical Classification system. Both classification systems are quite similar with only minor differences.

WHO Clinical Staging Of HIV for Infants and Children With Established HIV infection (Adapted from WHO 2007)
Clinical stage 1 (Asymptomatic)
Asymptomatic
Persistent generalized lymphadenopathy
Clinical stage 2 (Mild) *
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
Clinical stage 3 (Advanced) *
Unexplained moderate malnutrition not adequately responding to standard therapy
Unexplained persistent diarrhoea (14 days or more)
Unexplained persistent fever (above 37.5 ºC, intermittent or constant, for longer than one month)
Persistent oral candidiasis (after first 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 109/L) or chronic thrombocytopenia (<50 x 109/ L)

WHO Clinical Staging Of HIV for Infants and Children With Established HIV infection (Adapted from WHO 2007) *(continued)*
Clinical stage 4 (Severe) *
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 more than one month'sduration, or visceral at any site)
Extrapulmonary 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, with onset at age over 1 month
Extrapulmonary cryptococcosis (including meningitis)
Disseminated endemic mycosis (extrapulmonary 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
(*) Unexplained refers to where the condition is not explained by other causes.

Which drugs to use?

Always use combination of at least 3 drugs (see Table next page)

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; ABC + 3TC;
  - Alternative 2 NRTI combinations : d4T + 3TC ; ddI + 3TC
  - For infants exposed to maternal or infant NVP or other NNRTIs used for maternal treatment or PMTCT, start ART with PI (Lopinavir/r) + 2 NRTIs.

Not Recommended

- Mono or dual therapy (except mother-to-child transmission prophylaxis during neonatal period):
  - d4T + ZDV - pharmacologic and antiviral antagonism.
  - d4T + ddI - higher risk of lipodystrophy, peripheral neuropathy.
  - 3TC + FTC - similar resistance patterns and no additive benefit.

When to change?

- Treatment failure based on clinical, virologic and immunological parameters e.g. deterioration of condition, unsuppressed/rebound viral load 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 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 an infectious diseases specialist before switching.

Categories of antiretroviral drugs available in Malaysia					
Nucleoside / Nucleotide reverse transcriptase inhibitors (NRTI)	Non nucleoside reverse transcriptase inhibitor (NNRTI)	Protease inhibitors (PI)	Integrase inhibitors	CCR5 antagonists	Fusion inhibitors
Zidovudine (ZDV)	Nevirapine (NVP)	Ritonavir	Raltegravir	Maraviroc	Enfurvitide
Stavudine(d4T)	Efavirenz (EFZ)	Indinavir (IDV)			
Lamivudine (3TC)	Etravirine	Lopinavir/Ritonavir (Kaletra)			
Didanosine (ddI)		Saquinavir			
Abacavir (ABC)		Atazanavir (ATV)			
Tenofovir (TDF)		Nelfinavir			
Emtricitabine (FTC)		Darunavir			
Fixed-dose combination tablets FDC) ZDV + 3TC combined tablet (Combivir / Duovir) d4T + 3TC +NVP combined tablet (SLN 30) TDF + FTC combined tablet (Tenvir-EM) Footnote: Not all ARVs are suitable for use in children					

When to start ARV ?			
Age	Initiate Treatment*	Consider	Defer
<12 months	All infants regardless of clinical symptoms,immune status and viral load		
1-<5 years	AIDS or significant HIV-related symptoms (WHO Stage 3** or 4**) OR Asymptomatic or mild symptoms (WHO Stage 1 & 2) and CD4 < 25%	Asymptomatic or mild symptoms and • CD4 > 25 % or • VL ≥100,000 copies /ml	Asymptomatic and • CD4 ≥25 % and • VL <100,000 copies /ml
≥ 5 years	AIDS or significant HIV-related symptoms (WHO Stage 3** or 4**) OR Asymptomatic or mild symptoms (WHO Stage 1 & 2) and CD4 ≤ 350 cells /mm^3	Asymptomatic or mild symptoms and • CD4 > 350cells/mm^3 or • VL ≥100,000 copies /ml	Asymptomatic and • CD4 >350 cells/mm^3 and • VL <100,000 copies /ml

* Before making the decision to initiate therapy, the provider should fully assess, discuss, and address issues associated with adherence with the child and the caregiver

** Stabilize any opportunistic infection (OI) before initiating ART.

Antiretroviral drugs dosages and common side effects			
Drug	Dosage	Side effects	Comments
Zidovudine (ZDV)	180-240mg/m²/dose, bd Neonate: 4mg/kg bd (max. dose 300mg bd)	Anaemia, neutropenia, headache	Large volume of syrup not well tolerated in older children
Didanosine (ddI)	90-120mg/m²/dose, bd (max. dose 200mg bd)	Diarrhoea, abdo pain, peripheral neuropathy	Ideally taken on empty stomach (1hr before or 2h after food)
Lamivudine (3TC)	4mg/kg/dose, bd (max. dose 150mg bd)	Diarrhoea, abdo pain; pancreatitis (rare)	Well tolerated Use oral solution within 1 month of opening
Stavudine (d4T)	1mg/kg/dose, bd (max. dose 40mg bd)	Headache, peripheral neuropathy, pancreatitis (rare)	Capsule may be opened and sprinkle on food or drinks
Abacavir (ABC)	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)
Efavirenz (EFZ)	350mg/m2 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
Nevirapine (NVP)	150-200mg/m²/day od for 14 days, then increase to 300-400mg/m²/day, bd (max. dose 200mg bd)	Severe skin rash, headache, diarrhea, nausea	Take with food to increase absorption and reduce GI side effects Solution contains 43% alcohol and is very bitter!

Antiretroviral drugs dosages and common side effects *(continued)*			
Drug	Dosage	Side effects	Comments
Ritonavir (RTV)	350-450mg/m²/dose, bd (max. dose 600mg bd)	Vomiting, nausea, headache, diarrhoea; hepatitis (rare)	Take with food to increase absorption and reduce GI side effects Solution contains 43% alcohol and is very bitter!
Kaletra (Lopinavir/ ritonavir)	230/57.5mg/m²/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
Indinavir (IDV)	500mg/m²/dose, tds (max. dose 800mg tds)	Headache, nausea, abdominal pain, hyperbilirubinemia, renal stone	Use in older children that can swallow tablet; Take on an empty stomach Advise to drink more fluid

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_4 (amylase if on ddI) 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 have HIV and are not on follow up.
- Disclosure of diagnosis to the child (would-be teenager, 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.

Uncomplicated Malaria

Symptomatic infection with malaria parasitaemia without signs of severity or evidence (clinical or laboratory) of vital organ dysfunction.

Treatment

UNCOMPLICATED PLASMODIUM FALCIPARUM

First Line Treatment	
Preferred Treatment	**Alternative Treatment**
Artesunate/Mefloquine (Artequine)#	Artemether/Lumefantrine (Riamet)+
Dosage according to body wt	*Dosage according to body wt*
10-20kg:* Artesunate 50mg OD x 3d Mefloquine 125mg OD x 3d (Artequine pellets)	5 -14 kg: D1: 1 tab stat then 1 tab again after 8 hours D2-3: 1 tab BD
20-40kg: Artesunate: 100mg OD x 3d Mefloquine 250mg OD x 3d (Artequine 300/750)	15 – 24kg: D1: 2 tabs stat then 2 tabs again after 8 hours D2-3: 2 tablets BD
>40kg: Artesunate 200mg OD x 3d Mefloquine 500mg OD x 3d (Artequine 600/1500)	25 – 35kg: D1: 3 tabs stat then 3 tabs again after 8 hours D2-3: 3 tablets BD
	>35kg: D1: 4 tabs stat then again 4 tabs after 8 hours D2-3: 4 tabs BD

Add primaquine 0.75mg/kg single dose OD if gametocyte is present at any time during treatment. ***Check G6PD before giving primaquine.***

#. Avoid in children with epilepsy as well.

*Use Riamet for children below 10 kg as there is no artequine formulations for this group of children.

+ Riamet should be administered with high fat diet preferably to be taken with milk to enhance absorption.

Both Artequine and Riamet are Artemisinin-based Combination Treatment (ACT)

Second-line treatment for treatment failure
(in uncomplicated *Plasmodium Falciparum*):

- Recommended second-line treatment:
  - An alternative ACT is used (if Riamet was used in the first regimen, use Artequine for treatment failure and vice-versa).
  - Artesunate 4mg/kg OD plus Clindamycin 10mg/kg/dose bd for a total of 7 days.
  - Quinine 10mg salt/kg 8 hourly plus Clindamycin 10mg/kg/dose bd for a total of 7 days.
- Add primaquine 0.75mg base/kg single dose OD if gametocyte is present at any time during treatment. Check G6PD before giving Primaquine.

Treatment for Plasmodium vivax, knowlesi or malariae.	
Treatment for *P. vivax*	Treatment for *P. knowlesi* or *malariae*
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	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* 0.5 mg base/kg daily for 14 days	
Note: Chloroquine should be prescribed as mg base in the drug chart. *P. malariae* and *P. knowlesi* do not form hypnozoites, hence do not require radical cure with primaquine.	

Treatment of chloroquine-resistant *P. vivax, knowlesi or malariae.*

- ACT (Riamet or Artequine) should be used for relapse or chloroquine resistant *P. vivax*. For radical cure in *P. vivax*, ACT must be combined with supervised 14-day primaquine therapy.
- Quinine 10mg salt/kg three times a day for 7 days is also effective for chloroquine resistant *P. vivax* and this must be combined with primaquine for antihypnozoite activity.
- Mefloquine 15mg/kg single dose combined with primaquine have been found to be effective.

Primaquine may cause life threatening haemolysis in individuals with G6PD deficiency. G6PD testing is required before administration of Primaquine. For mild to moderate G6PD deficiency, an intermittent Primaquine regimen of 0.75mg base/kg weekly for 8 weeks can be given under medical supervision. ***In severe G6PD deficiency Primaquine is contraindicated.***

Severe and complicated *P. vivax, knowlesi or malariae* should be managed as for severe falciparum malaria *(see next page).*

Severe *P. falciparum* malaria

- All Plasmodium species can potentially cause severe malaria, the commonest being *P falciparum*.
- Young children especially those aged below 5 years old are more prone to develop severe or complicated malaria.

Recognising Severe P. falciparum malaria
Clinical features
Impaired consciousness or unarousable coma
Prostration
Failure to feed
Multiple convulsions (more than two episodes in 24 h)
Deep breathing, respiratory distress (acidotic breathing)
Circulatory collapse or shock
Clinical jaundice plus evidence of other vital organ dysfunction
Haemoglobinuria
Abnormal spontaneous bleeding
Pulmonary oedema (radiological)
Laboratory findings
Hypoglycaemia (blood glucose < 2.2 mmol/l or < 40 mg/dl)
Metabolic acidosis (plasma bicarbonate < 15 mmol/l)
Severe anaemia (Hb < 5 g/dL, packed cell volume < 15%)
Haemoglobinuria
Hyperparasitaemia (> 2%/100 000/µl in low intensity transmission areas or > 5% or 250 000/µl in areas of high stable malaria transmission intensity)
Hyperlactataemia (lactate > 5 mmol/l)
Renal impairment (serum creatinine > 265 µmol/l).

First-line Treatment

D1: IV Artesunate 2.4 mg/kg on admission, then rpt again at 12H & 24H
D2-7: IV Artesunate 2.4 mg/kg OD or switch to oral ACT

Parenteral Artesunate should be given for a minimum of 24h or until patient is able to tolerate orally and thereafter to complete treatment with a complete course of oral ACT (Artequine or Riamet). Avoid using Artequine (Artesunate + Mefloquine) if patient presented initially with impaired consciousness as increased incidence of neuropsychiatric complications associated with mefloquine following cerebral malaria have been reported.

IM Artesunate (same dose as IV) can be used in patients with difficult intravenous access.

Second-line Treatment

- D1:IV Quinine loading 7mg salt/kg over 1 hour followed by
  Infusion Quinine 10mg salt/kg over 4 hours then 10mg salt/kg q8hourly
  OR
- Loading 20mg salt/kg over 4 hours then IV 10mg salt/kg q8 hourly
  (Dilute quinine in 250ml of D5% over 4 hours)

- D2-7: IV Quinine 10mg salt/kg q8h
  AND

- Doxycycline (>8yrs) (3.5 mg/kg OD) OR Clindamycin (<8yrs)
  (10 mg/kg/dose bd) given for 7 days

Quinine infusion rate should not exceed 5 mg salt/kg body weight per hour. Change to Oral Quinine if able to tolerate orally.
(Maximum Quinine per dose = 600mg.) Reduce IV Quinine dose by one third of total dose if unable to change to Oral Quinine after 48hours or in renal failure or liver impairment.

Congenital malaria

Congenital malaria is rare. It is acquired from the mother prenatally or perinatally, usually occurring in the newborn of a non-immune mother with *P. vivax* or *P. malariae* infection, although it can be observed with any of the human malarial species.. The first sign or symptom most commonly occur between 10 and 30 days of age (range: 14hr to several months of age). Signs and symptoms include fever, restlessness, drowsiness, pallor, jaundice, poor feeding, vomiting, diarrhea, cyanosis and hepatosplenomegaly. It can mimic a sepsis like illness. Parasitemia in neonates within 7 days of birth implies transplacental transmission. Vertical transmission may be as high as 40% and is associated with anemia in the baby. Baby should been screened for malaria and be treated if parasitemia is present.

Treatment:

- Chloroquine, total dose of 25mg base/kg orally 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
- Primaquine is not required for treatment as the tissue/ exo-erythrocytic phase is absent in congenital malaria.

Mixed Malaria infections

Mixed malaria infections are not uncommon. ACTs are effective against all malaria species and are the treatment of choice. Treatment with Primaquine should be given to patients with confirmed *P. vivax* infection.

Malaria Chemoprophylaxis		
Prophylaxis	Duration of Prophylaxis	Dosage
Atovaquone/ Proguanil (Malarone)	Start 2 days before, continue daily during exposure and for 7 days thereafter	Pediatric tablet of 62.5 mg Atovaquone and 25 mg Proguanil: 5-8 kg: 1/2 tablet daily >8-10 kg: 3/4 tablet daily >10-20 kg: 1 tablet daily >20-30 kg: 2 tablets daily >30-40 kg: 3 tablets daily >40 kg: 1 adult tablet daily
Mefloquine (Tablet with 250mg base, 274mg salt)	Start 2-3 weeks before, continue weekly during exposure and for 4 weeks thereafter	<15 kg: 5mg of salt/kg; 15-19 kg: ¼ tab/wk; 20-30 kg: ½ tab/wk; 31-45 kg: ¾ tab/wk; >45 kg: 1 tab/wk
Doxycycline (tab 100mg)	Start 2 days before, continue daily during exposure and for 4 weeks thereafter	1.5mg base/kg once daily (max. 100 mg) <25kg or <8 yr: Do Not Use 25-35kg or 8-10 yr: 50mg 36-50kg or 11-13 yr: 75mg >50kg or >14 yr: 100mg

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 conjuctivitis, 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 - usually develops > 6 mths 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.

The diagnostic work-up for TB disease is tailored to the organ system most likely affected. The tests to consider include but are not limited to the following:
Pulmonary TB
• Chest radiograph
• Early morning gastric aspirates[1]
• Sputum (if >12 years, able to expectorate sputum)[1]
• Pleural fluid[1] or biopsy[1]
Central Nervous System (CNS) TB
• CSF for FEME , AFB smear and TB culture[1]
• CT head with contrast
TB adenitis
• Excisional biopsy or fine needle aspirate[1]
Abdominal TB
• CT abdomen with contrast
• Biopsy of mass / mesenteric lymph node[1]
TB osteomyelitis
• CT/MRI of affected limb
• Biopsy of affected site[1]
Miliary / Disseminated TB
• As for pulmonary TB
• Early morning urine[1]
• CSF[1]
[1]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, as well as HIV prevalence.
- Therapeutic choices are best made according to drug susceptibility of the organism cultured from the patient.
- Almost all recommended treatment regimens have 2 phases, an initial intensive phase and a second continuation phase.
- 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.

Tuberculosis Chemotherapy in Children					
Drug		Daily Dose		Intermittent Dose (Thrice Weekly)	
		mg/kg/day	Max dose (mg)	mg/kg/day	Max dose (mg)
Isoniazid	H	10-15	300	10	900
Rifampicin	R	10-20	600	10	600
Pyrazinamide	Z	30-40	2000	-	-
Ethambutol	E	15-25	1000	30-50	2500

Short course therapy

- This consists of a 6 month regimen, an initial 2 month intensive and subsequent 4 month continuation phase. Short course therapy is suitable for pulmonary tuberculosis and non-severe extrapulmonary tuberculosis. Children with tuberculous meningitis , miliary and osteoarticular tuberculosis should be treated for 12 months. 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 (Ethambutol) is added when initial drug resistance may be present or for extensive disease eg. miliary TB or where prevalence of HIV is high.
- *Maintenance Phase* (4 months)
  - Isoniazid and rifampicin for the remaining 4 months.
  - This should be given daily (preferred).
  - WHO does not recommend intermittent regimens but a thrice weekly regimen can be given in certain cases.
  - 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, bone / joint (single site) excluding spine, and skin.

WHO Recommendations

- Children living in settings where the prevalence of HIV is high or where resistance to isoniazid is high, or both, with suspected or confirmed pulmonary tuberculosis or peripheral lymphadenitis; or children with extensive pulmonary disease living in settings of low HIV prevalence or low isoniazid resistance, should be treated with a four-drug regimen (HRZE) for 2 months followed by a two-drug regimen (HR) for 4 months.
- Children with suspected or confirmed pulmonary tuberculosis or tuberculous peripheral lymphadenitis who live in settings with low HIV prevalence or low resistance to isoniazid and children who are HIV-negative can be treated with a three-drug regimen (HRZ) for 2 months followed by a two-drug (HR) regimen for 4 months
- Children with suspected or confirmed pulmonary tuberculosis or tuberculous peripheral lymphadenitis living in settings with a high HIV prevalence (or with confirmed HIV infection) should not be treated with intermittent regimens.
- Thrice-weekly regimens can be considered during the continuation phase of treatment, for children known to be HIV-uninfected and living in settings with well-established directly-observed therapy (DOT).
- Streptomycin should not be used as part of first-line treatment regimens for children with pulmonary tuberculosis or tuberculous peripheral lymphadenitis.
- Children with suspected or confirmed tuberculous meningitis as well as those with suspected or confirmed osteoarticular tuberculosis should be treated with a four-drug regimen (HRZE) for 2 months, followed by a two-drug regimen (HR) for 10 months; the total duration of treatment being 12 months.

Corticosteroids

- Indicated for children with TB meningitis.
- May be considered for children with pleural and pericardial effusion (to hasten reabsorption of fluid), severe miliary disease (if hypoxic) and endobronchial disease.
- Steroids should be given only when accompanied by appropriate antituberculous therapy.
- Dosage: prednisolone 1-2mg/kg per day (max. 40 mg daily) for first 3-4 week, then taper over 3-4 weeks.

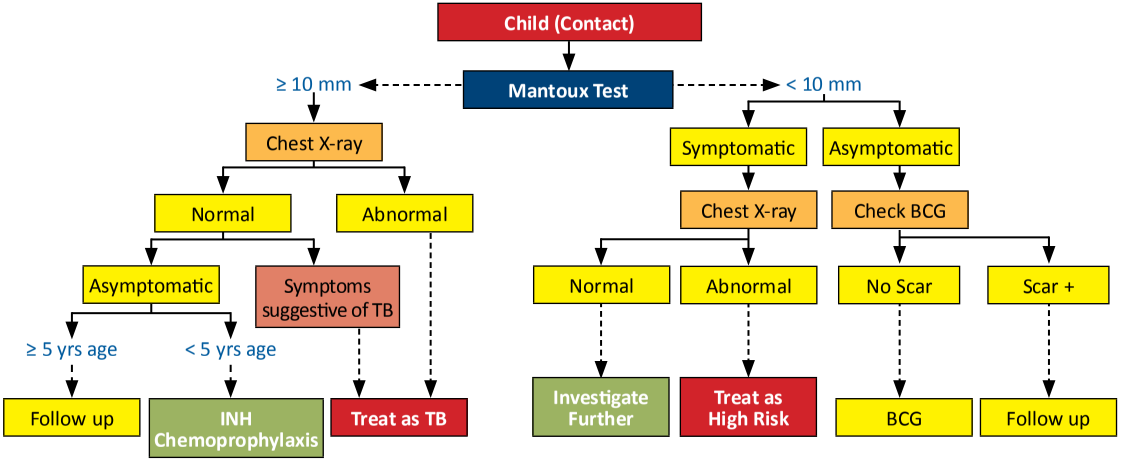
Monitoring of Drug Toxicity

- Indications for baseline and routine monitoring of serum transaminases and bilirubin are recommended for:
  - Severe TB disease.
  - Clinical symptoms of hepatotoxicity.
  - Underlying hepatic disease.
  - Use of other hepatotoxic drugs (especially anticonvulsants).
  - HIV infection.
- Routine testing of serum transaminases in healthy children with none of the above risk factors is not necessary.
- Children on Ethambutol should be monitored for visual acuity and colour discrimination.

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 one week while the mother is being treated. Mother should wear a surgical mask subsequently while breast feeding until she is asymptomatic and her sputum is AFB-smear negative .
  - 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 6 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.

MANAGEMENT OF CHILDREN WITH A POSITIVE HISTORY OF CONTACT WITH TUBERCULOSIS



- Regional lymphadenopathy is one of the more common complications of BCG vaccination and arises as a result of enlargement of ipsilateral lymph nodes, principally involving the axillary node.
- Differential diagnoses to consider are:
  - Pyogenic lymphadenitis.
  - Tuberculous lymphadenitis.
  - Non-tuberculous lymphadenitis.
- The following are features suggestive of BCG lymphadenitis
  - History of BCG vaccination on the ipsilateral arm.
  - Onset usually 2 to 4 months after BCG vaccination, although it may range from 2 weeks to 6 months. Almost all cases occur within 24 months.
  - There is absence of fever or other constitutional symptoms.
  - Absent or minimal local tenderness over the lesion(s).
  - >95% of cases involve ipsilateral axillary lymph nodes, but supraclavicular or cervical glands may be involved in isolation or in association with axillary lymphadenopathy.
  - Only 1 to 2 discrete lymph nodes are enlarged (clinically palpable) in the majority of cases. Involved lymph nodes are rarely matted together.
- Two forms of lymphadenitis can be recognized, non-suppurative or simple which may resolve spontaneously within a few weeks, or suppurative which is marked by the appearance of fluctuation with erythema and oedema of the overlying skin and increased pigmentation.
- Once suppuration has occurred, the subsequent course is usually one of spontaneous perforation, discharge and sinus formation. Healing eventually takes place through cicatrization and closure of the sinus, the process taking several months with possible scarring.

Correct Technique to give BCG Vaccination	
Needle:	Short (10mm) 26-27 gauge needle 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
Do not give BCG at other sites where the lymphatic drainage makes subsequent lymphadenitis difficult to diagnose and dangerous (especially on buttock where lymphatic drains to inguinal and deep aortic nodes).	

MANAGEMENT

Assessment

Careful history and examination are important to diagnose BCG adenitis

- 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 may be needed when needle aspiration has failed (as in the case of matted and multiloculated nodes) or when suppurative nodes have already drained with sinus formation.
  - Surgical incision is not recommended.

Needle aspiration

- Prevents spontaneous perforation and associated complications.
- Shortens the duration of healing.
- Is safe.

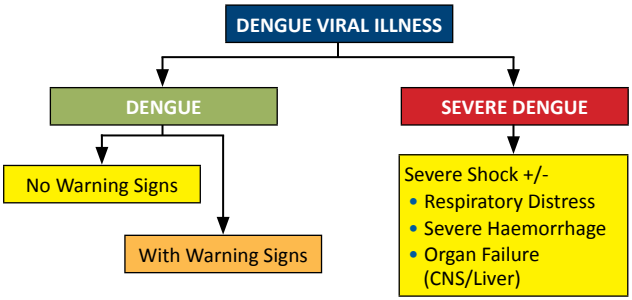
Persistent Lymphadenitis/ disseminated disease

- In patients with large and persistent or recurrent lymphadenopathy, constitutional symptoms, or failure to thrive, possibility of underlying immunodeficency should be considered and investigated. Thus all infants presenting with BCG lymphadenitis should be followed up till resolution.

Introduction

- Dengue virus infections affect all age groups and produce a spectrum of illness that ranges from asymptomatic to a mild or nonspecific viral illness to severe and occasionally fatal disease.
- The traditional 1997 World Health Organization classification of dengue was recently reviewed and changed. The new classification encompass various categories of dengue since dengue exists in continuum.
- The term DHF used in previous classification put too much emphasis on hemorrhage; However, ***the hallmark of severe dengue (and the manifestation that should be addressed early) IS NOT HEMORRHAGE but increased vascular permeability that lead to shock.***

NEW SIMPLIFIED CLASSIFICATION OF DENGUE VIRAL INFECTIONS, WHO 2009



This new system divides dengue into TWO major categories of severity:
- Dengue: with or without warning signs, and
- Severe dengue.

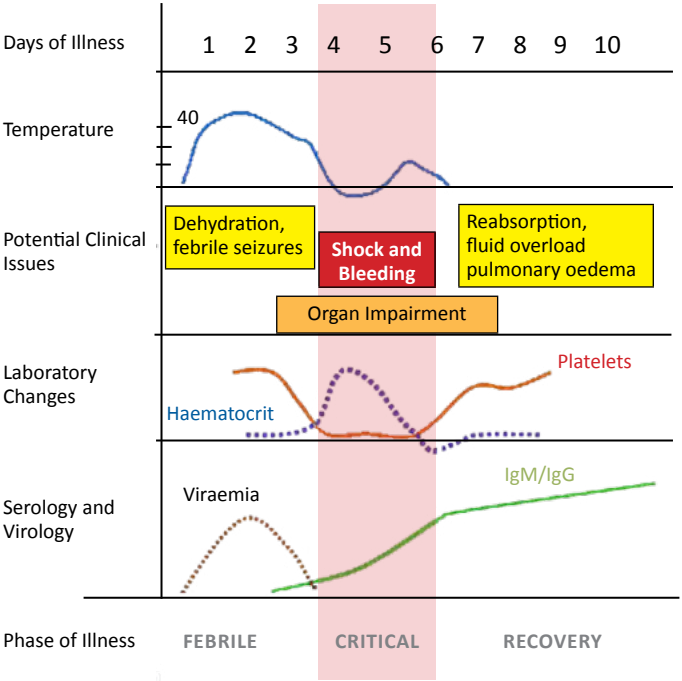
Probable Dengue	Warning Signs
• Lives in/travel to dengue endemic area	• Intense abdominal pain or tenderness • Persistent vomiting • Clinical fluid accumulation. • Mucosal bleed • Lethargy, restlessness • Liver enlargement > 2cm • Laboratory: Increase in hematocrit with concurrent rapid decrease in platelet count.
• Fever and 2 of the following:	
• Nausea, vomiting	
• Rash	
• Aches and pains	
• Positive Tourniquet test	
• Leucopenia	
• Any warning sign	
• Laboratory-confirmed dengue (important when no sign of plasma leakage)	

Criteria for Severe Dengue
Severe plasma leakage with rising hematocrit leading to:
• Shock
• Fluid accumulation (pleural,ascitic)
• Respiratory distress
• Severe bleeding
• Severe organ involvement
• Liver: Elevated transaminases (AST or ALT≥1000)
• CNS: Impaired consciousness, seizures.
• Heart and other organ involvement

Management of Patients with Dengue

- Dengue is a complex and unpredictable disease but success can be achieved with mortality rates of 1% when care is given in simple and inexpensive interventions provided they are given appropriately at the right time.
- The timing of intervention starts at frontline healthcare personnel whether they are in A&E or OPD or even health clinics.
- Early recognition of disease and careful monitoring of IV fluid is important right from beginning.
- The healthcare personnel involved in managing dengue cases day to day need to familiarize themselves with the THREE main well demarcated phases of dengue: febrile, critical; and recovery. *(see next page)*
- In early phase of disease, it is difficult to differentiate dengue with other childhood illness; therefore performing a tourniquet test with FBC at first encounter would be useful to differentiate dengue from other illness.
- Temporal relationship of fever cessation (defervescence) is important as in DENGUE (unlike other viral illness) manifest its severity (leakage/ shock) when temperature seems to have declined.

PHASES OF DENGUE IN RELATION TO SYMPTOMS AND LABORATORY CHANGES



Adapted from World Health Organization: Dengue Hemorrhagic Fever: Diagnosis, Treatment, Prevention and Control. Third Edition. Geneva, WHO/TDR, 2009.

Priorities during first encounter are:

1 - Establish whether patient has dengue

2 - Determine phase of illness

3 - Recognise warning signs and/or the presence of severe dengue if present.

- Most patients with DF and DHF can be managed without hospitalization provided they are alert, there are no warning signs or evidence of abnormal bleeding, their oral intake and urine output are satisfactory, and the caregiver is educated regarding fever control and avoiding non steroidal anti-inflammatory agents and is familiar with the course of illness.
- A dengue information/home care card that emphasizes danger/warning signs is important.
- These patients need daily clinical and/or laboratory assessment by trained doctors or nurses until the danger period has passed.

If dengue is suspected or confirmed, disease notification is mandatory.

Indication for Hospitalisation

- Presence of warning signs.
- Infants.
- Children with co-morbid factors (diabetes, renal failure, immune
- compromised state, hemoglobinopathies and obesity).
- Social factors - living far from health facilities, transport issues.

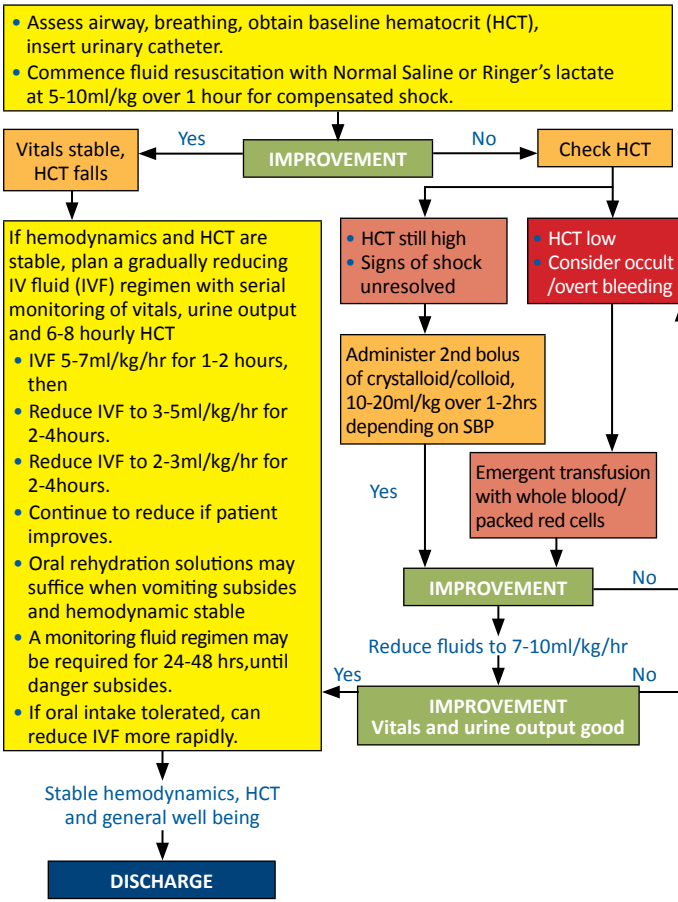
The THREE major priorities of managing hospitalized patient with dengue in the critical phase are:

A - Replacement of plasma losses.

B - Early recognition and treatment of hemorrhage.

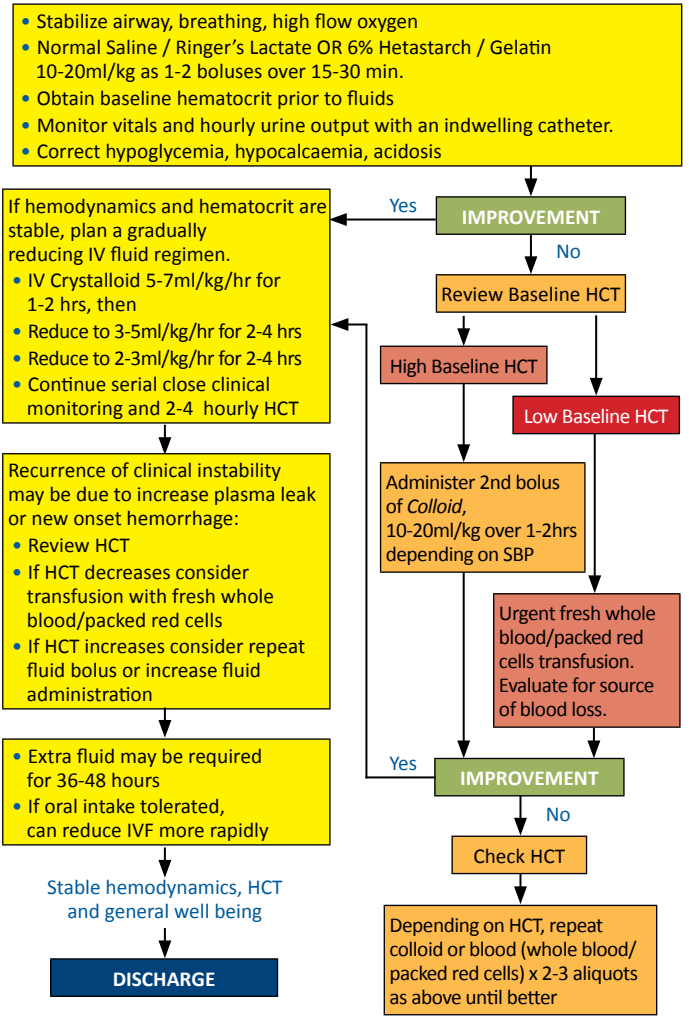
C - Prevention of fluid overload.

- Fluid therapy in a patient with dengue shock has two parts: initial, rapid fluid boluses to reverse shock followed by titrated fluid volumes to match ongoing losses.
- However, for a patient who has warning signs of plasma leakage but is not yet in shock, the initial fluid boluses may not be necessary.

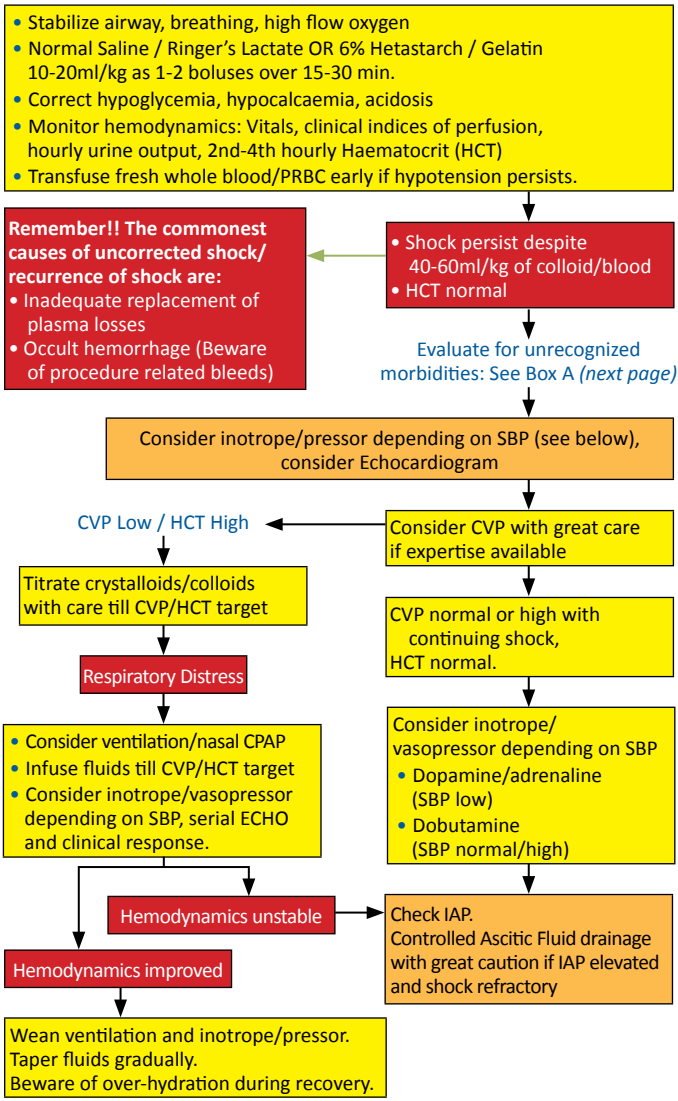


Note:

- ***Recurrence of clinical instability may be due to increased plasma leak or new onset hemorrhage:***
- ***Review HCT***



Remember!
The commonest causes of uncorrected shock/recurrence of shock are:
- ***Inadequate replacement of plasma losses***
- ***Occult hemorrhage (Beware of procedure related bleeds)***



SBP: Systolic blood pressure, PRBC: Packed red blood cell, CVP: Central venous pressure, ECHO: Echocardiogram, IAP: Intra-abdominal pressure

BOX A: Unrecognized morbidities that may contribute to refractory dengue shock.
Occult bleeds Rx: Whole blood/PRBC transfusion
Co-Existing bacterial septic shock/Malaria/leptospira, etc Rx: antibiotics/antimalarials, cardiovascular support, blood transfusion
Myocardial Dysfunction (systolic or diastolic) Rx: Cardiovascular support, evaluate with ECHO if available
Positive pressure ventilation contributing to poor cardiac output Rx: Titrated fluid and cardiovascular support
Elevated intra-abdominal pressure (IAP) Rx: Cautious drainage
Wide-Spread Hypoxic-ischemic injury with terminal vasoplegic shock No treatment effective
ECHO: Echocardiogram; IAP: Intra-abdominal pressure; Rx: Treatment

Volume replacement flowchart for patient with dengue with "warning signs"
• Assess airway and breathing and obtain baseline HCT level.
• Commence fluid resuscitation with normal saline/Ringers lactate at 5-7ml/kg over 1-2 hours.
• If hemodynamic and HCT are stable, plan a gradually reducing IVF regime.
• Titrate fluid on the basis of vital signs, clinical examination, urine output (aim for 0.5ml-1ml/kg/hr),and serial HCT level.
• IVF:5-7ml/kg/hr for 1-2 hours, then:
• Reduce IVFs to 3-5ml/kg/hr for 2-4hours;
• Reduce IVFs to 2-3ml/kg/hr for 2-4 hours;
• Continue serial close monitoring and every 6-8hourly HCT level.
• Oral rehydration solutions may suffice when vomiting subsides and hemodynamic stabilize.
• A monitored fluid regimen may be required for 24-48hours until danger period subsides
HCT-hematocrit; IVF, intravenous fluid

Guidelines for reversing dengue shock while minimizing fluid overload
Severe dengue with compensated shock: • Stabilize airway and breathing, obtain baseline Hct level, initiate fluid resuscitation with NS/RL at 5-10 mL/kg over 1 hr, and insert urine catheter early.
Severe dengue with hypotension: • Stabilize airway and breathing, obtain baseline Hct level, initiate fluid resuscitation with 1-2 boluses of 20 mL/kg NS/RL or synthetic colloid over 15-20 mins until pulse is palpable, slow down fluid rates when hemodynamics improve, and repeat second bolus of 10 mL/kg colloid if shock persists and Hct level is still high.
• Synthetic colloids may limit the severity of fluid overload in severe shock.
End points/goals for rapid fluid boluses: • Improvement in systolic BP, widening of pulse pressure, extremity perfusion and the appearance of urine, and normalization of elevated Hct level.
• If baseline Hct level is low or "normal" in presence of shock, hemorrhage likely to have worsened shock, transfuse fresh WB or fresh PRBCs early.
• After rapid fluid boluses, continue isotonic fluid titration to match ongoing plasma leakage for 24–48 hrs; if patient not vomiting and is alert then aftershock correction with oral rehydration fluids may suffice to match ongoing losses.
• Check Hct level 2-4 hourly for first 6 hrs and decrease frequency as patient improves.
Goals for ongoing fluid titration: • Stable vital signs, serial Hct measurement showing gradual normalization (if not bleeding), and low normal hourly urine output are the most objective goals indicating adequate circulating volume; adjust fluid rate downward when this is achieved.
• Plasma leakage is intermittent even during the first 24 hrs after the onset of shock; hence, fluid requirements are dynamic.
• Targeting a minimally acceptable hourly urine output (0.5-1 mL/kg/hr) is an effective and inexpensive monitoring modality that can signal shock correction and minimize fluid overload.
• A urine output of 1.5–2 mL/kg/hr should prompt reduction in fluid infusion rates, provided hyperglycemia has been ruled out.
• Separate maintenance fluids are not usually required; glucose and potassium may be administered separately only if low.

Guidelines for reversing dengue shock while minimizing fluid overload *(cont)*
• Hypotonic fluids can cause fluid overload; also, avoid glucose-containing fluids, such as 1/2Glucose Normal Saline (GNS or I/2 GNS): the resultant hyperglycemia can cause osmotic diuresis and delay correction of hypovolemia. Tight glucose monitoring is recommended to avoid hyper/hypoglycemia.
• Commence early enteral feeds when vital signs are stable, usually 4–8 hrs after admission.
• All invasive procedures (intubation, central lines, and arterial cannulation) must be avoided; if essential, they must be performed by the most experienced person. Orogastric tubes are preferred to nasogastric tubes.
• Significant hemorrhage mandates early fresh WB or fresh PRBC transfusion; minimize/avoid transfusions of other blood products, such as platelets and fresh-frozen plasma unless bleeding is uncontrolled despite 2–3 aliquots of fresh WB or PRBCs.
NS/RL, normal saline/Ringer's lactate; Hct, hematocrit; BP, blood pressure; WB, whole; HCT-hematocrit; IVF, intravenous fluid GNS-glucose/normal saline

*** It is recommended that baseline hematocrit is obtained for all cases and repeat hematocrit done following each fluid resuscitation to look at child 's response and to plan subsequent fluid administration. In PICU/HDW settings, ABG machine can be used to look at HCT and in general wards, either, SPIN PCV or FBC (sent to lab).*

Discharge of Children with Dengue

- Patients who are resuscitated from shock rapidly recover. Patients with dengue hemorrhagic fever or dengue shock syndrome may be discharged from the hospital when they meet the following criteria:
  - Afebrile for 24 hours without antipyretics.
  - Good appetite, clinically improved condition.
  - Adequate urine output.
  - Stable hematocrit level.
  - At least 48 hours since recovery from shock.
  - No respiratory distress.
  - Platelet count greater than 50,000 cells/µL.

HOME CARE CARD FOR DENGUE PATIENTS

(Please take this card to your health facility for each visit)

What should be done?

- Adequate bed rest.
- Adequate fluid intake:
  (>5 glasses for average-sized adults or accordingly in children)
  - Milk, fruit juice (caution with diabetes patient) and isotonic electrolyte solution (ORS) and barley/rice water.
  - Plain water alone may cause electrolyte imbalance.
- Take Paracetamol (not more than 4 grams per day for adults and accordingly in children).
- Tepid sponging.
- Look for mosquito breeding places in and around the home and eliminate them.

What should be avoided?

- Do not take acetylsalicylic acid (Aspirin), mefenamic acid (Ponstan), ibuprofen or other non-steroidal anti-inflammatory agents (NSAIDs), or steroids.
  If you are already taking these medications please consult your doctor.
- Antibiotics are not necessary.

If any of following is observed, take the patient immediately to the nearest hospital. These are warning signs for danger:

- Bleeding:
  - Red spots or patches on the skin; bleeding from nose or gum,
  - vomiting blood; black-colored stools;
  - heavy menstruation/vaginal bleeding.
- Frequent vomiting.
- Severe abdominal pain.
- Drowsiness, mental confusion or seizures.
- Pale, cold or clammy hands and feet.
- Difficulty in breathing.

Laboratory Monitoring					
Visit (date)					
White blood cells					
Hematocrit					
Platelets					

Introduction

- Diphtheria is a clinical syndrome caused by *Corynebacterium diphtheria.*
- Diphtheria can be classified based on site of disease: nasal diphtheria, pharyngeal and tonsillar diphtheria, laryngeal or laryngotracheal diphtheria, and cutaneous diphteria.
- Diphtheria may cause systemic complication such as myocarditis (mortality 50%), neuritis presenting as paralysis of soft palate and rarely non-oliguric acute kidney injury.

Management of an Acute Case

- All suspected and confirmed patients must be placed under strict isolation until bacteriological clearance has been demonstrated after completing treatment. Strict droplet precautions and hand hygiene must be observed by healthcare workers.
- Obtain specimens for culture from nose, throat, or any mucosal membrane (tissue). Obtain specimen before the commencement of antibiotic and specimen must be transported to the laboratory promptly. Notify laboratory personnel as special tellurite enriched culture media (Loffler's or Tindale's) are needed.

Diphtheria Antitoxin (derived from horse serum)

- Definitive treatment :
  - Early, single dose of IV infusion (over 60minutes) diphtheria antitoxin should be administered on the basis of clinical diagnosis, even before culture results are available.
  - Tests for hypersensitivity is recommended for IV administration.

Form of diphtheria	Dose (units)	Route
Pharyngeal/Laryngeal disease of 48 hours or less	20,000 to 40,000	IM OR IV
Nasopharyngeal lesions	40,000 to 60,000	IM OR IV
Extensive disease of 3 or more days durations or diffuse swelling of the neck (bull-neck diphtheria)	80,000 to 120,000	IM OR IV
Cutaneous lesions (not routinely given)	20,000 to 40,000	IM

Begin antibiotic therapy

Antibiotic is indicated to stop toxin production, treat localised infection, and to prevent transmission of the organism to contacts. It is not a substitute for antitoxin treatment.

REGIME

- Penicillin
  - IV aqueous crystalline Penicillin 100,000 to 150,000 U/kg/day in 4 divided doses, maximum 1.2 million U.

  Or
  - IM procaine Penicillin 25,000 to 50,000 U/kg/day (maximum 1.2million U, in 2 divided doses.
  - Change to oral Penicillin V 125-250mg QID once patient can take orally.
  - Total antibiotic duration for 14 days.

OR

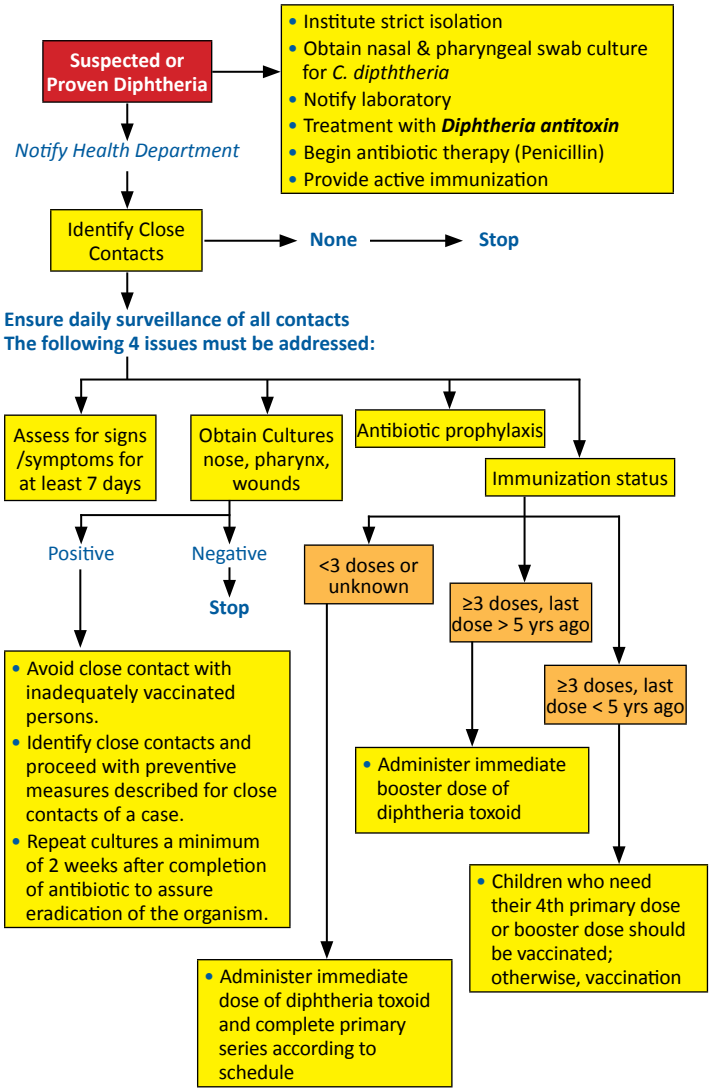
- Erythromycin
  - IV OR Oral 40-50 mg/kg/day, maximum 2g/day.
  - Total antibiotic duration for 14 days.

Immunization

- Before discharge, to catch up diphtheria toxoid immunization as diptheria infection does not necessary confer immunity

Management of close contacts and asymptomatic carriers

- Refer to diphtheria protocol.


Suspected or Proven Diphtheria
• Institute strict isolation
• Obtain nasal & pharyngeal swab culture for C. diptht heria
• Notify laboratory
• Treatment with Diphtheria antitoxin
• Begin antibiotic therapy (Penicillin)
• Provide active immunization
Notify Health Department
Identify Close Contacts
None
Stop
Ensure daily surveillance of all contacts
The following 4 issues must be addressed:
Assess for signs /symptoms for at least 7 days
Obtain Cultures nose, pharynx, wounds
Antibiotic prophylaxis
Immunization status
Positive
Negative
Stop
<3 doses or unknown
≥3 doses, last dose > 5 yrs ago
≥3 doses, last dose < 5 yrs ago
• Avoid close contact with inadequately vaccinated persons.
• Identify close contacts and proceed with preventive measures described for close contacts of a case.
• Repeat cultures a minimum of 2 weeks after completion of antibiotic to assure eradication of the organism.
• Administer immediate booster dose of diphtheria toxoid
• Children who need their 4th primary dose or booster dose should be vaccinated; otherwise, vaccination
• Administer immediate dose of diphtheria toxoid and complete primary series according to schedule

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Introduction

- A chronic inflammatory itchy skin condition that usually develops in early childhood and follows a remitting and relapsing course. It often has a genetic component.
- Leads to the breakdown of the skin barrier making the skin susceptible to trigger factors, including irritants and allergens, which can make the eczema worse.
- Although not often thought of as a serious medical condition, it can have a significant impact on quality of life.

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 rhinoconjuctivitis, atopic dermatitis)
Minor / less specific features
Xerosis
Preauricular fissures
Icthyosis / 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 virus)
Perifollicular accentuation (especially in pigmented races)

Triggering factors

- Infection: Bacterial, viral or fungal
- Emotional stress
- Sweating and itching
- Irritants: Hand washing soap, detergents
- Extremes of weathers
- Allergens
  - Food : egg, peanuts, milk, fish, soy, wheat.
  - Aeroallergens : house dust mite, pollen, animal dander and molds.

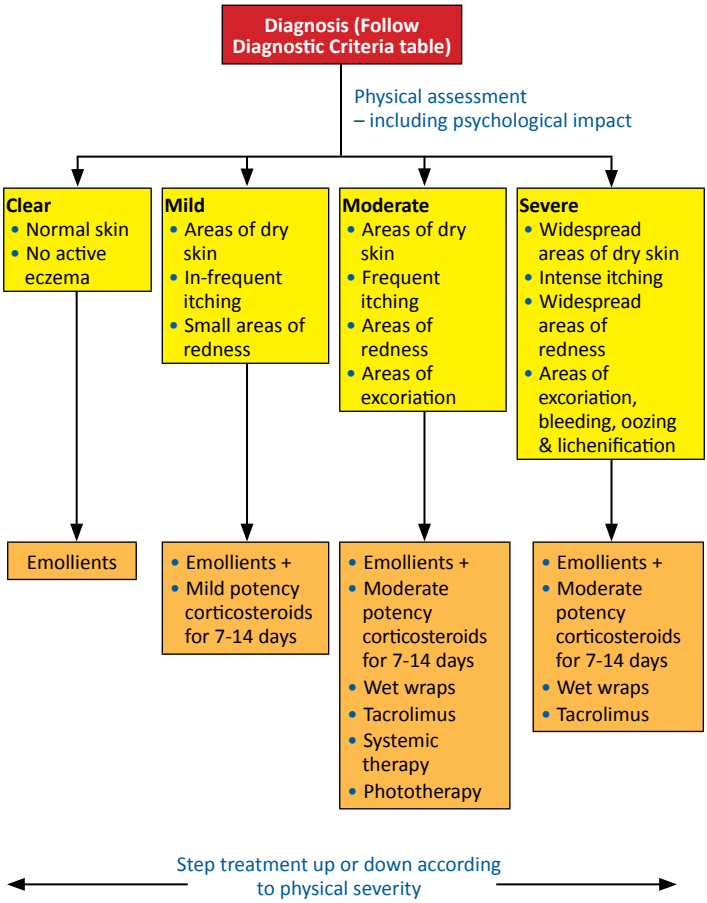
Management

- Tailor the treatment of atopic dermatitis individually depending on:
  - The severity.
  - Patient's understanding and expectation of the disease and the treatment process.
  - Patient's social circumstances.
- Comprehensive patient education is paramount, and a good doctor-patient relationship is essential for long-term successful management.
- In an acute flare-up of atopic dermatitis, evaluate for the following factors:
  - Poor patient compliance
  - Secondary infection: bacterial (e.g. *Staphylococcus aureus*), viral (e.g. herpes simplex virus)
  - Persistent contact irritant/allergen.
  - Physical trauma, scratching, friction, sweating and adverse environmental factors.

Bath & Emollients

- Baths soothe itching and removes crusting. They should be lukewarm and limited to 10 minutes duration. Avoid soaps. Use soap substitute e.g. aqueous cream or emulsifying ointment.
- Moisturizers work to reduce dryness in the skin by trapping moisture.
- Apply to normal and abnormal skin at least twice a day and more frequently in severe cases.
- Emollients are best applied after bath. Offer a choice of unperfumed emollients and suitable to the child's needs and preferences, e.g. Aqueous cream, Ung. Emulsificans, and vaseline.

N.B. Different classes of moisturizer are based on their mechanism of action, including occlusives, humectants, emollients and protein rejuvenators. In acute exudation form $KMNO_4$ 1:10,000 solutions or normal saline daps or soaks are useful – as mild disinfectant and desiccant.


Diagnosis (Follow Diagnostic Criteria table)
Physical assessment – including psychological impact
Clear
• Normal skin
• No active eczema
Mild
• Areas of dry skin
• In-frequent itching
• Small areas of redness
Moderate
• Areas of dry skin
• Frequent itching
• Areas of redness
• Areas of excoriation
Severe
• Widespread areas of dry skin
• Intense itching
• Widespread areas of redness
• Areas of excoriation, bleeding, oozing & lichenification
Emollients
• Emollients +
• Mild potency corticosteroids for 7-14 days
• Emollients +
• Moderate potency corticosteroids for 7-14 days
• Wet wraps
• Tacrolimus
• Systemic therapy
• Phototherapy
• Emollients +
• Moderate potency corticosteroids for 7-14 days
• Wet wraps
• Tacrolimus
Step treatment up or down according to physical severity

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 once or twice daily.
  - 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.

Steroid Potency	
Potency of topical steroid	Topical steroid
Mild	Hydrocortisone cream/ointment 1%
Moderate	Bethametasone 0.025% (1:4dilution)
	Eumovate (clobetasone butyrate)
Potent	Bethametasona 0.050%
	Elomet (mometasone furoate)
Super potent	Dermovate (clobetasone propionate)

Systemic Therapy

- Consist of:
  - Relief of pruritus
  - Treatment of secondary infection, and
  - Treatment of refractory cases

Relief of Pruritus

- Do not routinely use oral antihistamines.
- Offer a 1-month trial of a non-sedating antihistamine to:
  - Children with severe atopic eczema
  - Children with mild or moderate atopic eczema where there is severe itching or urticaria.
- If successful, treatment can be continued while symptoms persist. Review every 3 months.
- Offer a 7–14 day trial of a sedating antihistamine to children over 6 months during acute flares if sleep disturbance has a significant impact. This can be repeated for subsequent flares if successful.

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.
- Commonly *Staphyloccus aureus.*
- Useful in exudation form where superinfection occurs.
- Choice:
  - Oral cloxacillin 15mg/kg/day 6 hourly for 7-14 days, *or*
  - Oral Erythromycin / cephalosporin
- 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 response to conventional topical therapy and have extensive eczema. Refer to a Dermatologist (who may use systemic steroids, interferon, Cyclosporine A, Azathioprine or/and phototherapy).

Other Measures

- Avoid woolen toys, clothes, bedding.
- Reduce use of detergent (esp. biological).
- BCG contraindicated till skin improves.
- Swimming is useful (MUST apply moisturizer immediately upon exiting pool).
- Avoid Aggravating Factors.

For Relapse

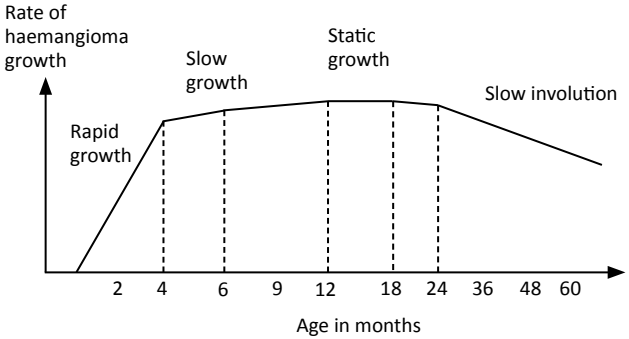
- Check compliance.
- Suspect secondary infection – send for skin swab; start antibiotics.
- Exclude scabies
- For severe eczema, emollient and topical steroid can be applied under occlusion with 'wet wrap'. This involves the use of a layer of wet, followed by a layer of dry Tubifast to the affected 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 excoriation.

Prognosis

- Tendency towards improvement throughout childhood.
- Two third will clear by adolescence.

Infantile haemangiomas

- Are the most common benign vascular tumour of infancy.
- Clinical course is marked by rapid growth during early infancy followed by slower growth, then gradual involution.
- A minority cause functional impairment and even more cause psychosocial distress.
- Once resolved, a significant minority (20-40%) leave residual scarring, fibrofatty tissue, telangiectases, and other skin changes which can have a lasting psychological effect.



- By 5 years of age, 50% of hemangiomas involute, 70% by age 7, and 90% by age 9. 20-40% leave residual changes in the skin.
- Approximately 10% require treatment, and < 1% are life threatening.
- In 95% of cases, diagnosis can be established on the basis of history and physical examination alone.
  - Typical-appearing vascular tumors.
  - History of the lesion seen at birth or shortly thereafter, with characteristic proliferation in early infancy.

Clinical subtypes of haemangiomas:

- *Superficial haemangiomas* are most common (50%-60%).
- *Deep haemangiomas* (15%): bluish soft-tissue swellings without an overlying superficial component.
- *Mixed haemangiomas* (both a superficial and deep component) (25%-35%).*Multiple neonatal haemangiomatosis* (15%-30%), consists of multiple small lesions ranging from a few millimeters to 1 to 2 cm.

Management

- Most hemangiomas require no treatment.
- Active nonintervention is recommended in order to recognize those that may require treatment quickly.
- When treatment is undertaken, it is important that it be customized to the individual patient, and that the possible physical, and psychological complications be discussed in advance. Often, a multidisciplinary approach is recommended.
- Individualized depending on: size of the lesion(s), location, presence of complications, age of the patient, and rate of growth or involution at the time of evaluation. The potential risk(s) of treatment is carefully weighed against the potential benefits.

No risk or low-risk haemangiomas

(Small, causing no functional impairment and unlikely to leave permanent disfigurement)

- Wait and watch policy (active non-intervention)
- Patient education: Parent education may include the following:
  - The expected natural history without treatment
  - Demonstration whenever possible serial clinical photographs of natural involution.

High-risk haemangiomas

(Large, prognostically poor location, likely to leave permanent disfigurement, causing functional impairment, or involving extracutaneous structures)

- Large cutaneous or visceral haemangiomas (particularly liver) can result in high-output cardiac failure.
- Haemangiomas on the 'special sites' with associated complications are given on the table below.

Special site	Complications
Beard	Airway compromise
Eye	Amblyopia, strabismus, astigmatism
Lumbar	Tethered cord, imperforate anus, renal anomalies, sacral anomalies.
Facial	PHACES

- Segmental haemangiomas, which cover a particular section or area of skin, may be markers for underlying malformations or developmental anomalies of the heart, blood vessels, or nervous system (PHACE and PELVIS syndromes and lumbosacral haemangiomas) and, depending on the severity of the associated anomaly, can result in increased morbidity or mortality.
- PHACE syndrome is posterior fossa structural brain abnormalities (Dandy-Walker malformation and various forms of hypoplasia); haemangiomas of the face, head, and neck (segmental, >5 cm in diameter); arterial lesions (especially carotid, cerebral, and vertebral); cardiac anomalies (coarctation of the aorta in addition to many other structural anomalies); eye abnormalities; and, rarely, associated midline ventral defects such as sternal cleft or supraumbilical raphe).
- PELVIS syndrome is perineal haemangioma with any of the following: external genital malformations, lipomyelomeningocele, vesicorenal abnormalities, imperforate anus, and/or skin tags.

Treatment

- The listed treatments may be used singly, in combination with each other, or with a surgical modality.

MEDICAL

- *Propranolol* is the first-line therapy; Patients are admitted to ward for propranolol therapy for close monitoring of any adverse effects.
  - *Dose:* Start at 0.5 mg/kg/d in 2 to 3 divided doses orally and then increased if tolerated. An increase in dose by 0.5 mg/kg/d is given until the optimal therapeutic dose of 1.5 to 2 mg/kg/day.
  - *Duration:* Ranges from 2 - 15 months but it is proposed that propranolol should be continued for 1 year or until the lesion involutes completely, as rebound growth has been noted if treatment is withdrawn too early.
  - Propranolol is withdrawn by halving the dose for 2 weeks, then halving again for 2 weeks, before stopping.
  - Adverse effects: hypotension, bradycardia, hypoglycemia, bronchospasm, sleep disturbance, diarrhea, and hyperkalemia.
- *Systemic corticosteroids* (indicated mainly during the growth period of haemangiomas):
  - Prednisolone 2 to 4 mg/kg/ day in a single morning dose or divided doses. Watch out for growth retardation, blood pressure elevation, insulin resistance, and immunosuppression.
  - Intralesional corticosteroid therapy for small, bossed, facial hemangioma.
  - Triamcinolone, 20mg/ml, should be injected at low pressure, using a 3 ml syringe and 25-gauge needle. Do not exceed 3-5mg/kg per procedure.
  - Periocular regions must be done only by an experienced ophthalmologist as there is a risk of embolic occlusion of the retinal artery or oculomotor nerve palsy.

- Other systemic therapy:
  - *Interferon alfa*. Very effective but is used mainly as a second-line therapy for lesions not responsive to corticosteroids because of the possible severe neurotoxicity, including spastic diplegia.
  - *Vincristine*. Some consider this as second-line treatment for corticosteroid resistant hemangiomas.

SURGERY

- The benefits and risks of surgery must be weighed carefully, since the scar may be worse than the results of spontaneous regression.
- Surgery is especially good for small, pedunculated hemangiomas and occasionally, in cases where there may be functional impairment. It is usually used to repair residual cosmetic deformities.
- Generally, it is recommended that a re-evaluation be done when the child is 4 years old, in order to assess the potential benefit of excision.

Definition

Infestation caused by the mite *Sarcoptes scabei*. 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

- Educate the parents about the condition and give clear written information on applying the treatment.
- Treat everyone in the household and close contacts.
- Only allow the patient to go to school 24 hours after the start of treatment.
- Wash clothing and bedding in hot water or by dry cleaning. Clothing that cannot be washed may be stored in a sealed plastic bag for three days.
- The pruritis of scabies may be treated with diphenhydramine or other anti-pruritic medication if necessary. The pruritis can persist up to three weeks post treatment even if all mites are dead, and therefore it is not an indication to retreat unless live mites are identified.
- Any superimposed bacterial skin infection should be treated at the same time as the scabies treatment.

Treatment

- Permetrin 5% lotion
  - Use for infants as young as 2 months and onwards. Children should be supervised by an adult when applying lotion.
  - Massage the lotion into the skin from the head to the soles of the feet, paying particular attention to the areas between the fingers and toes, wrists, axillae, external genitalia and buttocks. Scabies rarely infects the scalp of adults, although the hairline, neck, temple and forehead may be involved in geriatric patients.
  - Reapply to the hands if washed off with soap and water within eight hours of application.
  - Remove the lotion after 12 to 14 hours by washing (shower or bath).
  - Usually the infestation is cleared with a single application. However a second application may be given seven to 10 days after the first if live mites are demonstrated or new lesions appear.
- Benzyl Benzoate (EBB)
  - Use 12.5% emulsion in children age 7-12 years; 25% emulsion if above 12 years and adults.
  - Apply nightly or every other night for a total of three applications.
  - It can irritate the skin and eyes, and has caused seizures when ingested.
- Crotamiton (Eurax)
  - Apply 10% crotamiton cream to the entire body from the neck down, nightly, for two nights. Wash it off 24 hours after the second application.
- Sulfur (3-6% in calamine lotion)
  - Apply from the neck down, nightly, for three nights. Bathe before
  - reapplying and 24 hours after the last application. No controlled
  - studies of efficacy or safety are available.
- Lindane (1% gamma benzene hexachloride) Lotion.
  - Apply to cool, dry skin. Apply the lotion sparingly from the chin to the toes, with special attention to the hands, feet, web spaces, beneath the fingernails and skin creases. Wash off after eight to 12 hours.
  - 95% of patients require only one treatment. Re-treat only if
    i. Infestations with live mites is confirmed after one week.
    ii. Itching persist three weeks after the first treatment.

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 (Nikolksy' 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 conjuctival 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 surabasal cleavage plane.
- Renal profile – raised blood urea, hyperkalaemia and creatinine.
- Glucose - hypoglycaemia.

Aetiology in Steven Johnson Syndrome / TEN
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 0.4 Gm/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 and 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.
- Synechiea should be disrupted.

Oral care

- Good oral hygiene aimed at early restoration of normal feeds.

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Chapter 88: Inborn errors metabolism (IEM): Approach to Diagnosis and Early Management in a Sick Child

Introduction

- Over 500 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 divided into 5 useful groups:

Group	Diseases	Diagnosis and Treatment
Disorders that give rise to acute or chronic intoxication	Aminoacidopathies (MSUD, 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	• Readily diagnosed through basic IEM investigations: blood gases, glucose, lactate, ammonia, plasma amino acids, urinary organic acids and acylcarnitine profile • Specific emergency and long term treatment available for most diseases.
Disorders with reduced fasting tolerance	Glycogen storage diseases, disorders of gluconeogenesis, fatty acid oxidation disorders, disorders of ketogenesis/ketolysis	• Persistent/recurrent hypoglycemia is the first clue to diagnosis. • Specific emergency and long term treatment available for most diseases.
Neurotransmitter defects and related disorders	Nonketotic hyperglycinemia, serine deficiency, disorders of biogenic amine metabolism, disorders of GABA metabolism, antiquitin deficiency (pyridoxine dependent epilepsy), pyridoxal phosphate deficiency, GLUT1 deficiency	• Diagnosis requires specialized CSF analysis. • Some are treatable.

Classification *(continued)*		
Group	Diseases	Diagnosis and Treatment
Disorders of the biosynthesis and breakdown of complex molecules	Lysosomal storage disorders, peroxisomal disorders, congenital disorders of glycosylation, sterol biosynthesis disorders, purine and pyrimidine disorders	• Specialized diagnostic tests required. • Very few are treatable.
Mitochondrial disorders	Respiratory chain enzymes deficiencies, PDHc deficiency, pyruvate carboxylase deficiency	• Persistent lactate acidemia is often the first clue to diagnosis. • Mostly supportive care.

Screening for treatable IEM in a sick child

- In an acutely ill child, IEM should be considered a differential diagnosis along with other diagnoses:
  - In all neonates with unexplained, overwhelming, or progressive disease particularly after a normal pregnancy or birth, but deteriorates after feeding.
  - In all children with acute encephalopathy, particularly preceded by vomiting, fever or fasting.
  - In all children with unexplained symptoms and signs of metabolic acidosis, hypoglycaemia, acute liver failure or Reye-like syndrome.
- The aim is targeted to pick up treatable diseases in Group 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 syndrome, progressive neurological disease).
  - Consanguinity.
  - Deterioration after a symptom-free interval in a newborn.
  - Unusual smell - burn 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>
<tr><th colspan="2">Basic metabolic investigations [1]</th><th>Special metabolic investigations [1]</th></tr>
<tr><td>Ammonia[2]</td><td rowspan="5">Must be included in work-up of an acutely ill child of unknown aetiology [4]</td><td rowspan="2">Acylcarnitines (Dried blood spot on Guthrie card)</td></tr>
<tr><td>Glucose</td></tr>
<tr><td>Lactate[2]</td><td>Amino acids (plasma or serum)[3]</td></tr>
<tr><td>Blood gases</td><td>Organic acids (urine)</td></tr>
<tr><td>Ketostix (urine)</td><td>Orotate (urine): if suspected urea cycle defects</td></tr>
<tr><td colspan="2" rowspan="2">Blood count, electrolytes, ALT, AST, CK, creatinine, urea, uric acid, coagulation</td><td>[Send to the metabolic lab immediately (eg by courier) especially when the basic metabolic investigations are abnormal, particularly if there is hyperammonemia or persistent ketoacidosis]</td></tr>
<tr><td colspan="2">1, Will pick up most diseases from Group 1 and 2, and some diseases in other groups (which often require more specialized tests)
2, Send immediately (within 15 minutes) to lab with ice
3, Urinary amino acids are the least useful as they reflect urinary thresh old. Their true value is only in the diagnosis of specific renal tubular transport disorders (eg cystinuria).
4, Routine analysis of pyruvate is not indicated.</td></tr>
</table>

Useful normal/abnormal values		
Basic tests	**Values**	**Note**
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 not analyzed immediately. 2. Secondary elevated may occur in severe liver failure.
Anion Gap	*Calculation* [Na+] + [K+] – [Cl-] – [HCO3-] Normal :- 15-20mmol/L	1. Normal: renal / intestinal loss of bicarbonate. 2. Increased: organic acids, lactate, ketones.
Lactate	• Blood: < 2.4mmol/L • CSF: < 2.0mmol/L	False elevations are common due to poor collection or handling techniques

Disorders"Typical" basic laboratory constellations						
Disorders	Ammonia	Glucose	Lactate	pH	Ketonuria	Others
Urea cycle defects	↑↑↑	N	N	↑	N	
Organic acidemias	↑↑	↓, N, ↑	↑↑	↓↓↓	↑↑↑	↑anion gap, neutropenia, thrombocytopenia
MSUD	N	N	N	N	N,↑	
GSD	N	↓↓↓	↑↑	↓	N	↑triglyceride, ↑uric acid, ↑ALT
FAOD	↑	↓↓↓	↑	↓	↓↓↓	↑CK
Mitochondrial disorders	N	N	↑↑↑	↓↓	N	↑alanine
Tyrosinemia I	N	N-↓	N	N-↓	N	Liver failure, ↑α-fetoprotein, Renal fanconi

Early contact to 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 acidurias 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. ***However, the maximum duration without protein is 48 hours.***
- Correct hypoglycaemia and metabolic acidosis.
- Reduce catabolism by providing adequate calories.
  Aim 120kcal/kg/day, achieved by
  - IV Glucose infusion (D10%, 15% or 20% with appropriate electrolytes).
  - Intralipid 20% at 2-3g/kg/day ***(Except when a Fatty Acid Oxidation Disorder is suspected).***
  - Protein-free formula for oral feeding [eg Pro-phree® (Ross), Calo-Lipid (ComidaMed®), basic-p (milupa)].
- Anticipate complications
  - Hyperglycemia/glucosuria - Add IV Insulin 0.05U/kg/hr if blood glucose > 15mmol/L to prevent calories loss.
  - Fluid overload: IV Frusemide 0.5-1mg stat doses.
  - Electrolytes imbalances: titrate serum Na+ and K+.
  - Protein malnutrition – add IV Vamin or oral natural protein (eg milk) after 48 hours, starts at 0.5g/kg/day.
- Carry out detoxifying measures depending on the clinical and laboratory findings.
- Continue all conventional supportive/intensive care
  - Respiratory insufficiency: artificial ventilation.
  - Septicaemia: antibiotics.
  - Cerebral convulsions: anticonvulsants.
  - Cerebral edema: avoid hypotonic fluid overload, hyperventilation, Mannitol, Frusemide.
  - Early central line.
  - Consult metabolic specialist.

Specific detoxification measures for hyperammonemia
Hyperammonemia due to Urea cycle defects
Anti-hyperammonemic drugs cocktail
Loading dose • IV Sodium benzoate 250mg/kg • IV Sodium phenylbutyrate 250mg/kg • IV L-Arginine 250mg/kg (mix together in D10% to a total volume of 50mls, infuse over 90 min) *Maintanence dose* • Same dilution as above but infuse over 24 hours
Indication: 1. NH3 > 200µmol/L 2. Symptomatic (encephalopathic)
Dialysis
• Hemodialysis or hemofiltration if available. • If not, peritoneal dialysis is the alternative. • Exchange transfusion is not effective. *(Method of choice depends on local availability, experience of medical staff)*
Indication: 1. NH3 > 400µmol/L 2. Symptomatic (encephalopathic) 3.Inadequate reduction/raising NH3 despite drugs cocktail
Hyperammonemia due to Organic aciduria
Give oral Carglumic acid, 100 - 250mg/kg/day in divided doses

Other specific Detoxification measures		
Disorder	**Pharmacological**	**Non-pharmacological**
MSUD	nil	Dialysis. *Indication:* 1. Leucine >1,500µmol/L 2. Symptomatic (encephalopathic)
Organic acidurias	Carnitine 100mg/kg/day	Dialysis. *Indication:* 1. intractable metabolic acidosis 2. Symptomatic (encephalopathic)
Tyrosinemia type 1	NTBC 1-2mg/kg/day	Nil
Cobalamin disorders	IM Hydroxocobalamin 1mg daily	Nil

STEP 2

- Adaptation and specification of therapy according to the results of the special metabolic investigations/definitive diagnosis.
- For protein metabolism disorders, the long term diet is consists of
  - Specific precursor free formula
  - Natural protein (breast milk or infant formula). This is gradually added when child is improving to meet the daily requirement of protein and calories for optimal growth.
- Other long term treatment includes
  - Oral anti-hyperammonemic drugs cocktail (for urea cycle defects)
  - Carnitine (for organic acidemias)
  - Vitamin therapy in vitamin-dependent disorders (eg Vit B12-responsive methylmalonic acidemia and cobalamine disorders).
- Transfer the child to a metabolic centre for optimisation of therapy is often necessary at this stage in order to plan for the long term nutritional management according to child's protein tolerance

STEP 3

- Be prepared for future decompensation
  - Clear instruction to parents.
  - Phone support for parents.
  - Provide a letter that includes the emergency management protocol to be kept by parents.
- Role of first-line paediatric doctors
  1. Help in early diagnosis
  2. Help in initial management and stabilization of patient
  3. Help in long term care (shared-care with metabolic specialist)
  - Rapid action when child is in catabolic stress (febrile illness, surgery, etc)
  - Adequate hydration and temporary adjustment in nutrition management and pharmacotherapy according to emergency protocol will prevent catastrophic metabolic decompensation.

Key points in managing acute metabolic decompensation in children with known disorders of protein metabolism (UCD, MSUD, Organic acidurias)

- Consult metabolic specialist if you are uncertain.
- Perform clinical and biochemical assessment to determine the severity.
- Stop the natural protein but continue the special formula as tolerated (PO or per NG tube/perfusor).
- IV Glucose and Intralipid to achieve total calories 120kcal/kg/day.
- IV antiemetic (e.g. Kytril) for nausea or vomiting.
- Management of hypoglycemia, hyperammonemia and metabolic acidosis as above.
- Gradually re-introduce natural protein after 24-48 hours.

Acute intoxication due to classical galactossemia (Group 1)

- Clinical presentation: progressive liver dysfunction after start of milk feeds, cataract.
- Diagnosis: dry blood spots (Guthrie card) for galatose and galactose-1-P uridyltransferase (GALT) measurement
- Treatment: lactose-free infant formula
- ***Neonatal intrahepatic cholestasis caused by Citrin Deficiency (NICCD) may mimic classical Galactosemia.***

Disorders with reduced fasting tolerance (Group 2)

- Clinical presentation: recurrent hypoglycemia ± hepatomegaly.
- Treatment: - 10% glucose infusion, 120- 150ml/kg/day.
- This therapy is usually sufficient in acute phase.
- Long term: avoid fasting, frequent meals, nocturnal continuous feeding, uncooked cornstarch (older children).
  (refer Chapter on Hypoglycaemia)

Neurotransmitter defects and related disorders (Group 3)

- This group should be considered in children with neurological problems
- when basic metabolic investigations are normal.
- Diagnosis usually requires investigations of the CSF. Considers this in
  - Severe epileptic encephalopathy starting before birth or soon thereafter, especially if there is myoclonic component.
  - Symptoms of dopamine deficiency: oculogyric crises, hypokinesia, dystonia, truncal hypotonia/limb hypertonia.
  - Presence of vanillactate and 4(OH) Butyrate in urine.
  - Unexplained hyperprolactinemia.

Disorders of the biosynthesis and breakdown of complex molecules (Group 4)

Disorders in this group

- Typically show slowly progressive clinical symptoms and are less likely to cause acute metabolic crises.
- Are not usually recognised by basic metabolic analyses but require specific investigations for their diagnosis.
  - Lysosomal disorders:
    (1) screening tests: urine glycoaminoglycans (mucopolysacchardioses), urine oligosaccharides (oligosaccharidoses).
    (2) definitive diagnosis: enzyme assay, DNA tests.
  - Peroxisomal disorders: plasma very long chain fatty acids (VLCFA).
  - Congenital disorders of glycosylation: serum transferrin isoform analysis.

Mitochondrial disorders (Group 5)

- Clinical: suspect in unexplained multi-systemic disorders especially if involve neuromuscular system.
- Inheritance:
  (1) mtDNA defects –sporadic, maternal.
  (2) nuclear gene defects –mostly autosomal recessive.
- Laboratory markers: persistently elevated blood/CSF lactate and plasma alanine.
- Diagnosis: respiratory enzyme assay in muscle biopsy/skin fibroblast, targeted mtDNA mutation study etc (discuss with metabolic specialist).
- 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 websites: http://www.mitosoc.org/, www.umdf.org/

Management of a asymptomatic newborn but at risk of having potentially treatable IEM

- Ideally the diagnosis of treatable IEM should be made before a child becomes symptomatic and this may be possible through newborn screening for high risk newborns.
  - A previous child in the family has had an IEM.
  - Multiple unexplained early neonatal death.
  - Mother has HELLP/fatty liver disease during pregnancy (HELLP – Haemolytic Anaemia, Elevated Liver Enzymes, Low Platelets).
- 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: screens for the specific condition, e.g. urea cycle disorders – monitor NH_3 and plasma amino acid, MSUD – monitor plasma leucine (amino acids).
- If potential diagnosis is unknown: Guthrie cards, collect on 2nd or 3rd day after feeding, mails it immediately and get result as soon as possible. Other essential laboratory monitoring: NH_3, VBG, blood glucose. Please discuss with metabolic specialist.
- To prevent decompensation before baby's status is known: provide enough calories (oral/IV), may need to restrict protein especially if index case presented very early (before 1 week). Protein-free formula should be given initially and small amount of protein (eg breast milk) is gradually introduced after 48 hours depending on baby's clinical status.
- If the index patient presented after the first week, 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 tests result as soon as possible to decide weather the baby is affected or not.

Chapter 89: Investigating Inborn errors 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 two or more developmental domains.
- Investigation done only after a thorough history and physical examination.
- If diagnosis is not apparent after the above, then investigations may be considered as listed below.
- 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.

Basic screening Investigations
Karyotyping
Serum creatine kinase
Thyroid function test
Serum uric acid
Blood Lactate
Blood ammonia
Metabolic screening using Guthrie card[1]
Plasma Amino acids[2]
Urine organic acid[2]
Neuroimaging[3]
Fragile X screening (boy)

1, This minimal metabolic screen should be done in all even in the absence of risk factors.

2, This is particularly important if one or more of following risk factors: Consanguinity, family history of developmental delay, unexplained sib 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 (eg. macro/microcephaly; seizure; focal motor findings on neurologic examination such as hemiplegia, nystagmus, optic atrophy; and unusual facial features eg. hypo/hypertelorism)

- If history and physical examination reveals specific clinical signs and symptoms, a large number of potential further investigations for possible IEM may be available. Many of these are highly specialised investigations and are expensive – it is not suggested they are all undertaken but considered. Referral to a clinical geneticist or metabolic specialist is useful at this stage to help with test selection based on "pattern recognition".

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 increased? If yes, suggest true elevation of lactate*
Ammonia↑	• Sample contamination • Sample delayed in transport/processing • Specimen hemolysed • Urea cycle disorders • Liver dysfunction
Uric acids	An abnormality high or low result is significant: • Glycogen storage disorders↑ • Purine disorders↑ • Molybdenum cofactor deficiency ↓

Metabolic/Genetic tests for specific clinical features	
Developmental delay and ...	**Disorders and Tests**
Severe hypotonia	*Peroxisomal disorders* Very long chain fatty acids (B)
	Purine/pyrimidine disorders Purine/pyrimidine analysis (U)
	Neurotransmitters deficiencies Neurotransmitters analysis (C)
	Neuropathic organic acidemia Organic acid analysis (U)
	Pompe disease Lysosomal enzyme (G)
	Prader Willi syndrome Methylation PCR (B)
Neurological regression + organomegaly + skeletal abnormalities	*Mucopolysaccharidoses* Urine MPS (U)
	Oligosaccharidoses Oligosaccharides (U)
Neurological regression ± abnormal neuroimaging e.g. leukodystrophy	*Other lysosomal disorders* Lysosomal enzyme (B)
	Mitochondrial disorders Respiratory chain enzymes (M/S)
	Biotinidase deficiency Biotinidase assay (G)
	Peroxisomal disorders Very long chain fatty acids (B)
	Rett syndrome (girl) MECP2 mutation study (B)
Abnormal hair	*Menkes disease* Copper (B), coeruloplasmin (B)
	Argininosuccinic aciduria Amino acid (U/B)
	Trichothiodystrophy Hair microscopy
B=blood, C=cerebrospinal fluid, U=urine, G=Guthrie card	

Metabolic/Genetic tests for specific clinical features *(continued)*	
Developmental delay and ...	Disorders and Tests
Macrocephaly	*Glutaric aciduria type I* Organic acids (U)
	Canavan disease Organic acid (U)
	Vanishing white matter disease DNA test (B)
	Megalencephalic leukodystrophy with subcortical cysts (MLC) DNA test (B)
Dysmorphism	*Microdeletion syndromes* FISH, aCGH (B)
	Peroxisomal disorders Very long chain fatty acids (B)
	Smith Lemli Opitz syndrome Sterol analysis (B)
	Congenital disorders of glycosylation Transferrin isoform (B)
Dystonia	*Wilson disease* Copper (B), coeruloplasmin (B)
	Neurotransmitters deficiencies Phenylalanine loading test, Neurotransmitters analysis (C)
	Neuroacanthocytosis Peripheral blood film, DNA test (B)
B=blood, C=cerebrospinal fluid, U=urine, G=Guthrie card, aCGH=array comparative genomic hybridization	

Metabolic/Genetic tests for specific clinical features *(continued)*	
Developmental delay and ...	Disorders and Tests
Epileptic encephalopathy	*Nonketotic hyperglycinemia* Glycine measurement (B and C)
	Molybdenum cofactor deficiency/ sulphite oxidase deficiency Sulphite (fresh urine)
	Glucose transporter defect Glucose (blood and CSF)
	Pyridoxine dependency Pyridoxine challenge, alpha aminoadipic semiadehyde (U)
	PNPO deficiency Amino acid (C), Organic acid (U)
	Congenital serine deficiency Amino acid (B and C)
	Cerebral folate deficiency CSF folate
	Ring chromosome syndromes Karyotype
	Neuronal ceroid lipofuscinosis Peripheral blood film, lysosomal enzyme (B)
	Creatine biosynthesis disorders MR spectroscopy
	Adenylosuccinate lyase deficiency Purine analysis (U)
	Cerebral dysgenesis e.g. lissencephaly MRI brain
	Angelman syndrome Methylation PCR
Spastic paraparesis	*Arginase deficiency* Amino acid (B)
	Neuropathic organic academia Organic acid (U)
	Sjogren Larsson syndrome Detailed eye examination
B=blood, C=cerebrospinal fluid, U=urine, G=Guthrie card, aCGH=array 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 multisystemic disease.
- Hepatic clinical response to IEM or acquired causes such as infection is indistinguishable.
- 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, ↑ammonia, ↑lactate, ↑plasma amino acids (tyrosine, phenylalanine, methionine), positive urine reducing substances (including galactose), an abnormal urine organic acid/blood acylcarnitine profiles.

Citrin deficiency

Recognized clinical phenotypes:

- Neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD)
  - Characterized by transient neonatal cholestasis and variable hepatic dysfunction.
  - Diagnosis: elevated plasma citrulline, galactossemia (secondary).
  - Treatment: lactose-free and/or MCT-enriched formula.
- Failure to thrive and dyslipidemia caused by citrin deficiency (FTTDCD)
  - Characterized by post-NICCD growth retardation and abnormalities of serum lipid concentrations.
  - A strong preference for protein-rich and lipid-rich foods and an aversion to carbohydrate-rich foods.
  - Diagnosis: mutation testing (plasma citrulline is normal at this stage)
  - Treatment: diet rich in protein and lipids and low in carbohydrates, sodium pyruvate.
- Citrullinemia type II (CTLN2)
  - Characterized by childhood- to adult-onset, recurring episodes of hyper ammonemia and associated neuropsychiatric symptoms.
  - Treatment: liver transplant.

IEM presenting mainly with Liver disease			
Leading manifestation patterns	Metabolic/genetic causes to be considered	Clues	Diagnostic tests
Acute/subacute hepatocellular necrosis (↑AST, ↑ALT jaundice, hypoglycaemia, ↑NH3, bleeding tendency, ↓albumin, ascitis)	Neonatal/ early infantile		
	*Neonatal haemochromatosis	↑↑↑ferritin	Buccal mucosa biopsy
	*Galactosemia	Positive urine reducing sugar, cataract	GALT assay
	*Long-chain fatty acid oxidation disorders	Associated (cardio)myopathy	Blood acylcarnitine
	*mtDNA depletion syndrome	Muscular hypotonia, multi-systemic disease, encephalopathy, nystagmus, ↑↑lactate (blood and CSF)	Liver biopsy for mtDNA depletion study
	*tyrosinemia type I	Severe coagulopathy, mild ↑AST/ALT, renal tubulopathy, ↓PO_4,↑↑↑AFP	Urine succinylacetone
	*Congenital disorders of glycosylation	Multi-system disease, protein-losing enteropathy	Transferrin isoform analysis
	Must rule out infections	Aetiology: TORCHES, parvovirus B19, echovirus, enteroviruses, HIV,EBV, HepB, Hep C	Serology, urine/stool viral culture

IEM presenting mainly with Liver disease *(continued)*			
Leading manifestation patterns	Metabolic/genetic causes to be considered	Clues	Diagnostic tests
Acute/subacute hepatocellular necrosis (↑AST, ↑ALT jaundice, hypoglycaemia, ↑NH3, bleeding tendency, ↓albumin, ascitis)	Late infancy to childhood		
	* above causes		
	*α-1-antitrypsin deficiency	Commonly presents as cholestatic jaundice, gradually subsides before 6 months. Some develop cirrhosis later. Less commonly may present as liver failure in early infancy	α-1-antitrypsin
	*Fructosemia	Symptoms after fructose intake, renal tubulopathy	
	*Wilson disease	KF ring, neurological symptoms, haemolysis	Serum/urine copper, coeruloplasmin
	Must rule out chronic viral hepatitis and autoimmune diseases		

IEM presenting mainly with Liver disease *(continued)*			
Leading manifestation patterns	Metabolic/genetic causes to be considered	Clues	Diagnostic tests
Cholestastic liver disease (conjugated bilirubin >15%, acholic stool, yellow brown urine, pruritus, ↑↑ALP) GGT may be low, normal or high - useful to differentiate various causes	Neonatal		
	*Alagille syndrome	Eye/cardiac/vertebral anomalies	DNA study
	*Inborn error bile acid synthesis	↓ or normal GGT	Liver biopsy,DNA study
	*Progressive familial intra-hepatic 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, opthalmoplegia, hepatosplenomegaly	Bone marrow examination
	* Peroxisomal disorders	Severe hypotonia, cataract, dysmorphic, knee calcification	Plasma VLCFA
	*α-1-antitrypsin deficiency	see above	α-1-antitrypsin
	Must exclude extrahepatic biliary disease		

IEM presenting mainly with Liver disease *(continued)*			
Leading manifestation patterns	Metabolic/genetic causes to be considered	Clues	Diagnostic tests
Cholestastic liver disease (conjugated bilirubin >15%, acholic stool, yellow brown urine, pruritus, ↑↑ALP) GGT may be low, normal or high - useful to differentiate various causes	Late infancy to childhood		
	* above causes		
	* Rotor syndrome	Normal liver function	Diagnosis by exclusion
	* Dublin-Johnson	Normal liver function	Diagnosis by exclusion
Cirrhosis (end stage of chronic hepato-cellular disease) chronic jaundice, clubbing, spider angiomatoma, ascites, portal HPT	*Wilson disease	KF ring, neurological symptoms, haemolysis	Serum/urine copper, coeruloplasmin
	*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
	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 a child with an apparently isolated cardiomyopathy, must actively screen for subtle/additional extra-cardiac involvement included studying renal and liver function as well as ophthalmological and neurological examinations.
- Cardiomyopathy may be part of clinical features of some genetic syndromes especially Noonan syndrome, Costello syndrome, Cardiofaciocutaneous syndrome.
- Sarcomeric protein mutations are responsible for a significant cases of familial cardiomyopathy.

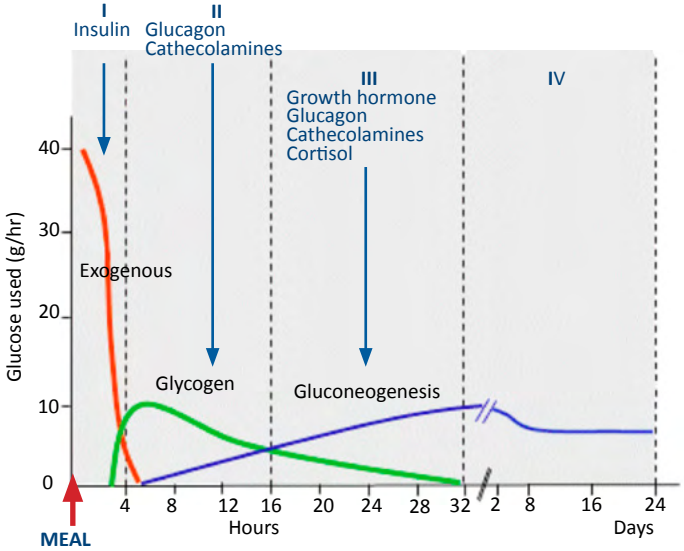
IEM that may present predominatly as Cardiomyopathy (CMP)		
Disorder	**Cardiac finding**	**Clues**
Primary carnitine deficiency	Dilated CMP	Low serum free carnitine
Long chain fatty acid oxidation disorders	Hypertrophic/ Dilated CMP	Myopathy, retinopathy, hypoketotic hypoglycaemia, abnormal acylcarnitne profile
Mitochondrial disorders	Hypertrophic/ Dilated CMP	Associated with multi-system abnormalities, ↑↑lactate *Kearns– Sayre syndrome:* Chronic progressive external ophthalmoplegia ,complete heart block
Barth syndrome	Dilated CMP	Neutropenia, myopathy, abnormal urine organic acid (↑3 methylglutaconic aciduria)
Infantile pompe disease	Hypertrophic CMP	Short PR, very large QRS, ↑CK, ↑AST, ↑ALT, deficient alpha acid glucosidase enzyme activity (could be done using dried blood spots)
Glycogen Storage Disease type III	Hypertrophic CMP	Hepatomegaly, ↑CK, ↑AST, ↑ALT, ↑postprandial lactate, ↑uric acid, ↑TG

IEMs presenting as mainly a Haematological disorder	
Clinical problem	**Metabolic/Genetic causes and Clues/tests**
Megaloblastic anemia	*Defective transportation or metabolism of B12* Methylmalonic aciduria, ↑homocysteine, low/normal serum B12.
	Orotic aciduria ↑↑ urinary orotate.
	Disorders of folate metabolism ↓serum folate.
Global marrow failure	*Pearson syndrome* Exocrine Pancreatic dysfunction, lactate, renal tubulopathy.
	Fanconi anemia Cafe au lait spots, hypoplastic thumbs, neurological abnormalities, increased chromosomal breakage.
	Dyskeratosis congenita Abnormal skin pigmentation, leucoplakia and nail dystrophy; premature hair loss and/or greying.

Introduction

Definition of hypoglycemia:

- Consensus for thresholds at which intervention should be considered:
  - <2.2 mmol/L (40 mg/dl) on first day of life.
  - 2.2–2.8 mmol/L (40-50 mg/dl) after 24 hours of age.



Phase	I: Post Prandial	II: Short to Middle Fast	III: Long Fast	IV: Very Long Fast
Glucose source	Exogenous	Glycogen Gluconeo-genesis	Gluconeo-genesis (hepatic) Glycogen	Gluconeo-genesis (hepatic and renal)
Counsuming tissues	All	All but liver, muscle	-	Brain, blood cell, medullary kidney
Greatest brain nutrient	Glucose	Glucose	Glucose	Ketone bodies Glucose

Clinical classification of hypoglycemia

- According to its timing:
  - Only postprandial.
  - Only at fast.
  - Permanent/hectic.
- According to liver findings:
  - With prominent hepatomegaly.
  - Without prominent hepatomegaly.
- According to lactic acid:
  - With lactic acidosis (lactate > 6mmol/l).
  - With hyperlactatemia (lactate 2.5–6mmol/l).
  - With normal lactate (lactate < 2.5 mmol/l).
- According to ketosis:
  - Hyper/normoketotic.
  - Hypoketotic/nonketotic.

Laboratory tests during symptomatic hypoglycemia

- Adequate laboratory tests must be done to identify the cause, or else the diagnosis may be missed.
- Ensure samples are taken before correcting the hypoglycemia.

Laboratory tests during symptomatic hypoglycemia	
Essential Tests	Other tests
Ketone (serum or urine)	Serum cholesterol/triglyceride
Acylcarnitine (dry blood spots on Guthrie card)	Serum uric acid
Blood lactate	Liver function
VBG	Creatine kinase
Blood ammonia	Urine reducing sugar
Urine organic acids	Urine tetraglucoside
Free fatty acids (if available)	Plasma amino acid
Serum insulin	Consider toxicology tests (C-peptide)
Serum cortisol	Fasting tolerance test (only by metabolic specialist/ endocrinologist)
Serum growth hormone	Other special tests e.g. fatty oxidation study in cultured fibroblasts

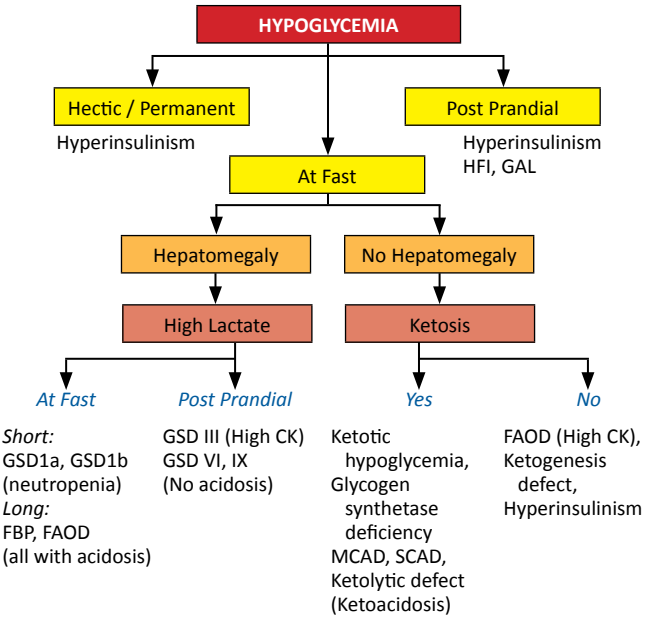
DETERMINE THE CAUSE

This can be approached using the following algorithm which is based first on 2 major clinical findings :

(1) Timing of hypoglycemia and

(2) Permanent hepatomegaly.

Then looking carefully at the metabolic profile over the course of the day, checking plasma glucose, lactate, and ketones before and after meals and ketones in urines will allow one to reach a diagnosis in almost all cases..



Abbreviations:

HFI, Hereditary fructose intolerance; GAL, Galactosemia; GSD, Glycogen storage disease; FBP, Fructose-1,6-bisphosphatase deficiency; FAOD, Fatty acid oxidation disorders; MCAD, Medium chain acyl dehydrogenase deficiency; SCAD, Short chain acyl dehydrogenase deficiency.

GLYCOGEN STORAGE DISEASE

- *Hepatic type:* Type Ia, Ib, III, IV, VI, IX.
- *Clinical presentation:* Recurrent hypoglycemia, hepatomegaly, failure to thrive, "doll face", bleeding tendency (GSD I), hypertrophic cardiomyopathy (GSD III).
- *Laboratory findings:* ↑lactate, ↑uric acid, ↑triglycerides, (↑) transaminases, ↑CK (GSD III), ↑ urine tetraglucosides.
- *Glucose challenge test:* Type Ia, Ib: ↓in lactate; Type III, VI, IX: ↑in lactate.
- *Diagnosis:* enzyme studies (liver), mutation analysis.
- *Treatment:*
  - Avoid hypoglycemia by means of continuous carbohydrate intake.
  - Frequent meals (every 2-3 hours): Slowly resorbed carbohydrates (glucose polymer/maltodextrin, starch), avoid lactose.
  - Nights: Continous intake of glycose polymer/maltodextrin via nasogastric tube, uncooked cornstarch in children > 1 year age.
- *Complications:* liver tumours, osteoporosis, cardiomyopathy (GSD III).

HYPERINSULINAEMIC HYPOGLYCAEMIA

Diagnostic criteria

- Glucose infusion rate > 8mg/kg/min to maintain normoglycaemia.
- Detectable serum insulin (+/- C-peptide) when blood glucose < 3mmol/l.
- Low or undetectable serum fatty acids.
- Low or undetectable serum ketone bodies.
- Serum ammonia may be high (Hyperinsulinism/hyperammonaemia syndrome).
- Glycaemic response to glucagon at time of hypoglycaemia.
- Absence of ketonuria.

Causes

- Congenital Hyperinsulinism (Mode of inheritance)
  - ABCC8 (AR, AD)); KCNJ11 (AR, AD); GLUD1 (AD); GCK (AD); HADH (AR); HNF4A (AD); SLC16A1 (Exercise induced)(AD).
- Secondary to (usually transient)
  - Maternal diabetes mellitus (gestational and insulin dependent).
  - IUGR.
  - Perinatal asphyxia.
  - Rhesus isoimmunisation.
- Metabolic conditions
  - Congenital disorders of glycosylation (CDG), Tyrosinaemia type I.
- Associated with Syndromes
  - Beckwith-Wiedemann, Soto, Kabuki, Usher, Timothy, Costello, Trisomy 13, Mosaic Turner, Central Hypoventilation Syndrome.
- Other causes: Dumping syndrome, Insulinoma (sporadic or associated with MEN Type 1), Insulin gene receptor mutations, Factitious HH (Munchausen-by-proxy).

Treatment for Recurrent Hypoglycaemia	
Medication	**Route / Dose**
Diazoxide	Oral, 5–20mg/kg/day divided into 3 doses
Side Effects	• Common: fluid retention, hypertrichosis. • Others: hyperuricaemia, eosinophilia, leukopenia.
Practical Management	• Use in conjunction with cholorothiazide especially in newborns. • Restrict fluid intake, especially on the higher doses. • Carefully monitor fluid balance.
Chlorothiazide	Oral, 7–10mg/kg/day divided into 2 doses
(used in conjunction with diazoxide)	
Side Effects	Hyponatraemia, hypokalaemia
Practical Management	Monitor serum electrolytes
Nifedipine	Oral, 0.25-2.5mg/kg/day divided into three doses
Side Effects	Hypotension
Practical Management	• Monitor blood pressure. • Not effective in patients with CHI due to defective KATP channels.
Glucagon (± Octreotide)	SC/IV infusion, 1–20µg/kg/hour
Side Effects	• Nausea, vomiting, skin rashes. • Paradoxical hypoglycaemia in high doses.
Practical Management	• Avoid high doses. • Watch for rebound hypoglycaemia when used as an emergency treatment for hypoglycaemia.
Octreotide (± Glucagon)	SC/IV continuous infusion or 6–8-hourly SC injections; 5–25µg/kg/day
Side Effects	• Common- tachyphylaxis • Others- Suppression of GH, TSH, ACTH, glucagon; diarrhoea, steatorrhoea, cholelithiasis, abdominal distension, growth suppression.
Practical Management	• Use with caution in infants at risk of necrotising enterocolitis, (reduces blood flow to the splanchnic circulation). • Follow-up with serial ultrasound scans of the biliary tree, if on long-term treatment with Octreotide. • Monitor long-term growth.

Incidence of Down syndrome	
Maternal Age-Specific Risk for Trisomy 21 at Livebirth	
Overall Incidence: 1 in 800-1000 newborns	
Age (years)	**Incidence**
20	1 in1500
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	

Medical problems

Newborn

- Cardiac defects (50%): AVSD [most common], VSD, ASD, TOF or PDA
- Gastrointestinal (12%): duodenal atresia [commonest], pyloric stenosis, anorectal malformation, tracheo-oesophageal fistula, and Hirshsprung disease.
- Vision: congenital cataracts (3%), glaucoma.
- Hypotonia and joint laxity
- Feeding problems. Usually resolves 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%), glau coma, 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.
  - 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:
  - Echocardiogram by 2 weeks (if clinical examination or ECG were abnormal) or 6 weeks.
  - Chromosomal analysis.
  - T4 /TSH at birth or by 1-2 weeks of life.
- 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 below*

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 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.

Karyotyping in Down syndrome	
Non-disjunction trisomy 21	95%
Robertsonian Translocation	3%
Mosaicism	2%
Recurrence Risk by Karyotype	
Nondisjunction Trisomy	
47(XX or XY) + 21	1%
Translocation	
Both parents normal	low; <1%
Carrier Mother	10%
Carrier Father	2.5%
Either parent t(21q;21q)	100%
Mosaics	< 1%

Useful web resources

- The Down Syndrome Medical Interest Group (UK)
  www.dsmig.org.uk
- Down Syndrome: Health Issues
  www.ds-health.com
- Growth charts for children with Down Syndrome
  www.growthcharts.com
- Educational issues
  www.downsed.org
- Kiwanis Down Syndrome Foundation
  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/

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 tests[1]	T4, TSH		T4, TSH, antibodies		T4, TSH, antibodies	
Growth monitoring [2]	Length, weight and head circumference checked regularly and plotted on Down's syndrome growth charts.			Length and weight should be checked at least annually and plotted on Down's syndrome growth charts.		
Eye examination	Visual behaviour. Check for congenital cataract	Visual behaviour. Check for congenital cataract	Visual behaviour. Check for congenital cataract	Orthoptic, refraction, ophthalmic examination[3]		Visual acuity, refraction, ophthalmic examination[3]
Hearing check	Neonatal screening	Full audiological review (hearing, impedance, otoscopy) by 6-10 months and then annually.				
Cardiology, Other advice	Echocardiogram 0-6 weeks			Dental assessment		

Age 5 to 19 years	
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 and employment	To discuss when appropriate, in adolescence.

Note: The above table are suggested ages. Check at any other time if parental or other concerns. Perform developmental assessment during each visit.

Footnote:
1, Asymptomatic patients with mildly raised TSH (<10mu/l) but normal T4 does not need treatment but test more frequently for uncompensated hypothyroidism.
2, Down syndrome centile charts at www.growthcharts.com. Consider weight for length charts of typically developing children for weight assessment. If BMI > 98th centile or underweigh, refer for nutritional assessment and guidance. Re-check thyroid function if accelerated weight gain.
3, Performed by optometrist/ophthalmologist.

Adapted from Down Syndrome Medical Interest Group (DSMIG) guidelines

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Ch 88 Inborn errors metabolism (IEM): Approach to Diagnosis and Early Management in a Sick Child

1.Saudubray JM, van den Berghe G, Walter J, eds. Inborn Metabolic Diseases: Diagnosis and Treatment. Berlin: Springer-Verlag, 5th edition, 2011

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5.T. Ohura, et al. Clinical pictures of 75 patients with neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD). J Inherit Metab Dis 2007.

Ch 90 Recurrent Hypoglycemia

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2.Saudubray JM, et al. Genetic hypoglycaemia in infancy and childhood : Pathophysiology and diagnosis J. Inherit. Metab. Dis. 23 (2000) 197-214

3.Khalid Hussain et al. Hyperinsulinaemic hypoglycaemia. Arch. Dis. Child (2009).

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3.The Down Syndrome Medical Interest Group (UK). Guidelines for Essential Medical Surveillance for Children with Down Syndrome.

Chapter 92: 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 and diarrhoea, tachycardia, poor urine output and poor perfusion of the peripheries are indicators of dehydration.
- *Tenderness* on palpation or percussion is essential for the diagnosis. 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. Eliciting 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, obese 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 as the cause of the abdominal pain.
- *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.

- If unsure of the diagnosis, the child is very ill or there are no facilities or personnel for intensive care, the child must be referred to the nearest paediatric surgical unit.

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.
- A*ppendicular abscess*, mass and perforation may be treated with IV 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. The heart rate, blood pressure, 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 aliquots of normal saline or Hartmann's solution (Ringer's lactate) given fast over ½ - 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 – ½ saline + 5% D/W + KCl.
- Antibiotics must be started early, soon after the diagnosis is made.
- Inotropes may need to be started early if the child is in severe sepsis.
- Operation - There is no rush to take the child to the operating theatre. 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.

- Vomiting in the child is NOT normal.
- Bilious vomiting is ALWAYS significant until otherwise proven

Causes of Persistent Vomiting
Neonates
General
• Sepsis
• Meningitis
• Hydrocephalus/ neurological disorder
• Urinary tract infection
• Motility disorder
• Inborn errors of metabolism
• Congential adrenal hyperplasia
• Poor feeding techniques
Oesophageal
• Atresia
• Webs
• Swallowing disorders
Stomach
• Gastro-oesophageal reflux
• Duodenal atresia/ stenosis
Small intestines
• Malrotation
• Stenosis/ atresia
• Adhesions/ Bands
• Meconium peritonitis/ ileus
• Enterocolitis
Large intestine/ rectum
• Stenosis/ atresia
• Hirschprung's disease
• Anorectal malformation

Causes of Persistent Vomiting *(continued)*
Infants
General
• Sepsis
• Meningitis
• Hydrocephalus/ neurological disorder
• Urinary tract infection
• Tumours eg neuroblastoma
• Metabolic disorders
• Oesophageal stricture
Stomach
• Gastro-oesophageal reflux
• Pyloric stenosis
Small intestines
• Malrotation/ volvulus
• Adhesions
• Meckel's diverticulum
• Hernias
• Appendix- rare
Large intestines
• Intussusception
• Hirschprung's disease
• Enterocolitis/gastroenteritis

Causes of Persistent Vomiting *(continued)*
Older Child
General
• Sepsis
• Neurological disorder
• Tumours
• Metabolic disease
• Oesophageal stricture
Stomach
• Gastro-oesophageal stricture/ reflux
• Peptic ulcer disease
• Gastric volvulus
Small intestines
• Malrotation/ volvulus
• Adhesions
• Meckel's diverticulum
• Appendicitis/ peritonitis
Large intestines
• Intussusception
• Foreign body
• Worm infestation
• Constipation: habitual

When is the vomiting significant?

- Vomiting from Day 1 of life.
- Vomit contains blood (red/black).
- Bilious vomiting: green, not yellow. Bowel obstruction must be ruled out.
- Faeculent vomiting.
- Projectile vomiting.
- Baby is unwell - dehydrated/septic.
- Associated failure to thrive.
- Associated diarrhoea/constipation.
- Associated abdominal distension.

GASTRO-OESOPHAGEAL REFLUX

- More common in infancy than generally recognized.
- Majority (>90%) resolve spontaneously within the first year of life.
- Small percentage develop complications.
- Please refer Ch 74 Gastroesophageal Reflux Disease (GERD)

PYLORIC STENOSIS

- Cause- unknown.
- Usually first born baby boy; usual presentation at 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.

Investigations

Investigation to confirm diagnosis are usually unnecessary.

- Ultrasound.
- Barium meal.

However, 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
  - Slow (rapid will cause cerebral oedema) unless the child is in shock
- Fluid
  - ½ saline + 10%D/W (+ 5-10 mmol KCL/kg/day) .
  - Rate (mls/hr) = [Maintenance (150 ml/kg body weight) + 5-10 % dehydration {% dehydration x body weight (kg) x 10}] /24 hours.
  - Replace gastric losses with normal saline.

Do NOT give Hartmann's solution (the lactate will be converted to bicarbonate which worsens the alkalosis)

- Insert a nasogastric tube – 4 hourly aspiration with free flow.
- Comfort glucose feeds maybe given during the rehydration period but the nasogastric tube needs to be left on free drainage.
- Pyloromyotomy after the electrolytes have been corrected.

MALROTATION

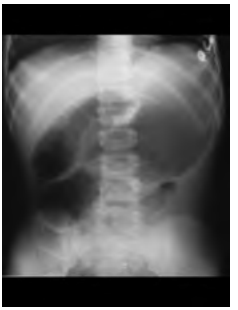
- A term that embraces a number of different types of abnormal rotation that takes place when the bowel returns into the intra-abdominal cavity in utero. This is Important because of the propensity for volvulus of the mid-gut around the superior mesenteric artery causing vascular compromise of most of the small bowel and colon.

Types of Clinical Presentation

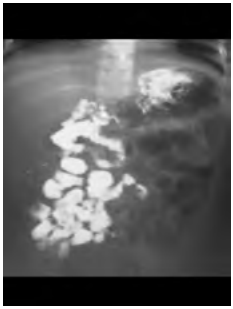
- Acute Volvulus
  - Sudden onset of bilious/ non-bilious vomiting.
  - Abdominal distention with/without a mass (late sign).
  - Bleeding per rectum (late sign).
  - Ill baby with distended tender abdomen.
- Chronic Volvulus
  - Caused by intermittent or partial volvulus resulting in lymphatic and venous obstruction.
  - Recurrent colicky abdominal pain.
  - Vomiting (usually bilious).
  - Malabsorption.
  - Failure to thrive.
- Internal Herniation
  - Due to lack of fixation of the colon.
  - Results in entrapment of bowel by the mesentery of 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.



- Upper Gastrointestinal contrast study with follow through
  - Duodeno-jejunal flexure to the right of the vertebra.
  - Duodenal obstruction, often with spiral or corkscrew appearance of barium flow.
  - Presence of small bowel mainly on the right side.



Treatment

Pre-operative Management

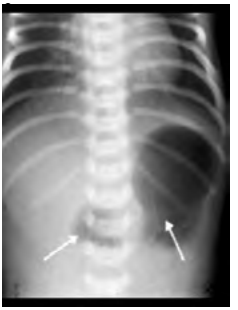
- Rapid rehydration and correction of electrolytes
- Fluids
  - Maintenance – ½ saline + 5% (or 10% if neonate) Dextrose Water with added KCl.
  - Rehydration – Normal saline or Hartmann's Solution (Ringer's Lactate)
- Orogastric or nasogastric tube with 4 hourly aspiration and free drainage
- Antibiotics (+ inotropes) if septic.

Operative

- De-rotation of volvulus.
- ± Resection with an aim to preserve maximum bowel length (consider a second look operation if most of the bowel appears of doubtful viability).
- Division of Ladd's bands to widen the base of the mesentery to prevent further volvulus.
- Appendicectomy.

Duodenal Stenosis/ Atresia

- Usually at the second part of the duodenum
- Presents with bilious/non-bilious vomiting
- Can be associated with Down's Syndrome and gastro-oesophageal reflux.
- Abdominal X-Ray – double – bubble with or without gas distally



Management

- Slow rehydration with correction of electrolytes and nutritional deficiencies.
- Duodeno-duodenostomy as soon as stabilized.
- Postoperatively, the bowel motility may be slow to recover.

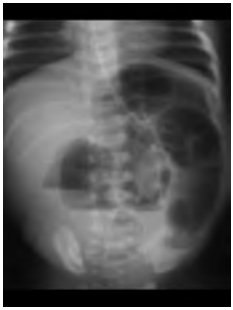
Ileal /Jejunal Atresia

- Atresia anywhere along the small bowel. Can be multiple.
- Presents usually with abdominal distension and vomiting (non-bilious initially and then bilious)
- Usually pass white or pale green stools, not normal meconium.
- Differential diagnoses – Long segment Hirschsprung's disease, Meconium ileus.

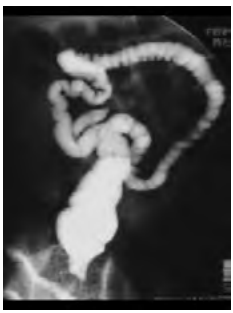
Management

- Evaluation for associated anormalities.
- Insertion of an orogastric tube – 4 hourly aspiration and free drainage.
- Replace losses with Hartmann's solution (Ringer's lactate).
- Rehydration of the baby with correction of the electrolytes and acidosis.
- Laparotomy and resection of the dilated bowels with primary anastomosis, preserving as much bowel length as possible.
- Parenteral nutrition as the motility of the bowel can be abnormal and take a long time to recover.

- AXR – dilated loops of small bowel.



- Contrast enema – microcolon



Chapter 94: 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 IV 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 4 years. Majority of the children in this age group have no pathological lead point. Lymphoid hyperplasia has been implicated. 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

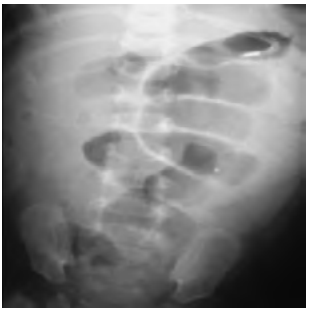
- Previously healthy or preceding viral illness.
- Pain - Sudden onset, severe intermittent cramping pain lasting seconds to minutes.
- During the time in-between attacks lasting between 5 to 30 minutes, the child may be well or quiet.
- Vomiting – Early reflex vomiting consists of undigested food but 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

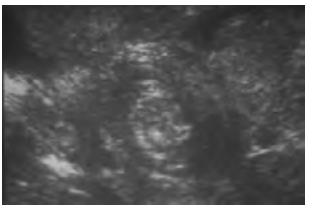
- Well- looking/drowsy/dehydrated/fitting (due to hyponatremia) depending on the stage of presentation.
- Abdominal mass (sausage shaped but may be difficult to palpate in a distended abdomen).
- Abdominal distension is a late sign.

Investigations

- Plain abdominal X-ray – Absence of caecal gas, paucity of bowel gas on the right side with loss of visualization of the lower border of the liver, dilated small bowel loops (see figure below).



- Ultrasound – Useful diagnostic tool. Target sign (see figure below) on transverse section and pseudo-kidney sign on longitudinal section. May also help to identify lead points if present.



- Barium enema – for diagnosis and reduction if required.

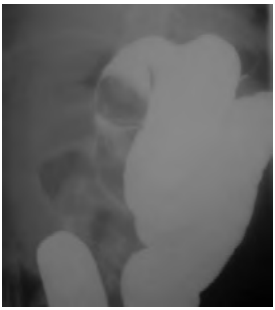
Management

Resuscitation

- Aggressive rapid rehydration with boluses of 20 mls/kg of Normal saline/Hartmann's solution (Ringer's lactate) till parameters are normal.
- Do NOT proceed to hydrostatic 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, successful reduction rate is about 80-90%.
- Types
  - Barium enema reduction. (see figure below: "claw sign" of intussusceptum is evident).
  - Air/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.

Contraindications to enema reduction

- Peritonitis.
- Bowel Perforation.
- Severe Shock.
- Neonates or children more than 4 years old (relative contraindication).
- History more than 48 hours.

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 about 30-60%.

Successful management of intussusception depends on high index of suspicion, early diagnosis, adequate resuscitation and prompt reduction.

Both are due to a patent processus vaginalis peritonei. The patent communication in the hydrocoele is smaller, so the 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.
- *Boy:girl* ratio = 6 : 1.
- *Site:* 60% right side but 10% may be bilateral.

Presentation

- Reducible bulge in groin – extends into scrotum when crying/straining.
- With complications.
- Lump in groin (girls) – sliding hernia containing ovary (rule out testicular feminization syndrome if bilateral)

Complications

- Incarceration/Irreducibility – Highest incidence (2/3) before age of 1 year.
- Testicular atrophy.
- Torsion of ovary.

Management

Reducible hernia:

- To operate (herniotomy) as soon as possible.
- *Premature:* before discharge (if possible at corrected age-44 to 60 week)
- *Infant:* as soon as possible.
- *Older child:* on waiting list.

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.
- If the manual reduction is successful, herniotomy is performed 24-48 hours later when the oedema subsides. If the reduction is not successful, the operation is performed immediately.

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 drainage of hydrocoele is done.

Chapter 96: 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 3.4%
  Premature 30.3%
- At 1 year: Full term 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). Surgery makes the testis more accessible to palpation and thus an earlier 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

- Ask mother whether she has ever felt the testis in the scrotum, more easily felt during a warm bath and when squatting.
- 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.
- If bilateral need to rule out dysmorphic syndromes, hypopituitarism, and chromosomal abnormalities (e.g. Klinefelter). Exclude virilized female (Congenital Adrenal Hyperplasia).
- 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. Results of hormonal therapy (HCG, LH-RH) have not been good.
- 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.

Causes of Acute Scrotum
Acute testicular torsion.
Torsion of epididymal and testicular appendages.
Epididymo-orchitis.
Incarcerated inguinal hernia.
Idiopathic scrotal oedema.
Acute hydrocele.
Henoch-Schonlein purpura.
Tumours.
Trauma.
Scrotal (Fournier's) gangrene.
Symptomatic varicocele.

TORSION OF THE TESTIS

Torsion of the testis is an emergency as failure to detort testis within 6 hours will lead to testicular necrosis.

Symptoms

- Sudden severe pain (scrotum and referred to lower abdomen)
- Nausea and vomiting
- No fever or urinary tract infection symptoms until later

Physical Findings

- Early
  - Involved testis - high, tender, swollen.
  - Spermatic cord – swollen, shortened and tender.
  - Contralateral testis - abnormal lie, usually transverse.
- Late
  - Reactive hydrocele.
  - Scrotal oedema.

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. The deformity is usually bilateral.

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, may be confused with torsion of testis.

Symptoms
- Age – 8-10 years old.
- Sudden onset of pain, mild initially but gradually increases in intensity.

Physical Examination
- Early
  - Minimal redness of scrotum with a normal non-tender testis
  - Tender nodule "blue spot" (upper pole of testis) is pathognomonic.
- Late
  - Reactive hydrocele with scrotal oedema makes 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.

Symptoms

- Gradual onset of pain with fever.
- May have a history of mumps.
- ± Dysuria/ frequency.

Physical examination

- 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.

Phimosis

Definition - True preputial stenosis
(In a normal child the foreskin is non-retractile till age of 5 years)

Causes

- Congenital - rare
- Infection- balanoposthitis
- Recurrent forceful retraction of foreskin
- *Balanoxerotica obliterans (BXO)

Symptoms

- Ballooning of foreskin on micturition.
- Recurrent balanoposthitis.
- Urinary retention.
- Urinary tract infection.

Management

- Treat infection if present.
- Elective circumcision.

**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)

Balanoposthitis

(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.

OESOPHAGEAL ATRESIA WITH OR WITHOUT A TRACHEO-OESOPHAGEAL FISTULA

Presentation

- Antenatal: polyhydramnios, diagnosed on ultrasound.
- "Mucousy" baby with copious amount of secretions.
- Unable to insert orogastric tube.
- Respiratory distress syndrome.
- Aspiration pneumonia and sepsis.

Problems

- Oesophageal Atresia: Inability to swallow saliva with a risk of aspiration pneumonia.
- Tracheo-oesophageal fistula: Reflux of gastric contents, difficult to ventilate.
- Distal obstruction: If present and the baby is ventilated, prone to perforation of bowel.
- Prematurity: If present, associated problems.

Management

- Evaluation for other anomalies/problems e.g. cardiac, intestinal atresias, pneumonia.
- Suction of the upper oesophageal pouch: A Replogle (sump suction) tube should be inserted and continuous suction done if possible. Otherwise, frequent intermittent suction (every 10-15 minutes) of oropharynx is done including throughout the journey to prevent aspiration pneumonia.
- Ventilation if absolutely necessary.
- Fluids - Maintenance and resuscitation fluids as required.
- Position - Lie the baby horizontal and lateral or prone to minimise aspiration of the saliva and reflux.
- Monitoring – Pulse oximetry and cardiorespiratory monitoring.
- Keep baby warm.
- Refer to nearest centre with neonatal and paediatric surgical facilities

Types

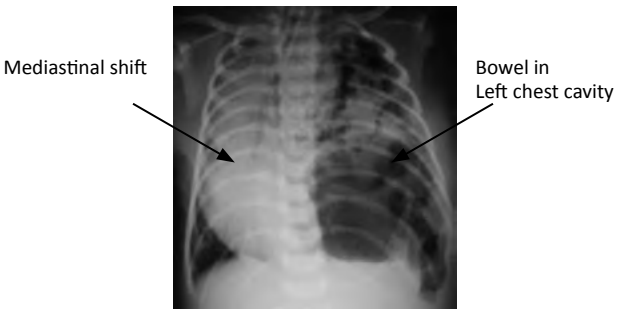
- Bochdalek: Posterolateral, commonest, more common on left side.
- Eventration of the diaphragm.
- Morgagni – anterior, retrosternal.

Problems

- Associated pulmonary hypoplasia.
- Herniation of the abdominal viscera into thoracic cavity causing mechanical compression and mediastinal shift.
- Reduced and abnormal pulmonary arterial vasculature resulting in persistent pulmonary hypertension of the newborn (PPHN) and reversal to foetal circulation.
- High mortality rate (40-60%) associated with early presentation.

Presentation

- Antenatal: Fluid filled stomach or bowel with/without liver in the left chest cavity.
- Mediastinal shift.
- Birth: Respiratory distress with cyanosis.
- Absent breath sounds on left side, scaphoid abdomen.
- Chest X-Ray: bowel loops within the chest and minimal bowel in abdomen.
- Late presentation
  - Left side: Gastrointestinal symptoms- bowel obstruction.
  - Right side: Respiratory symptoms including recurrent respiratory infections.
  - Asymptomatic: Abnormal incidental chest x-ray



Differential Diagnoses

- Congenital cystic adenomatoid malformation.
- Pulmonary sequestration.
- Mediastinal cystic lesions e.g. teratoma.

Management

- Evaluation for associated anomalies and persistent pulmonary hypertension of the newborn (PPHN).
- Ventilation - Intubation and ventilation may be required soon after delivery and pre-transport. Ventilation with a face-mask should be avoided. Low ventilatory pressures are to be used. A contralateral pneumothorax or PPHN need to be considered if the child deteriorates. If the baby is unstable or high ventilatory settings are required, the baby should not be transported.
- Frequent consultation with a paediatrician or paediatric surgeon to decide when to transport the baby.
- Chest tube - If inserted, it should not be clamped during the journey.
- Orogastric Tube: Gastric decompression is essential here. A Size 6 or 8 Fr tube is inserted, aspirated 4 hourly and placed on free drainage.
- Fluids – Caution required as both dehydration and overload can precipitate PPHN.
- May need inotropic support and other modalities to optimize outcome.
- Monitoring: Pre-ductal and post-ductal pulse oximetry to detect PPHN.
- Position: Lie baby lateral with the affected side down to optimise ventilation.
- Warmth.
- Consent: High risk.
- Air transport considerations.
- Referral to the paediatric surgeon for surgery when stabilised.

Factors most affecting the outcome

- Birth weight ≥ 2kg: Good outcome.
- Apgar score at 5 minutes of 7-10: Good outcome.
- Size of defect: If primary repair is achieved, 95% survival vs 57% survival in agenesis.
- Willford Hall/Santa Rosa predictive formula (WHSRpf) = Highest PaO2 – Highest PaCo2 (using arterial blood sample within 24 hours of life). If WHSRpf > 0, survival was 83 – 94%. If WHSRpf < 0, survival was only 32-34%.
- Cardiac anomalies- Survival was low for patients with haemodynamically significant cardiac defects (41.1%), compared to patients without cardiac lesions (70.2%)
- Late presentation more than 30 days of life: 100% survival.

ABDOMINAL WALL DEFECTS

- Exomphalos and Gastroschisis are commoner abdominal wall defects.
- Gastroschisis: Defect in the anterior abdominal wall of 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 may just be bowel loops.

Problems

- Fluid loss: Significant in gastroschisis due to the exposed loops of bowel.
- Hypothermia: Due to the larger exposed surface area.
- High incidence of associated syndromes and anomalies especially in exomphalos.
- Hypoglycemia can occur in 50% of babies with Beckwith-Wiedermann's Syndrome (exomphalos, macroglossia, gigantism).

Management

- Evaluation: for hydration and associated syndromes and anomalies.
- Fluids: IV fluids are essential as losses are tremendous especially from the 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 Saline + 10% D/W at 60 – 90 mls/kg (Day 1 of life) should also be given.
- 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 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 without compressing, twisting and kinking the bowel. Please do NOT use "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 to keep the child dry.
- Monitoring: Heart rate, Capillary refill time, Urine output (the baby may need to be catheterised to monitor urine output or have the nappies weighed).
- Position: The baby should be placed in a lateral position to prevent tension and kinking of the bowel.
- Referral to the surgeon as soon as possible.

INTESTINAL OBSTRUCTION

- *Cause* -May be functional e.g. Hirschsprung's disease or mechanical e.g. atresias, midgut malrotation with volvulus.

Problems

- Fluid loss due to the vomiting, bowel dilatation and third space losses.
- Dehydration.
- Diaphragmatic splinting.
- Aspiration secondary to the vomiting.
- Nutritional deficiencies.

Presentation

- Antenatal diagnosis – dilated fluid-filled bowels.
- Delay in passage of meconium (Hirschsprung's disease, atresias).
- Vomiting – bilious/non-bilious (Bilious vomiting is due to mechanical obstruction until proven otherwise).
- Abdominal distension.
- Abdominal X-ray – dilated loops of bowel.

Management

- Evaluation – for onset of obstruction and associated anomalies (including anorectal anomalies).
- Fluids – Intravenous fluids are essential.
- Boluses - 10-20 mls/kg Hartmann's solution/Normal Saline to correct dehydration and replace the measured orogastric losses.
- Maintenance - ½ Saline + 10% D/W + KCl as required.
- Orogastric tube – Gastric decompression is essential, a Size 6 or 8 Fr tube is inserted, aspirated 4 hourly and placed on free drainage.
- If Hirschsprung's disease is suspected, rectal washout can be performed after consultation with a paediatrician or a paediatric surgeon.
- Warmth.
- Monitoring – vital signs and urine output.
- Air transport considerations during transfer to the referral centre.

ANORECTAL MALFORMATIONS

- Incidence – 1: 4,000-5,000 live births
- Cause- unknown
- Newborn check – important to clean off the meconium to check if a normal anus is present.

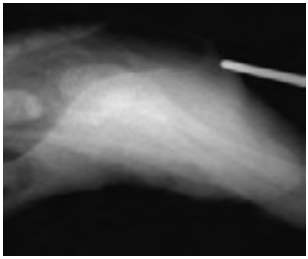
Classification (Pena)		
Type	**Clinical Features**	**Management**
Boys		
Perineal (cutaneous) fistula	• Low type. • Midline "snail-track". • "Bucket handle".	No colostomy required
Rectourethral fistula • Bulbar • Prostatic	• Most common. • Pass meconium in urine.	Colostomy
Rectovesical fistula	• High type. • Associated sacral anomalies.	Colostomy
Imperforate anus without fistula	• Usually Down syndrome. • Sacrum/sphincter - normal.	Colostomy
Rectal atresia	• Normal anal opening. • Atresia-2cm from anal verge. • Rare.	Colostomy
Girls		
Perineal (cutaneous) fistula	• Rectum and vagina well separated.	No colostomy required
Vestibular fistula	• Common • Fistula opening just posterior to hymen. • Common wall; rectum and vagina.	Colostomy
Persistent cloaca	• Rectum, Urethra, Vagina: Single common channel of variable length. • Single external opening. • Associated urogenital anomalies.	Colostomy + vesicostomy + vaginos-tomy
Imperforate anus without fistula	• Usually Down syndrome • Sacrum/sphincter - normal	Colostomy
Rectal atresia	• Rare. • Normal anal opening. • Atresia 2cm from anal verge.	Colostomy

Associated Anomalies

- Sacrum and Spine
  - Anomalies and spinal dysraphism is common.
  - Good correlation between degree of sacral development and final prognosis. Absence of more than 3 sacrum: poor prognosis.
- Urogenital
  - Common anomalies – vesicoureteric reflux, renal agenesis.
  - Incidence – low in low types and high in cloaca (90%).
  - Vaginal anomalies – about 30%.
- Others
  - Cardiac anomalies.
  - Gastrointestinal anomalies e.g. duodenal atresia.
  - Syndromes e.g. Trisomy 21.

Investigations

- Chest and Abdominal X-ray.
- Lateral Pronogram. (see Figure)
- Echocardiogram.
- Renal and Sacral Ultrasound.
- Micturating cystourethrogram.
- Distal loopogram.



Management

- Boys and Girls
  - Observe for 12-24 hours.
  - Keep nil by mouth.
  - If abdomen is distended, to insert an orogastric tube for 4 hourly aspiration and free drainage.
  - IV fluids – ½ saline with 10% Dextrose Water with KCl. May need rehydration fluid boluses if child has been referred late and dehydrated.
  - Start IV antibiotics.
  - Assess for urogenital, sacral and cardiac anomalies.

Boys

- Inspect the perineum and the urine – if there is clinical evidence of a low type, the child needs to be referred for an anoplasty. If there is evidence of meconium in the urine, the child requires a colostomy followed by the anorectoplasty a few months later.
- If there is no clinical evidence, a lateral pronogram should be done to check the distance of the rectal gas from the skin to decide if a primary anoplasty or a colostomy should be done.

Girls

- Inspect the perineum.
- If there is a rectovestibular fistula or a cutaneous fistula, then a primary anoplasty or a colostomy is done.
- If it is a cloacal anomaly, the child needs to be investigated for associated genitourinary anomalies. The baby then requires a colostomy with drainage of the bladder and hydrocolpos if they are not draining well. The anorectovaginourethroplasty will be done many months later.
- If there is no clinical evidence, a lateral pronogram should be done to check the distance of the rectal gas from the skin to decide if a primary anoplasty or a colostomy should be done.

HIRSCHSPRUNG'S DISEASE

- Common cause of intestinal obstruction of the newborn.

Aetiology

- Aganglionosis of the variable length of the bowel causing inability of the colon to empty due to functional obstruction of the distal bowel.
- The primary aetiology has been thought to be due to cellular and molecular abnormalities during the development of the enteric nervous system and migration of the neural crest cells into the developing intestine.
- Genetic factors play a role with an increased incidence in siblings, Down Syndrome, congenital central hypoventilation syndrome and other syndromes.

Types

- Rectosigmoid aganglionosis: commonest, more common in boys.
- Long segment aganglionosis.
- Total colonic aganglionosis: extending into the ileum or jejunum, almost equal male: female ratio.

Clinical Presentation

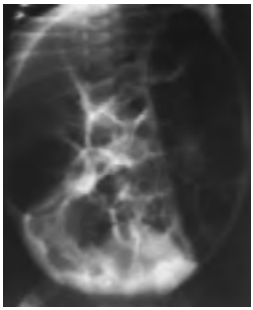
- May present as a neonate or later in life.
- Neonate.
  - Delay in passage of meconium (94-98% of normal term babies pass meconium in the first 24 hours).
  - Abdominal distension.
  - Vomiting – bilious/non-bilious.
  - Hirschsprung-associated enterocolitis (HAEC) – fever, foul smelling, explosive diarrhoea, abdominal distension, septic shock. Has a high risk of mortality and can occur even after the definitive procedure.
- Older child.
  - History of constipation since infancy.
  - Abdominal distension.
  - Failure to thrive.
  - Recurrent enterocolitis.

Other causes of delay in passage of meconium

- Prematurity.
- Sepsis, including urinary tract infection.
- Intestinal atresias.
- Meconium ileus.
- Hypothyroidism.

Investigation

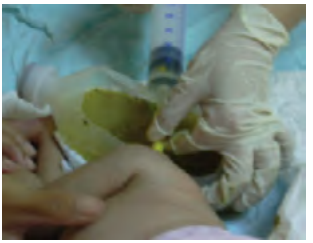
- Plain Abdominal X-ray – dilated loops of bowel with absence of gas in the rectum, sometimes a megacolon is demonstrated. (Figure below)



- Contrast enema – presence of a transition zone with an abnormal rectosigmoid index.
- Rectal Biopsy: Absence of ganglion cells and presence of acetylcholinesterase positive hypertrophic nerve bundles confirms the diagnosis

Management

- Enterocolitis (HAEC) – high risk of mortality. Can occur even after the definitive procedure.
- Aggressive fluid resuscitation.
- IV broad-spectrum antibiotics.
- Rectal washouts-Using a large bore soft catheter inserted into the colon past the transition zone, the colon is washed out with copious volumes of warm normal saline (in aliqouts of 10-20mls/kg) till toxins are cleared. (Figure below)



- If the decompression is difficult with rectal washouts, a colostomy or ileostomy is required.
- Definitive surgery, with frozen section to confirm the level of aganglionosis, is planned once the diagnosis is confirmed.
- Postoperatively, the child needs close follow-up for bowel management and the development of enterocolitis.

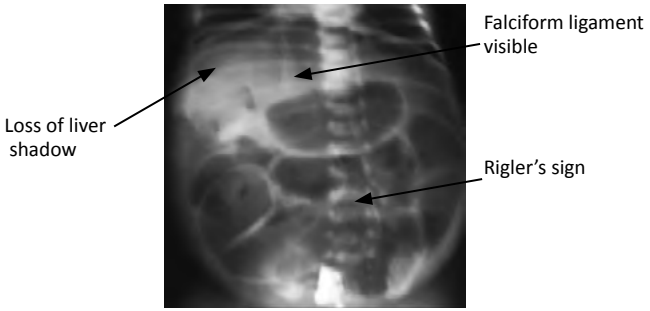
PERFORATED VISCUS

Causes

- Perforated stomach.
- Necrotising enterocolitis.
- Spontaneous intestinal perforations.
- Intestinal Atresias.
- Anorectal malformation.
- Hirschsprung's disease.

Management

- Evaluation: These babies are usually septic with severe metabolic acidosis, coagulopathy and thrombocytopenia.
- Diagnosis: A meticulous history of the antenatal, birth and postnatal details may elicit the cause of the perforation. Sudden onset of increased abdominal distension and deteriorating general condition suggests perforation.
- Supine abdominal x-ray showing free intraperitoneal gas. (Figure below)



- Ventilation: Most of the babies may require intubation and ventilation if they are acidotic and the diaphragm is splinted.
- Fluids: Aggressive correction of the dehydration, acidosis and coagulopathy should be done.
- Orogastric tube: It should be aspirated 4 hourly and left on free drainage.
- Urinary Catheter: Monitor hourly urine output
- Drugs: Will require antibiotics and possibly inotropic support
- Consultation with the paediatrician or paediatric surgeon of the regional referral centre before transfer of the baby.
- Peritoneal Drain: If there is a perforation of the bowel, insertion of a peritoneal drain (using a size 12-14 Fr chest tube or a peritoneal dialysis drain into the right iliac fossa) with/without lavage with normal saline or an isotonic peritoneal dialysate solution should be considered as a temporising measure while stabilising the baby prior to surgery. This can help to improve the ventilation as well as the acidosis.

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Definition

Definite arthritis of

- Unknown aetiology.
- Onset before the age 16 yrs.
- Persists for at least 6 wks.

Symptoms and Signs in JIA	
Articular	Extra-articular
Joint swelling	General • Fever, pallor, anorexia, loss of weight
Joint pain	
Joint stiffness / gelling after periods of inactivity	Growth disturbance • General: growth failure, delayed puberty • Local: limb length / size discrepancy, micronagthia
Joint warmth	
Restricted joint movements	Skin • subcutaneous nodules • rash – systemic, psoriasis, vasculitis
Limping gait	
	Others • Hepatomegaly, splenomegaly, lymphadenopathy, • Serositis, muscle atrophy / weakness • Uveitis: chronic (silent), acute in Enthesitis related arthritis (ERA)
	Enthesitis*
* inflammation of the entheses (the sites of insertion of tendon, ligament or joint capsule into bone)	

Helpful pointers in assessing articular symptoms			
	Inflammatory	Mechanical	Psychosomatic
Pain	+/-	+	+++
Stiffness	++	-	+
Swelling	+++	+/-	+/-
Instability	+/-	++	+/-
Sleep disturbance	+/-	-	++
Physical signs	++	+	+/-

Diagnosis and Differential diagnosis

- JIA is a diagnosis of **exclusion.**

Differential diagnosis of JIA	
Monoarthritis	**Polyarthritis**
Acute	JIA – polyarthritis (RF positive or negative), ERA, psoriatic arthritis
Acute rheumatic fever	
Reactive arthritis: Post viral/ post enteric /post streptococcal infection	Reactive arthritis
	Lyme disease
Septic arthritis / osteomyelitis	SLE
Early JIA	Other connective tissue diseases
Malignancy: leukaemia, neuroblastoma	Inflammatory bowel disease
Haemophilia	Sarcoidosis
Trauma	Familial hypertrophic synovitis syndromes
Chronic	Immunodeficiency syndromes
JIA: oligoarthritis, ERA, psoriatic	Mucopolysaccharidoses
Chronic infections: TB, fungal, brucellosis	
Pigmented villonodular synovitis	
Sarcoidosis	
Synovial haemangioma	
Bone malignancy	

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 being 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.

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 – exclude leukaemia. BMA may be required if there are any atypical symptoms/signs even if PBF is normal
  - 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 neccesary : complement levels, ASOT, Ferritin, immunoglobulins (IgG, IgA and IgM), HLA B27, synovial fluid aspiration for microscopy and culture, echocardiography, MRI/CT scan of joint, bone scan .*

Management

- Medical treatment
  - Refer management algorithm *(see following pages)*

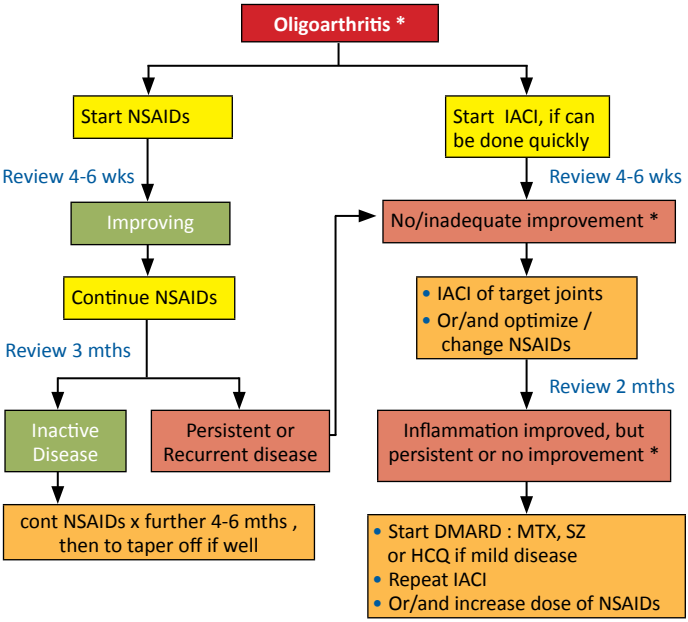
Dosages of drugs commonly used in JIA

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^2/dose (max 25 mg/dose)	1/week
Folic acid	2.5 - 5.0 mg per dose	1/week
Sulphasalazine	15 - 25 mg/kg/dose (start 2.5 mg/kg/dose and 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.

- Physiotherapy
  - Avoid prolonged immobilisation
  - Strengthens muscles, improves and maintains range of movement
  - Improves balance and cardiovascular fitness
- Occupational Therapy
  - Splinting when neccesary to reduce pain and preserve joint alignment.
  - To improve daily quality of life by adaptive aids and modifying the environment.
- 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.
- 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.

Oligoarthritis (1-4 joints)

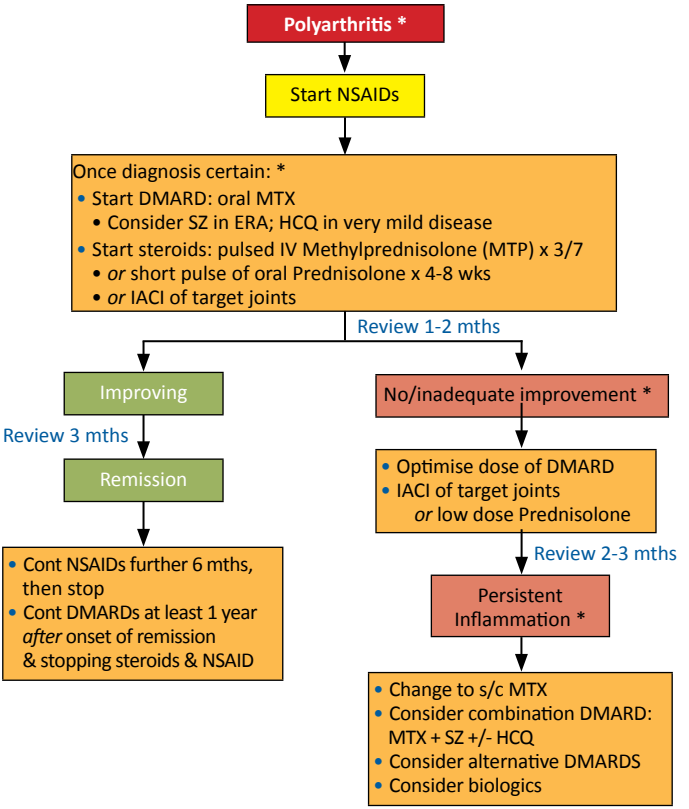


Remember to Screen for Uveitis

All patients with persistent inflammation should be on DMARDs within 6 months of diagnosis even if only having oligoarthritis.

Footnote:
**, Consider referral to Paeds Rheumatologist / reconsider diagnosis;*
Abbreviations:
IACI, Intra-articular corticosteroid injection; MTX , Methotrexate;
SZ, Sulphasalazine; HCQ, Hydroxychloroquine; DMARD, Disease modifying anti-rheumatic drugs.

Polyarthritis (> 5 joints)

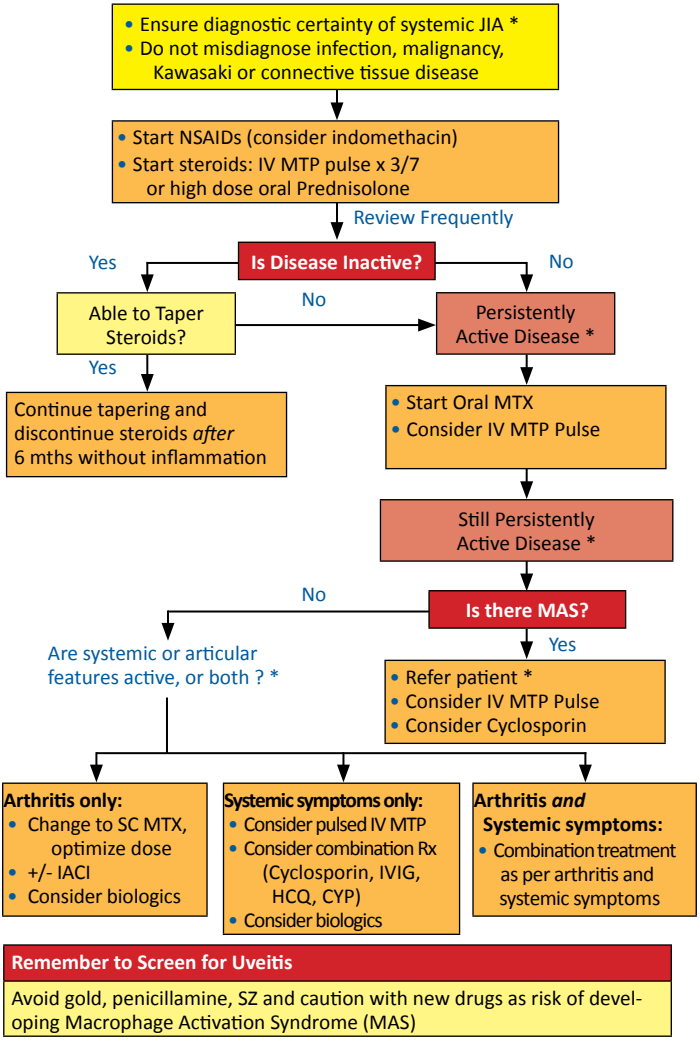


Remember to Screen for Uveitis

Best opportunity to achieve remission in first two years of disease
Avoid accepting low grade inflammation until all avenues explored

Footnote:
**, Consider referral to Paeds Rheumatologist / reconsider diagnosis;*
Abbreviations:
IACI, Intra-articular corticosteroid injection; MTX , Methotrexate;
SZ, Sulphasalazine; HCQ, Hydroxychloroquine; ERA, enthesitis related arthritis;
DMARD, Disease modifying anti-rheumatic drugs.

Systemic onset JIA



Footnote:
**, Consider referral to Paeds Rheumatologist / reconsider diagnosis;*
Abbreviations: as previous page; CYP, cyclophosphamide; IVIG, IV immunoglobulins.

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Section 14 Rheumatology

Chapter 100 Juvenile Idiopathic Arthritis

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Introduction

- In Malaysia there are approximately 40 species of venomous snakes (18 land snakes and all 22 of sea snakes) belonging to two families – elapidae and viperidae.
- 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 especially in the northern part of Peninsular Malaysia and 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 are complex substances proteins with enzymatic activity. Although enzymes play an important role the lethal properties are caused by certain smaller polypeptides. Components such as procoagulant enzymes activate the coagulation cascade, phospholipase A2 (myotoxic, neurotoxic, cardiotoxic causes haemolysis and increased vascular permeability), proteases (tissue necrosis), polypeptide toxins (disrupt neuromuscular transmissions) and other components.

Clinical features

- Cobra usually cause pain and swelling of the bite site but more worrying is the neurological dysfunctions: ptosis, ophthalmoplegia, dysphagia, aphasia and 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.
- Pit vipers – cause extensive local effects: immediate pain, swelling, blisters and necrosis, vascular effects and hemolysis and systemic effects such as coagulopathies. Bleeding occurs at bite site, gingival sulci and venepuncture sites. Venom alters capillary permeability causing extravasation of electrolytes, albumin and rbcs through the vessel wall into envomated site.
- 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 bitten limb with splint or sling (retard venom absorption).
  - Apply a firm bandage for 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 the hospital for identification. Do not handle the snake with bare hands as even a severed head can bite!
- Transfer the victim quickly to the nearest health facility.

Treatment at 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, 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. Effectiveness is time and dose related. It is most effective within 4 hrs after envenomation and less effective after 12 hrs although it may reverse coagulopathies after 24 hrs.

Indications for antivenom

- Should be given only in the presence of envenomation as evidenced by:
  - Coagulopathy.
  - Neurotoxicity.
  - Hypotension or shock, arrhythmias.
  - Generalised rhabdomyolysis (muscle aches and pains).
  - Acute renal failure.
  - Local envenomation e.g. local swelling more than half of bitten limb, extensive blistering/bruising, bites on digit, rapid progression of swelling.
  - Helpful laboratory investigations suggesting envenomation include anaemia, thrombocytopenia, leucocytosis, raised serum enzymes (creatine 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 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.

Guide to initial dosages of important Antivenoms		
Species	Antivenom manufacturer	Initial dose
Malayan pit viper	Thai Red Cross (Monovalent)	100 mls
Cobra	Twyford Pharmaceuticals (monovalent) Serum Institute of India; Biological E. Limited, India (Polyvalent)	50 mls (local) 100 mls (systemic) 50 mls (local) 100 - 150 mls (systemic)
King Cobra	Thai Red Cross (Monovalent)	50 – 100 mls
Common sea snake	CSL, Australia (polyvalent)	1 000 units (1 vial)

- 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.
- Prepare adrenaline, hydrocortisone, antihistamine and resuscitative equipment and be ready if allergic reactions occur.
- Pretreatment with adrenaline SC 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 occurs in 20% of patients

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.

  Treatment of anaphylactic reactions:
  - Stop antivenom infusion.
  - Give adrenaline IM (0.01ml/kg of 1 in 1000) and repeat every 5-10mins till symptoms subside. In case of persistent hypotension, life threatening anaphylaxis, adrenaline can be given IV 0.1mg of 1:10,000 dilution bolus over 5 mins. If hypotension is refractory to bolus dose start IV infusion at 1 microgm/kg/min. Close monitoring of heart rate is required.
  - Give antihistamine, e.g. chlorpheniramine 0.2mg/kg, hydrocortisone 4mg/kg/dose and IV fluid resuscitation (if hypotensive).
  - Nebulised adrenaline in the presence of stridor or partial obstruction
  - Nebulised salbutamol in the presence of bronchospasm or wheeze
  - If only mild reactions, restart infusion at a slower rate.
- *Pyrogenic reactions* – develop 1-2 hours after treatment and are due to pyrogenic contamination during the manufacturing process. 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. It is 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.

When to restart the antivenom after a reaction:

- Once the patient has stabilized, BP under control, manifestations of the reaction has subsided.
- In severe reactions restart antivenom under cover of adrenaline infusion. Rate of antivenom infusion is decreased initially and done under close monitoring in the ICU. Weigh the need for antivenom versus the potential risk of a severe anaphylactic reaction.

Anticholinesterases

- They 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 Edrophonium chloride (Tensilon) IV (0.25mg/kg, adult 10mg) with Atropine sulphate IV (50µg/kg, adult 0.6mg). If patients respond convincingly, maintain with Neostigmine methylsulphate IV (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 but consider only after sufficient antivenom has been given and correction of coagulation abnormalities with fresh frozen plasma and platelets before any surgical intervention as bleeding may be uncontrollable.
- 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.

Principles in approach to poisoning

- There is no role for the use of emetics in the 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 perhaps > 1 hour in the case of a slow release drug preparation.
- Gastric lavage is not recommended unless the patient has ingested a potentially life threatening amount of a poison and the procedure can be undertaken within 1 hour of ingestion.
- When in doubt about the nature of poison, contact the poison centre for help:

National Poison Centre (Pusat Racun Negara)
Tel: 1800-888099 OR 04-6570099 Mon – Fri: 8.10 am – 4.40 pm; Sat: 8.10 am – 1 pm Tel: 012-4309499 After Office Hours

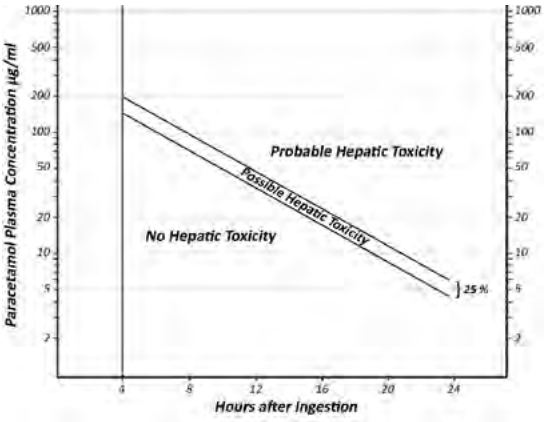
Laboratory investigations

- A careful history may obviate the need for blood tests.
- Blood glucose should be taken in all cases with altered sensorium
- Blood gas analysis in any patient with respiratory insufficiency, hyperventilation or metabolic acid base disturbance is suspected.
- Electrolyte estimation may be useful as hypokalaemia has been seen in acute poisoning.
- A wide anion gap is seen in methanol, paraldehyde, iron, ethanol, salicylate 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 an invaluable tool in detection of dysrhythmia and conduction abnormalities such as widened QRS or prolonged QT interval. Tricyclic Antidepressant poisoning.may manifest as myocardial depression, ventricular fibrillation or ventricular tachycardia.

PARACETAMOL

• Paracetamol is also called acetaminophen. Poisoning occurs when > 150mg/kg ingested. Fatality is unlikely if < 225mg/kg is ingested.

Clinical Manifestations of Paracetamol poisoning	
Stage 1	Nausea vomiting within 12 -24 hours, some asymptomatic.
Stage 2	Liver enzymes elevated by 24 hours after ingestion. Symptoms often abate.
Stage 3	Liver enzymes abnormalities peak at 48 -72 hours and symptoms of nausea, vomiting and anorexia return. The clinical course may result 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 in the first 2 days.	



NORMOGRAM FOR ACUTE PARACETAMOL POISONING.
Adapted from Rumack BH, Matthew H. Acetaminophen poisoning and toxicity. Pediatrics1975;55(6):871–876

The most efficacius therapy involves the administration of N-acetylcysteine which serves as a precursor to facilitate the synthesis of glutathione.

Management

- Measure the 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 but it is still beneficial up to 24 hours of ingestion.
  - IV NAC if the 4 hour plasma paracetamol level exceeds 150µg/ml.
  - Dose: 150mg/kg in 3mls/kg 5%Dextrose over 15 min, followed by 50mg/kg in 7mls/kg 5% Dextrose over 4 hours,
    then 100mg/kg in 14mls/kg 5% Dextrose over 16 hours.
  - It is much less effective if given later than 15 hours after ingestion.
  - Decision is based on the Rumack- Matthew normogram. Plot the serum level of paracetamol drawn at least 4 hrs following ingestion.
  - If patients are on 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.
  - It may be necessary to continue the NAC beyond 24 hrs in massive overdose.
  - The paracetamol level should be checked before disontinuing and if still high rebolus and continue at 6-5 mg/kg till level is < 10µg/ml. Advisable to contact the poison centre.
  - Ensure the NAC is appropriately diluted and patient does not become fluid overloaded.
  - Adverse reactions to NAC.
  - Flushing, aching, rashes, angioedema, bronchospasm and hypertension.
  - NAC should be stopped and if necessary, IV antihistamine given.
    Once adverse reactions resolved, NAC restarted at 50mg/kg over 4 hrs
- If PT ratio exceeds 3.0, give Vitamin K 1 10mg IM.
  FFP or clotting factor concentrate may be necessary.
- Treat complications of acute hepatorenal failure.

Management of a single overdose is straightforward and is guided by the above. However when cases are associated with staggered overdoses or repeated supratherapeutic doses, patients with high risk factors or late presentations, management decisions become more complex.

HIGH RISK TREATMENT LINE

At Risk Patients
Regular use of enzyme inducing drugs e.g. Carbamazepines, phenytoin, phenobarbitone, rifampicin
Conditions causing glutathione depletion Malnutrition, HIV, eating disorders, cystic fibrosis

- Repeated supratherapeutic ingestion or when timing of ingestion is uncertain:
  - Children under 6 years of age who have ingested
    200mg/kg or more over a single 24 hr period
    150 mg/kg or more per 24 hr period for the preceding 48 hrs
    100 mg/kg or more per 24 hr period for the preceding 72 hrs or longer
  - Children over 6 years of age who have ingested
    At least 10g or 200mg/kg (whichever is less) over a single 24 hr period
    At least 6g or 150mg/kg (whichever is less) over a single 24 hr period for the preceding 48hrs or longer.
- Levels are difficult to interpret, advice should be sought from the Poison Centre. If in doubt treat first.

Prognosis

- Younger children who accidentally ingest a single dose were less at risk for hepatotoxicity and have a good prognosis.
- Older children who self harm with overdoses and young children who ingest repeated overdosings may suffer severe morbidity and mortality.

Indicators of severe paracetamol poisoning and when to refer to a specialist centre:

- Progressive coagulopathy:
  INR >2 at 24hrs, INR > 4 at 48hrs or INR >6 at 72 hrs.
- Renal impairment creatinine > 200 µmol/l.
- Hypoglycemia.
- Metabolic acidosis despite rehydration.
- Hypotension despite fluid resuscitation.
- Encephalopathy.

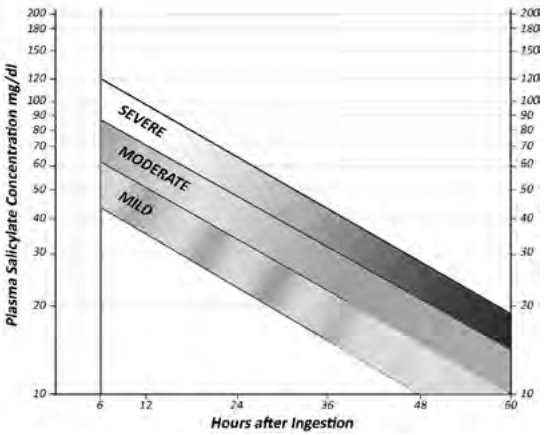
SALICYLATE

- Ingestion of > 0.15 mg/kg will cause symptoms.
- The fatal dose is estimated to be 0.2 0.5g/kg.
- Its main effects are as a metabolic poison causing metabolic acidosis and hyperglycaemia.

Clinical Manifestations of Salicylate poisoning	
General	Hyperpyrexia, profuse sweating and dehydration
CNS	Delirium, seizures, cerebral oedema, coma, Reye's syndrome
Respiratory	Hyperventilation
GIT	Epigastric pain, nausea, vomiting, UGIH, acute hepatitis
Renal	Acute renal failure
Metabolic	Hyper/hypoglycaemia, anion gap metabolic acidosis, hypokalaemia
Cardiovascular	Non-cardiogenic pulmonary oedema
Investigation : FBC, PCV, BUSE/Serum creatinine LFT/PT/PTT, RBS; ABG Serum salicylate level at least 6 hours after ingestion	

Management

- Use activated charcoal to reduce absorption and alkalinisation to enhance elimination. Activated charcoal 1-2g/kg/dose 4-8 hourly. Meticulous monitoring of urine pH to avoid significant alkalemia
- Correct dehydration, hypoglycaemia, hypokalaemia, hypothermia and metabolic acidosis.
- Give vitamin K if there is hypoprothrombinaemia.
- Plot the salicylate level on the normogram.
  - Forced alkaline diuresis (* Needs close monitoring as it is potentially dangerous) for moderate to severe cases.
    (For salicylate level > 35 mg/dl 6 hrs after ingestion)
  - Give 30mls/kg in 1st hour (1/5 DS + 1ml/kg 8.4% $NaHCO_3$).
    Give IV Frusemide (1mg/kg/dose) after 1st hr and then 8hrly.
  - Continue at 10mls/kg/hr till salicylate level is at a therapeutic range.
  - Add 1g KCl to each 500mls of 1/5 DS to the above regime (discontinue KCl if Se K+ > 5mmol/L).
  - Aim for plasma pH of >7.5 and urine output of > 3-6ml/kg/h.
  - BUSE/RBS/ABG every 6 hrs.
  - Treatment of Hypoglycaemia (5ml/kg of 10% dextrose).



DONE NORMOGRAM FOR ACUTE SALICYLATE POISONING.
Adapted from Done AK. Salicylate intoxication: Significance of measurements of salicylate in blood in cases of acute ingestion. Pediatrics 1960;26:800-7.

Haemodialysis in

- 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 intensive treatment.

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 Manifestations in Iron poisoning	
Stage 1 (6 - 12hrs)	Gastrointestinal bleeding, vomiting, abdominal pain, diarrhoea, hypotension, dehydration, acidosis and coma.
Stage 2 (8 - 16hrs)	Symptom free period but has nonspecific malaise.
Stage 3 (16-24hrs)	Profound hemodynamic instability and shock.
Stage 4 (2 - 5wks)	Liver failure and gastrointestinal scarring with pyloric obstruction.

Management

Emphasis is on supportive care with an individualised approach to gastrointestinal decontamination and selective use of antidotes.

- Ingestion < 30mg/kg - patients are unlikely to require treatment.
- Ingestion of > 30mg/kg - perform an abdominal XRay. If pellets are seen then use gastric lavage with wide bore tube or whole bowel irrigation with polyethylene glycol if pellets are seen in small bowel.
  (500ml/h in children < 6 yrs, 1000ml/h in children 6-12 yrs and 1500 – 2000ml/h in children >12 yrs old.
  Contraindications: Paralytic ileus, significant haematemesis, 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 i.e. hemetemesis or malaena.
  - If level > 90µmol/l or significant symptoms, chelation with IV Desferrioxamine 15 mg/kg till max of 80 mg/kg in 24 hours.
  - If serum Iron is not available, severe poisoning is indicated by nausea, vomiting, leucocytosis >15 X 10^9 and hyperglycaemia > 8.3 µmol/l
- Administer Desferrioxamine with caution because of hypotension and pulmonary fibrosis. Continue chelation therapy till serum Iron is normal, metabolic acidosis resolved and urine colour returns to normal.
- If symptoms are refractory to treatment following 24 hrs of chelation, reduce rate of infusion because of its association with acute respiratory distress syndrome.
- Critical care management includes management of cardiopulmonary failure, hypotension, severe metabolic acidosis, hypoglycaemia or hyperglycaemia, anaemia, GIT bleed, liver and renal failure.

Prognosis

- Gastrointestinal bleeding, hypotension, metabolic acidosis, coma and shock are poor prognostic features.

KEROSENE INGESTION AND HYDROCARBONS

- 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 Manifestations of Tricyclic Antidepressant poisoning	
Anticholinergic effects	Fever, dry mouth, mydriasis, urinary retention, ileus.
CNS	Agitation, confusion, convulsion,drowsiness, coma
Respiratory	Respiratory depression
Cardiovascular	Sinus tachycardia, hypotension, complex arrhythmias

Management

- There is no specific antidote.
- Give activated charcoal 1-2 g/kg/dose 4-8hourly.
- Place patient on continuous ECG monitoring. Meticulous monitoring is required. In the absence of 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 arrythmias. QRS > 100ms (seizures) and QRS >160ms (arrhythymia).
- Correct the metabolic acidosis. Give bicarbonate (1-2mmol/kg) to keep pH 7.45 – 7.55 when QRS is widened or in the face of ventricular arrhthymias. Administration of $NaHCO_3$ 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 benzodiazepines.
- Use propranolol to treat life-threatening arrhythmias.
- If *torsades de pointes* occurs treat with $MgSO_4$.
- Treat hypotension with Norepinephrine and epinephrine. Dopamine is not effective.
- Haemodiaysis/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 Manifestations in Organophosphate poisoning	
Cholinergic effects	Miosis, sweating, lacrimation, muscle twitching, urination, excessive salivation, vomiting, diarrhoea
CNS	Convulsions, coma
Respiratory	Bronchospasm, pulmonary oedema, respiratory arrest
Cardiovascular	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
- Give IV atropine 0.05mg/kg every 15 minutes till fully atropinized. Atropine administration is guided by the drying of secretions rather than the heart rate and the 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 Frusemide 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 amounts.
- General supportive care.

Introduction

- Anaphylaxis is a severe, life threatening, generalised or systemic hypersensitivity reaction. It is characterized by rapidly (minutes to hours) developing life threatening airway and/or breathing and /or circulation problems usually associated with skin and/ or mucosa changes.

Life threatening features

- Airway problems:
  - Airway swelling e.g. throat and tongue swelling.
  - Hoarse voice.
  - Stridor.
- Breathing problems:
  - Shortness of breath (bronchospasm, pulmonary oedema).
  - Wheeze.
  - Confusion cause by hypoxia.
  - Cyanosis is usually a late sign.
  - Respiratory arrest.
- Circulation problems
  - Shock.
  - Cardiovascular collapse with faintness, palpitations, loss of consciousness.
  - Cardiac arrest

Key points to severe reaction

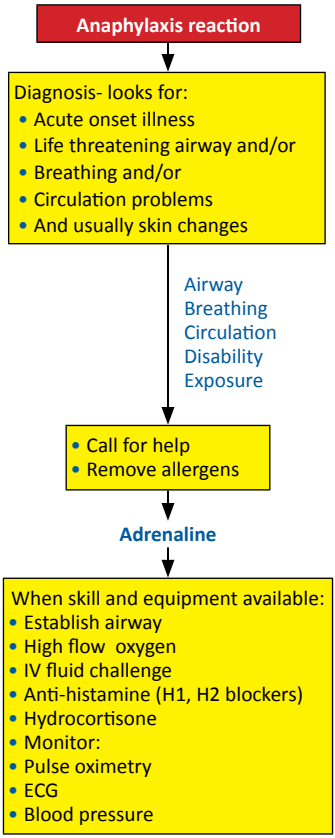
- Previous severe reaction.
- History of increasingly severe reaction.
- History of asthma.
- Treatment with β blocker.

Approach to treatment (see following pages)

- The clinical signs of critical illness are generally similar because they reflect failing respiratory, cardiovascular and neurological system.
- Use ABCDE approach to recognise and treat anaphylaxis.

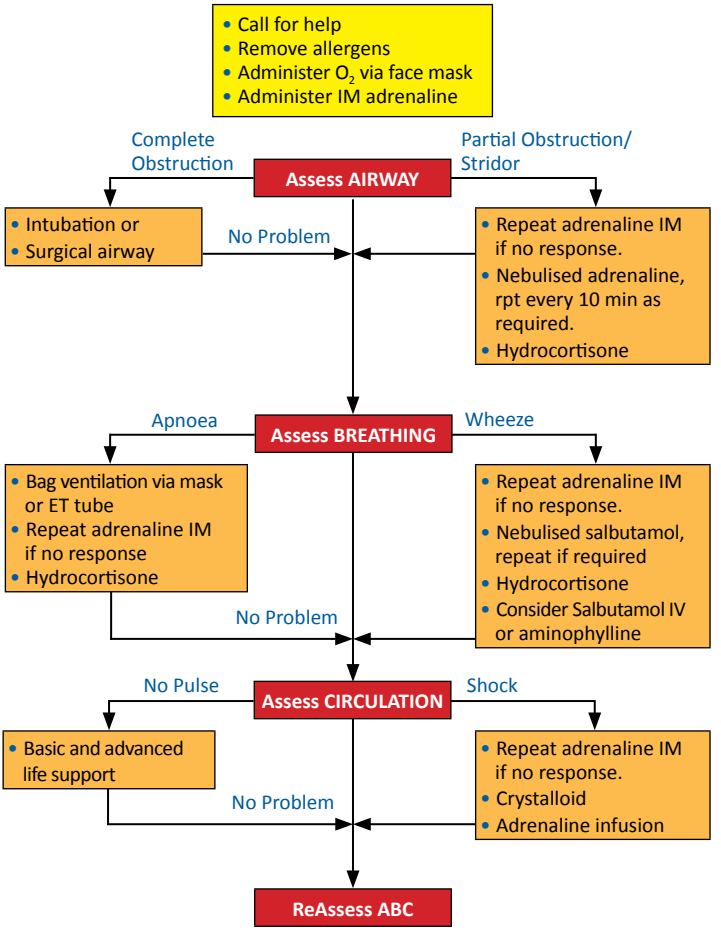
Discharge Planning

- Prevention of further episodes.
- Education of patients and caregivers in the early recognition and treatment of allergic reaction.
- Management of co-morbidities that increase the risk associated with anaphylaxis.
- An adrenaline auto injector should be prescribed for those with history of severe reaction to food, latex, insect sting, exercise and idiopathic anaphylaxis and with risk factor like asthma.


Anaphylaxis reaction
Diagnosis- looks for:
• Acute onset illness
• Life threatening airway and/or
• Breathing and/or
• Circulation problems
• And usually skin changes
Airway
Breathing
Circulation
Disability
Exposure
• Call for help
• Remove allergens
Adrenaline
When skill and equipment available:
• Establish airway
• High flow oxygen
• IV fluid challenge
• Anti-histamine (H1, H2 blockers)
• Hydrocortisone
• Monitor:
• Pulse oximetry
• ECG
• Blood pressure

Emergency treatment in anaphylaxis				
Drugs in anaphylaxis	Dosage by age			
	< 6 months	6 mths to 6 years	6 years-12 years	> 12 years
Adrenaline IM- pre hospital practitioners	150 micrograms (0.15ml of 1000)		300micrograms (0.3ml of 1:1000)	500microgram (0.5ml of 1:1000)
Adrenaline IM- in hospital practitioners (rpt after 5 mins if no improvement)	10 micrograms/kg 0.1ml/kg of 1:10000 (infants/young children) OR 0.01ml/kg of 1:1000 (older children)			
Adrenaline IV	Start with 0.1microgram/kg/min and titrate up to 5microgram/kg/min*			
Crystalloid	20 mls/kg			
Hydrocortisone ** IM or Slow IV)	25mg	50mg	100mg	200mg

- *If hypotensive persist despite adequate fluid (CVP>10), obtain echocardiogram and consider infusing noradrenaline as well as adrenaline.
- ** Dose of intravenous corticosteroid should be equivalent to 1-2mg/kg/dose of methylprednisolone every 6 hours (prevent biphasic reaction).
- Oral prednisolone 1m/kg can be used in milder case.
- Antihistamine are effective in relieving cutaneous symptoms but may cause drowsiness and hypotension.
- If the patient is on β-blocker, the effect of adrenaline may be blocked; Glucagon administration at 20-30µg/kg, max 1mg over 5 minutes followed by infusion at 5-15µg/min is useful.
- Continue observation for 6-24 hours depending on severity of reaction because of the risk of biphasic reaction and the wearing off of adrenaline dose.


• Call for help
• Remove allergens
• Administer O_2 via face mask
• Administer IM adrenaline
Complete Obstruction
Partial Obstruction/ Stridor
Assess AIRWAY
• Intubation or
• Surgical airway
No Problem
• Repeat adrenaline IM if no response.
• Nebulised adrenaline, rpt every 10 min as required.
• Hydrocortisone
Apnoea
Assess BREATHING
Wheeze
• Bag ventilation via mask or ET tube
• Repeat adrenaline IM if no response
• Hydrocortisone
No Problem
• Repeat adrenaline IM if no response.
• Nebulised salbutamol, repeat if required
• Hydrocortisone
• Consider Salbutamol IV or aminophylline
No Pulse
Assess CIRCULATION
Shock
• Basic and advanced life support
No Problem
• Repeat adrenaline IM if no response.
• Crystalloid
• Adrenaline infusion
ReAssess ABC

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Section 15 Poisons And Toxins

Ch 101 Snake Bite

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- The health care provider should decide on an appropriate level of pain relief for a child in pain and also before a diagnostic or therapeutic procedure.
- We can assess a child in pain using an observational-based pain score or a self-assessment pain score. Repeated assessment needs to be done to guide further analgesia.

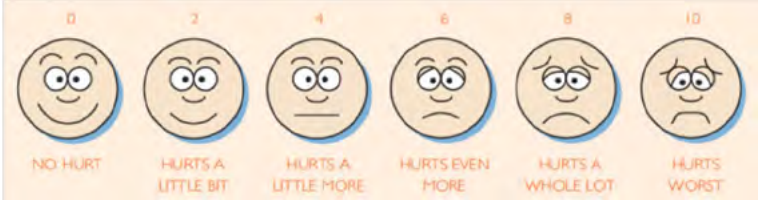
Observational-based Pain Score: The Alder Hey Triage Pain Score				
No.	Response	Score 0	Score 1	Score 2
1	Cry or voice	No complaint or cry Normal conversation	Consolable Not talking negative	Inconsolable Complaining of pain
2	Facial expression – grimace*	Normal	Short grimace <50% time	Long grimace >50% time
3	Posture	Normal	Touching / rubbing / sparing / limping	Defensive / tense
4	Movement	Normal	Reduced or restless	Immobile or thrashing
5	Colour	Normal	pale	Very pale / 'green'

*grimace – open mouth, lips pulled back at corners, furrowed forehead and /or between eye-brows, eyes closed, wrinkled at corners.

From Appendix F, APLS 5th Edition; Score range from 0 to 10

Self Assessment Pain Score:
The two examples are FACES Pain Scale (Wong & Baker) and Verbal Pain Assessment Scale (Likert Scale).

FACES Pain Scale - The child is more than 3 years old and he or she is asked to choose a face on the scale which best describes his / her level of pain. Score is 2, 4, 6, 8, or 10.



Verbal Pain Assessment Scale
A child who is more than 8 years old is asked to rate his or her pain by circling on any number on the scale of 0 to 10.

Chapter 105: Sedation and Analgesia 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 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

Personnel

- At least a senior medical officer, preferably PALS or APLS trained.
- A nurse familiar with monitoring and resuscitation.

Facilities

- Oxygen source.
- Suction.
- Resuscitation equipment.
- Pulse oximeter.
- ECG monitor.
- Non-invasive BP monitoring.
- Defibrillator.

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 anaesthesised area prior to prolonged needling procedure, e.g. insertion of chest drainage.

- Medications (see table next page)
  Many sedative and analgesic drugs are available; however, it is advisable to use the following frequently used medications:

  1. *Narcotics (analgesia)* also have sedative effects
  - Fentanyl
  - Naloxone (narcotic reversal)
    - For respiratory depression* caused by narcotics.
  - Morphine - general dissociative anaesthesia

  2. Benzodiazepines (sedatives) have no analgesia effects
  - Diazepam
  - Flumazenil (benzodiazepine reversal)
    - Can reverse respiratory depression* and paradoxical excitatory reactions
  - Midazolam.

  3. Ketamine (to be used by senior doctors preferably in the presence of an anaesthesia doctor).
  Adverse effects include
  - Increased systemic, intracranial and intraocular pressures.
  - Hallucinogenic emergence reactions (usually in older children).
  - Laryngospasm.
  - Excessive airway secretions.

**provide bag-mask positive pressure ventilation whilst waiting for reversal agent to take effect.*

Post sedation monitoring and discharge

Patient can be discharged when:
- Vital signs and SaO_2 normal.
  And
- Arousable.
- Baseline level of verbal ability and able to follow age-appropriate commands.
- Sit unassisted (if appropriate for age).

Drug dosages used for sedation and analgesia in children			
Drug	Dose	Onset of action	Duration of action
Chloral Hydrate	Oral 25 - 50 mg/kg; Max 2g. For higher doses, i.e. 50 -100 mg/kg, please consult paediatrician or anaesthesiologist.	15 – 30 mins	2 -3 hours
Narcotics			
Morphine	IV >1 year: 200-500 mcg/kg <1 year: 80 mcg/kg	5 – 10 mins	2 – 4 hours
Fentanyl	IV 1 – 2 mcg/kg	2 – 3 mins	20 -60 mins
Benzodiazepines			
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
Reversal agents			
Naloxone	Repeated small doses IV 1 - 10 mcg/kg every 1-2 mins		
Flumazenil	IV 0.01 – 0.02 mg / kg every 1 -2 minutes up to a maximum dose of 1 mg		

Headings

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
- **2.4** Central venous access - Femoral vein cannulation in children.

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.
(see Ch 105: Sedation and Analgesia for Diagnostic and Therapeutic Procedures)

1. AIRWAY ACCESS - ENDOTRACHEAL INTUBATION

(Please request for assistance from the Doctor from Anaesthesiology Department if necessary).

Introduction:

- APLS courses have been conducted locally since October 2010.
  Kindly refer to APLS 5th Ed:-
  - Chapter 20: Practical procedures: airway and breathing
  - Chapter 21: Practical procedures: circulation
- 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 or continuous positive airway pressure (CPAP) 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 blade for infants, curved blades for an older child.
  - Size 0 for neonates, 1 for infants, 2 for children.
- Endotracheal tube – appropriate size as shown.
- Stylet (optional).
- Suction catheter and device.
- Scissors and adhesive tape.
- Pulse oximeter.
- Sedation (Midazolam or Morphine).
- Muscle relaxant (Succinylcholine).

Size of ETT (mm):
2.5 for < 1kg
3.0 for 1-2kg
3.5 for 2-3kg
3.5 - 4.0 for > 3kg
Oral ETT length in cm for neonates: 6 + (weight in kg) cm
For Children > 1 year: ETT size (mm) = 4 plus (age in years /4) Oral ETT length (cm) = 12 plus (age in years /2)

Procedure

1. Position infant with head in midline and slightly extended.
2. Continue bag and mask ventilation with 100% oxygen till well saturated. In newborns adjust FiO_2 accordingly until oxygen saturation is satisfactory. (Refer NRP Program 6th edition).
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).

   Caution: must be able to bag the patient well or have good intubation skills before giving muscle relaxant.
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 secures the head.
6. When epiglottis is seen, lift blade upward and outward to visualize the vocal cords.
7. Suction secretions if necessary.
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 or resuscitation bag.
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 the PALS Provider Manual.

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 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 giving slow bolus drugs.
  - Redness.
  - Swelling.
  - Reduced movement of affected site.

  (Note – the inflammatory response can be reduced in neonates especially 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 – observation should be done more often, that is, 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 (glucose concentration >10g%, sodium bicarbonate, calcium solution, dopamine, cloxacillin, fusidic acid)

  Consider:
  - Refer to plastic surgeon / orthopaedics surgeon.
  - Performing 'subcutaneous saline irrigation' especially in neonates *(ref Davies, ADC, Fetal and Neonatal edition 1994).*

    Give IV analgesia morphine, then perform numerous subcutaneous punctures around the extravasated tissue and flush slowly with generous amount of normal saline to remove the irritant. Ensure that the flushed fluid flows out through the multiple punctured sites.

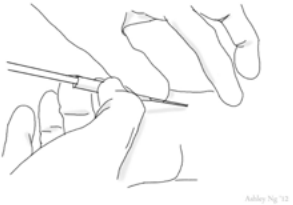
Pitfalls

- If the patient is in shock, the venous flow back and the arterial flow
- (in event of accidental cannulation of an artery) is sluggish.
- ***BEWARE!*** An artery can be accidentally cannulated, e.g. 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. Check for resistance to flow during slow bolus or infusion (e.g. frequent alarming of the perfusor pump) or watch for pulsation in the backflow or a rapid backflow. Rapid bolus or infusion of drugs can cause ischaemia of the limb. Where in doubt, gently remove the IV cannula.
- Ensure prescribed drug 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.
- Avoid medication error (correct patient, correct drug, correct DOSE, correct route).
- Avoid nosocomial infection.

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 arterial line if close monitoring cannot be done.

Equipment

- Topical anaesthetic (TA) like lignocaine EMLA® 5%.
- Alcohol swab.
- Needle size 27.
- Catheter size 25.
- Heparinised saline in 5cc syringe (1 ml for neonate), T-connector.
- Heparinised saline (1u/ml) for infusion.

Procedure

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 gently with a small amount of 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.
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 tape, taking care not to make the tape too tight.

Complications and Pitfalls

- Arteriospasm which may lead to ischaemia and gangrene.
- Neonates especially – digital and distal limb ischaemia.

Precautions

Prevention of digital, distal 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' especially in ill patients with shock).
- *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 dorsalispedis artery on one foot is chosen, ensure that these 2 arteries are palpable before cannulation.
- *Circulation chart*
  Perform observation and record circulation of distal limb every hour in the NICU/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 or limb ischaemia*
  - This is difficult as the artery involved is of small calibre.
  - Remove IV cannula.
  - Confirm thrombosis with ultrasound doppler.
  - May consider warming the contralateral unaffected limb to induce reflex vasodilatation if part of one limbis affected
    (see Ch 14 Vascular spasm and Thrombosis).
  - Ensure good peripheral circulation and blood pressure
  - Anticoagulant drugs and thrombolytic agents should be considered.
  - Refer orthopaedic surgeon if gangrene is inevitable
- *Reminders*:
  - PREVENTION of limb ischaemia is of utmost importance.
  - Early detection of ischaemia is very important in order 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.
  - 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

Notes:

- Intraosseous 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/adult - distal tibia, medial malleolus, anterior superior iliac spine, distal radius, distal ulna.
- All the fluids and medications can be given intraosseously.
- IO infusion is not recommended for use longer than a 24 hour period.

Indications

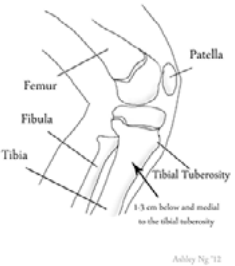
- Emergency access for IV fluids and medications when other methods of vascular access failed.
- In certain circumstances, e.g. severe shock with severe vasoconstriction or cardiac arrest, IO access may be the INITIAL means of vascular access attempted.

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 inthe same bone.
- Infection over the overlying tissues.

Equipment

- Sterile dressing set.
- EZ-IO drill set if available.
- Intraosseous needle.
- Syringes for aspiration.
- Local anaesthesia.



Procedure

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
- Lancet or heel prick device.
- Alcohol swab.

Procedure
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 lancet 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 ventilator.
- Occasionally it is used for continuous BP monitoring and infusion.

Contra-indications
- Local vascular compromise in lower extremities.
- Peritonitis, necrotising enterocolitis.
- Omphalitis.

Prior to setting
- Examine the infant's lower extremities and buttocks for any signs of vascular insufficiency.
- Palpate femoral pulses for their presence and equality.
- Evaluate the infant's legs, feet, and toes for any asymmetry in colour, visible bruising, or vascular insufficiency.
- Document the findings for later comparison. Do not set if there is any sign of vascular insufficiency.

Equipment
- UAC/UVC set.
- Umbilical artery catheter, appropriate size.
- 5 cc syringes filled with heparinized saline.
- Three-way tap.
- Heparinized saline (1u/ml) for infusion.

Size of UAC in mm:
3.5 for < 1.25 kg
5.0 for 1.25 - 3.5 kg

Procedure
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.

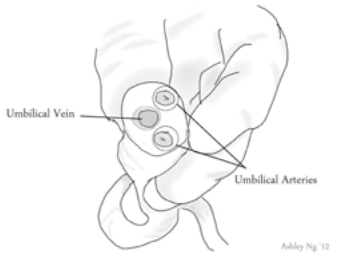
The formula for UAC is:
- (Body weight in kg x 3) + 9 + 'stump length' in cm *(high position - recommended)*
- Height in kg + 7 cm (low position)

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 umbilical artery.
   - 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 in 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 patient's folder for future reference (brand and material of catheter) in the event of limb ischaemia or thrombosis of femoral artery occurring later.
5. Observe for signs of arterial occlusion to the lower limbs and buttocks (colour, cold skin, capillary refill delayed, poor dorsalis pedis and posterior tibial pulses) during and after the proceduredue to arterial vasospasm. Lift 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 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, as soon as position is ascertained, 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 and thrombotic events.
10. Note the catheter length markings every day 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 aorta, iliac, femoral or obturator artery leading to limb or buttock ischaemia.
  (see Ch 14 Vascular spasm and Thrombosis)
- Thrombosis of renal artery (hypertension, haematuria, renal failure), mesenteric artery (gut ischaemia, necrotising enterocolitis).
- Vascular perforation of umbilical arteries, haematoma and retrograde arterial bleeding.
- Infection.

2.4.3. UMBILICAL VEIN CATHETERISATION (UVC)

Indications

- UVC is used for venous access in neonatal resuscitation.
- As a venous access in preterm babies especially ELBW babies (<1000g) and also in sick babies in shock with peripheral vasoconstriction.
- For doing exchange transfusion for severe neonatal jaundice.

Contra-indications

- Omphalitis, omphalocoele.
- Necrotising enterocolitis.
- Peritonitis.

Size of UVC mm:
5.0 for <2kg
8.0 for 2-3.5kg
10.0 for>3.5kg

Equipment

- UVC set.
- Umbilical venous catheter, appropriate size.
- 5 cc syringes filled with heparinized saline.
- Three-way tap.
- Heparinized saline (1u/ml) for infusion.

Procedure

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 x UAC cm (high position)] + 1 cm.
  (Refer to information on use of "Shoulder - umbilical length" , in Ch 13 NICU guidelines)

Or

- 2 x weight in kg + 5 + 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.
  - Stand to the right of the baby (if you are right handed). Tilt the umbilical stump inferiorly at an angle of 45 degrees from the abdomen. Advance the catheter superiorly and posteriorly towards the direction of the right atrium.

- Central venous pressure
  - The UVC tip is sited in the upper IVC (inferior vena cava).
    The right atrial pressure in a term relaxed baby normally ranges 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) in the event of thrombosis occurring in the cannulated vessel.

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.
6. Consider removing the UVC after 5 - 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).

Pifalls

- 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 Ch 14 Vascular spasm and Thrombosis.

2.5 CENTRAL VENOUS ACCESS: FEMORAL VEIN CANNULATION IN CHILDREN

- The routes of central venous access includes peripherally inserted central catheter - PICC (eg through cubital fossa vein into SVC) and femoral, external / internal jugular and subclavian veins.
- These lines must be inserted by trained senior doctors in selected seriously ill paediatrics patients requiring resuscitation and emergency treatment.
- The benefits of a successfully inserted central venous access must be weighed against the numerous potential complications arising from the procedure.
- This includes pneumothorax and life-threatening injuries of the airway, lungs, great vessels and heart.
- The basic principle of Seldinger central line insertion applies to all sites and the femoral vein cannulation is described.
- For insertion of central lines by experts in other sites, please refer to Chapter 21, APLS 5th Ed 2011 and PALS 6 PALS 2002.

Indications

- Seriously ill ventilated paediatrics patients.
- To obtain central venous pressure.
- Longer term intravenous infusion (compared to IO access).
- Haemodialysis.

Contra-indications

- Absence of trained doctors for this procedure.
- Bleeding and clotting disorders.
- Risk of contamination of the cannulation site by urine and faeces.

Equipment

- Sterile set.
- Lidocaine (Lignocaine) 1% for local anaesthetic, 2 mL syringe, 23 G needle.
- 5 mL syringe and normal saline, t-connector and 3-way tap.
- Seldinger cannulation set – syringe, needle, guide wire, catheter.
- Sterile dressing.

Procedure

1. In a ventilated child, give a dose of analgesia (eg Morphine, Fentanyl) and sedation (e.g. Midazolam).
2. In the supine position, expose the chosen leg and groin in a slightly abducted position.
3. Clean the inguinal region thoroughly using iodine and 70% alcohol.
4. Infiltrate local lidocaine if necessary.
5. Identify the landmark by palpating the femoral artery pulse in the mid-inguinal region. The femoral vein is medial to the femoral artery.
6. Insert the saline filled syringe and needle at 45 degrees angle to the skin and 1 cm medial (depends on the age of child) and parallel to the femoral artery pulsation. Pull the plunger gently and advance superiorly in-line with the leg.
7. When there is a backflow of blood into the syringe, stop suction, and disconnect the syringe from the needle. The guide wire is then promptly and gently inserted into the needle.
8. Withdraw the needle gently without risking damage to the guide wire
9. Insert the cannula over the wire without risking displacement of the wire into the patient.
10. Once the cannula has been inserted, remove the guide wire and attach the infusion line securely onto the hub of the cannula. Check for easy backflow by gentle suction on the syringe.
11. Secure the line using sterile dressing and ensure the insertion site is clearly visible at all times.

Pitfalls

- Do not lose the guide wire (inserted too deep into patient)
- Do not fracture the guide wire accidentally with the needle
- Do not accidentally cannulate the femoral artery (blood pressure could be low in a patient with shock)
- Beware of local haematoma at injection site.
- Always check the distal perfusion of the leg and toes before and after procedure.

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.

Contraindications

- Increased intracranial pressure (signs and symptoms, raised blood pressure, fundoscopic signs).
- Bleeding tendency - platelet count <50,000/mm^3, prolonged PT or APTT.
- Skin infection over the site of lumbar puncture
- Patient with hypertensive encephalopathy

Equipment

- Sterile set.
- Sterile bottles for CSF, bottle for RBS (random blood sugar).
- Spinal needle 20-22G, length 1.5 inch with stylet; length 3.5 inches for children > 12 years old.

Procedure

1. Give sedation (midazolam), apply local anaesthetic.
2. Take a random blood sugar sample (RBS).
3. Place child in lateral recumbent position with neck, body, hips and knees flexed. Monitor oxygen saturation continuously.
4. 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).
5. Clean area using standard aseptic techniques: povidone-iodine and 70% alcohol.
6. 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.
7. 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.
8. Gently withdraw needle, spray with op-site, cover with gauze and bandage.
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).

3.2. CHEST TUBE INSERTION

Indications

- Pneumothorax with respiratory distress.
- Significant pleural effusion.
- Empyema.

Equipment

- Suturing set.
- Local anaesthetic +/- sedation.
- Chest tube, appropriate size.
- Underwater seal with sterile water.
- Suction pump – optional.

Size of chest tube (mm)
8 for < 2kg
10 for > 2kg
Older children
12-18 depending on size

Procedure

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. Check approximate length of the chest tube to be inserted.

For Open Method

i. The open method (without the metal introducer) of chest tube cannulation is the preferred method except in neonates

ii. Make a small incision in the skin just above the rib. Bluntly dissect through the subcutaneous tissue and puncture the parietal pleura with the tip of the clamp. Put a gloved finger into the incision and clear the path into the pleura. This will not be possible in a small child. Advance the chest tube into the pleural space during expiration.

iii. For drainage of air, roll the child slightly to the opposite side for easier manoeuvring and advancement of the chest tube. Place the tip of the chest tube at the incision. Point the catheter tip anteriorly and slowly advance the chest tube. However, for drainage of empyema, roll the child slightly towards same side and point the catheter tip posteriorly and proceed with the rest of the procedure.

iv. Connect the chest tube to underwater seal.

For Closed Method

i. Make a small incision just above the rib down to the subcutaneous tissue.

ii. 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 by exerting a firm continuous pressure until a 'give' is felt.

iii. Withdraw the introducer partially and advance the chest tube till the desired length.

iv. Remove introducer fully and clamp the chest tube.over a gauze. May not be necessary if patient receiving positive pressure ventilation.

v. Connect the chest tube to underwater seal.

Then continue with the following for both methods:

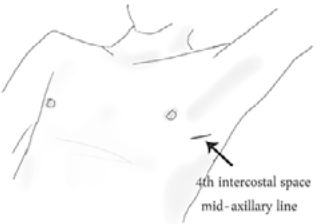
6. The water should bubble (if pneumothorax) and the fluid moves with respiration if chest tube is in the pleural space.
7. Secure the chest tube with pulse string sutures or sterile tape strips in neonates.
8. Connect the underwater seal to suction pump if necessary.
9. Confirm the position with a chest 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.

SITE FOR CHEST TUBE INSERTION



Ashley Ng '12

3.3. PERICARDIOCENTESIS

Indications

- Symptomatic collection of air.
- Blood or other fluids / empyema in pericardial sac.

Equipment

- Suturing set.
- Angiocatheter – size 20G for newborn,18G for older children.
- T connector.
- 3-way stopcock.

Procedure

1. Place patient in 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 newborn.

Equipment

- Nasogastric tube size 8-12.
- Syringes- 5cc for neonate, 25-50cc for older children.
- Sterile water.

Procedure

1. Put the child in left semiprone position.
2. Estimate the length of *nasogastric* tube inserted by measuring the tube from the nostril and extending it over and around the ear and down to the epigastrium.

   For *orogastric* tube insertion, the length of tube inserted equal to the bridge of the nose to the ear lobe and to appoint halfway between the lower tip of sternum and the umbilicus.
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. decompress. Insert a chest tube as described above as soon as feasible.

Complications

- Discomfort.
- Trauma to upper GIT.
- Aspiration of stomach contents.

3.4.2. ABDOMINAL PARACENTESIS

Indications

- Diagnostic procedure.
- Drain ascites.

Equipment

- Dressing set.
- Cannula size 21,23.
- Syringes 10cc.

Procedure

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 illiac 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 Ch 61 Acute Peritoneal Dialysis)

3.4.4. SUPRAPUBIC BLADDER TAP

Indication

- Urine culture in a young infant.

Equipment

- Dressing set.
- Needle size 21, 23.
- Syringe 5cc.
- Urine culture bottle.

Procedure

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 hematuria.
- Infection.
- Viscus perforation.

3.4.5. BLADDER CATHETERIZATION

Indications

- Monitor urine output.
- Urinary retention.
- MCUG - Patient for MCU needs to given stat dose of IV Gentamicin or TMP 2mg/kg bd for 48 hours.
- Urine culture.

Size of Catheter:
Size 4 for <3kg
Size 6 for >3kg
Older children:
Foley's catheter 6-10

Equipment

- Dressing Set.
- Urinary catheter.
- LA / K-Y jelly.
- Syringe and water for injection.

Procedure

1. Position the child in a frog-leg position. Clean and drape the perineum.
2. In girls, separate the labia majora with fingers to expose the urethra opening.
3. In boys, 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 lead to urethral stricture.

3.5. BONE MARROW ASPIRATION AND TREPHINE BIOPSY

Indications

- Examination of bone marrow in a patient with haematologic or oncologic disorder.

Contra-indications

- Bleeding tendency, platelet count < 50,000/mm^3.
  Consider transfusion of platelet concentrates prior to procedure.

Equipment

- Bone marrow set (Islam) 16 – 18G

Procedure

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 diasthesis.

Complications

- Bleeding, haematoma.
- Infection.

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Section 16 Sedation, Procedures

Ch 104 & 105 Recognition and assessment of pain, Sedation and Analgesia

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