PATENT DUCTUS ARTERIOSUS IN PRETERM INFANT

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.

Diagnosis
1) May be asymptomatic, picked up on routine echocardiography
2) Physical findings include:
   - Systolic or continuous murmur
   - Tachycardia
   - Hyperactive precordium
   - Prominent epigastric pulsation
   - Apnoea
   - Increase in ventilatory requirements

Complications
- Congestive cardiac failure
- Intraventricular haemorrhage
- Pulmonary haemorrhage
- Renal impairment
- Necrotising enterocolitis

How to close the preterm duct?
Both Indomethacin and Ibuprofen work by inhibiting prostaglandin synthesis. Indomethacin has some worrying side effects like reduced blood flow to the brain, kidneys and gut. Infusing Indomethacin slowly over 30 minutes may reduce the effect on cerebral blood flow. Ibuprofen has been shown to have similar efficacy in closing the duct with lower risk of oliguria. Surgical closure is indicated if the duct is persistently symptomatic and medical treatment has failed or is contraindicated.

Note: IV Indomethacin has to be freshly prepared as it is unstable once the vial is opened. It should be shared among a few babies if possible.

Recommended approaches to closing the PDA

1. Prophylactic Indomethacin
   - This approach may be used where facility for early bedside echocardiogram is not available and the unit has no ready access to cardiology services including cardiac surgery.
   - Prophylactic indomethacin may be given to:
     i) All babies born before 28 weeks
     ii) In babies born between 28 and 30 weeks who had no antenatal steroids and / or have RDS requiring surfactant.
   - IV Indomethacin 0.1mg/kg every 24 hours for 3 doses starting between 2 and 6 hours of age.
   - This approach has a number of immediate benefits, in particular a reduction in symptomatic patent ductus arteriosus, the need for duct ligation and severe intraventricular haemorrhage. There is no evidence to
suggest either benefit or harm in longer term outcomes including neurodevelopment.

2. **Targeted Early Closure**
   - This approach is recommended in units where facility for early bedside echocardiogram is available.
   - Compared to the above approach, fewer babies will need to be treated.
   - An echocardiogram should be performed to assess the status of ductal constriction between 3 and 5 hours after birth in:
     i) All babies born before 28 weeks
     ii) In babies born between 28 and 30 weeks who had no antenatal steroids and / or have RDS requiring surfactant.
   - Colour Doppler ductal diameters greater than the median (2.0mm at 3 hours or 1.6mm at 5-10 hours) should be considered for early medical closure.
   - Babies identified for early treatment should be given 0.1mg/kg of Indomethacin intravenously over 30 minutes.
   - Babies will often close their duct very quickly after one or two doses of IV Indomethacin. The number of doses can be tailored to the individual baby’s needs. An echocardiogram is repeated 24 hours after the first dose and if the duct is completely closed on colour Doppler, subsequent doses of Indomethacin need not be given.

3. **Treating Clinically Apparent Ducts.**
   - This approach may be used if there is great concern regarding potential adverse effects of Indomethacin or in tertiary units with ready access to cardiac surgical services.
   - IV Indomethacin 0.1 mg/kg/dose every 24 hours for 6 days. Oral indomethacin may be given in place of IV if there is no contraindication to enteral medication or feeding.

4. **Asymptomatic PDA** (only cardiac murmur present) in an otherwise well baby who is gaining weight normally should not be treated with Indomethacin. Most PDA in this group will close spontaneously.

**Contraindications to indomethacin therapy:**
- Infants with proven or suspected infection that is untreated.
- Bleeding, especially active gastrointestinal or intracranial.
- Platelet count < 50-80,000
- NEC or suspected NEC.
- Duct dependant congenital heart disease.
- Impaired renal function.
- Urine output < 0.6 ml/kg/hr after a dose given (withhold next dose until back to normal).

**Fluid restriction and/or diuretic therapy**
There is no evidence that fluid restriction and/or diuretic therapy improves outcome in the premature babies. These measures may result in electrolyte imbalance, hypovolemia and renal failure and are not generally recommended.
References

Perinatally Acquired Varicella

1. In maternal infection (onset of rash) **within 5 days before and 2 days after delivery** 17-30% develops neonatal varicella with lesions appearing 5-10 days of life. Mortality is high (20%-50%). Cause of death is due to severe pulmonary disease or widespread necrotic lesions of viscera.

2. 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.

3. Infants born to mothers who develop varicella between 7 days antenatally and 14 days postnatally should receive
   - **125µ Zoster immunoglobulin (ZIG)** as soon as possible. If vesicles develop to give
   - **Acyclovir 20 mg/kg** over 1 hour every 8hrly (total 60mg /kg/day) for 7 days.
   - If Zoster immunoglobulin is not available give **IV Immunoglobulin 400 mg/kg** (this is less effective) **AND**
   - **Acyclovir 20 mg/kg** over 1 hour every 8hrly (total 60mg /kg/day) for 7 days.

   **Women with varicella at time of delivery should be isolated from their new-borns, 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.

4. Infants whose mothers develop Zoster before or after delivery have maternal antibodies and will babies not need ZIG.

5. **Gestational Chicken Pox/Congenital varicella**
   - Transplacental transmission occurs.
   - 5% develop congenital malformations. Most common congenital abnormality are unilateral cicatricial lesions involving a hypoplastic limb. Others include LBW, microcephaly, chorioretinitis and cataract.
   - ¼ of new-borns delivered to mothers who contract varicella during the last 4 weeks of pregnancy will develop infection.
   - Not associated with increased prematurity or foetal death.
   - Increased risk of leukaemia described.

Reference
Textbook of Neonatology by Rennie & Roberton 1999
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. Associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment.

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

Important Points In The History:

- Current symptoms
- Pattern of symptoms
- Precipitating factors
- Present treatment
- Previous hospital admission
- Typical exacerbations
- Home/ School environment
- Impact on life style
- History of atopy
- Response to prior treatment
- Prolonged URTI symptoms
- Family history

Physical examination

ABSENCE OF PHYSICAL FINDINGS DOES NOT EXCLUDE ASTHMA!

Signs of chronic illness

- Harrison sulci
- Hyperinflated chest
- Eczema/ dry skin
- Hypertrophied turbinates

Signs in acute exacerbation

- Tachypnea, wheeze/ rhonchi/ hyperinflated chest
- Cyanosis/ drowsiness/ accessory muscles/ tachycardia
Management of Chronic Asthma

1. Assessment of Severity

Classification based on frequency, chronicity and severity of symptoms as below;

### CLASSIFICATION OF SEVERITY OF CHILDHOOD ASTHMA

<table>
<thead>
<tr>
<th>Category</th>
<th>Clinical Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent</td>
<td>Daytime symptoms less than once a week</td>
</tr>
<tr>
<td></td>
<td>Nocturnal symptoms less than once a month</td>
</tr>
<tr>
<td></td>
<td>No exercise induced symptoms</td>
</tr>
<tr>
<td></td>
<td>Brief exacerbations not affecting sleep and activity</td>
</tr>
<tr>
<td></td>
<td>Normal lung function</td>
</tr>
<tr>
<td>Persistent (Threshold for preventive treatment)</td>
<td></td>
</tr>
<tr>
<td>Mild persistent</td>
<td>Daytime symptoms more than once a week</td>
</tr>
<tr>
<td></td>
<td>Nocturnal symptoms more than twice a month</td>
</tr>
<tr>
<td></td>
<td>Exercise induced symptoms</td>
</tr>
<tr>
<td></td>
<td>Exacerbations once a month affecting sleep and activity</td>
</tr>
<tr>
<td></td>
<td>PEFR / FEV&lt;sub&gt;1&lt;/sub&gt; &gt; 80%</td>
</tr>
<tr>
<td>Moderate Persistent</td>
<td>Daytime symptoms daily</td>
</tr>
<tr>
<td></td>
<td>Nocturnal symptoms more than once a week</td>
</tr>
<tr>
<td></td>
<td>Exercise induced symptoms</td>
</tr>
<tr>
<td></td>
<td>Exacerbations more than twice a month affecting sleep and activity</td>
</tr>
<tr>
<td></td>
<td>PEFR / FEV&lt;sub&gt;1&lt;/sub&gt; 60 – 80%</td>
</tr>
<tr>
<td>Severe Persistent</td>
<td>Daytime symptoms daily</td>
</tr>
<tr>
<td></td>
<td>Daily nocturnal symptoms</td>
</tr>
<tr>
<td></td>
<td>Daily exercise induced symptoms</td>
</tr>
<tr>
<td></td>
<td>Frequent exacerbations more than twice a month affecting sleep and activity</td>
</tr>
<tr>
<td></td>
<td>PEFR / FEV&lt;sub&gt;1&lt;/sub&gt; &lt; 60%</td>
</tr>
</tbody>
</table>

**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<sub>1</sub> = Forced Expiratory Volume in One Second
2. Management

2.1 Prevention
Identifying and avoiding the following common triggers may be useful

a. 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.

b. Cigarette smoke


d. Food allergy - Uncommon trigger occurring in 1-2% of children

e. Exercise
   Although it is a recognised trigger, activity should not be limited. Symptoms can be controlled by taking a beta agonist prior to a strenuous exercise as well as optimising treatment

2.2 Drug Therapy

2.2.1 Drug therapy: Delivery systems available & recommendation for the different ages.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Oral</th>
<th>MDI + Spacer + Mask</th>
<th>MDI + Spacer</th>
<th>Dry Powder Inhaler</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5</td>
<td>+</td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5 - 8</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>&gt; 8</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

MDI = Meter dose inhaler
Mask used should be applied firmly to the face of the child
### 2.2.2 Drug Dosages

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Relieving Drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Beta2-agonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salbutamol</td>
<td>Oral, Metered dose inhaler,</td>
<td>0.15 mg/kg/dose TDS-QID/PRN, 100-200 mcg/dose QID/PRN, 100-200 mcg/dose QID/PRN</td>
</tr>
<tr>
<td>- <strong>Terbutaline</strong></td>
<td>Oral</td>
<td>0.075 mg/kg/dose TDS-QID/PRN, 250-500 mcg/dose QID/PRN, 500-1000 mcg/dose QID/PRN (maximum 4000 mcg/day)</td>
</tr>
<tr>
<td>- Fenoterol</td>
<td>Metered dose inhaler</td>
<td>200 mcg/dose QID/PRN</td>
</tr>
<tr>
<td><strong>Ipratropium Bromide</strong></td>
<td>Metered dose inhaler</td>
<td>40-60 mcg/dose TDS/QID/PRN</td>
</tr>
<tr>
<td><strong>Preventive Drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Corticosteroids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Oral</td>
<td>1-2 mg/kg/day in divided doses</td>
</tr>
<tr>
<td>- Beclomethasone dipropionate</td>
<td>Metered dose inhaler, dry powder inhaler</td>
<td>Doses for either beclomethasone or budesonide</td>
</tr>
<tr>
<td>- Budesonide</td>
<td>Metered dose inhaler, dry powder inhaler</td>
<td>&lt;400 mcg/day : low dose, 400-800 mcg/day : Moderate dose, 800-1200 mcg/day : High dose</td>
</tr>
<tr>
<td>Fluticasone propionate</td>
<td>Metered dose inhaler, dry powder inhaler</td>
<td>Doses for fluticasone:</td>
</tr>
<tr>
<td>Sodium cromoglycate</td>
<td>Dry powder inhaler, metered dose inhaler</td>
<td>20 mg QID, 1-2 mg QID or 5-10mg BID-QID</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Oral syrup, slow release</td>
<td>5 mg/kg/dose TDS/QID, 10 mg/kg/dose BD</td>
</tr>
<tr>
<td><strong>Long acting Beta2 Agonist</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Metered dose inhaler, dry powder inhaler</td>
<td>50-100 mcg/dose BD, 50-100 mcg/dose BD</td>
</tr>
<tr>
<td><strong>Combination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol / Fluticasone</td>
<td>Metered dose inhaler, dry powder inhaler</td>
<td>25/50 mcg, 25/125 mcg, 25/250 mcg, 50/100 mcg, 50/250 mcg, 50/500 mcg</td>
</tr>
<tr>
<td>Budesonide/Formoterol</td>
<td>Dry powder</td>
<td>160/4.5 mcg, 80/4.5 mcg</td>
</tr>
<tr>
<td><strong>Antileukotrienes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montelukast</td>
<td>Oral</td>
<td>5 mg/tablet on night chewable, 10 mg/tablet on</td>
</tr>
</tbody>
</table>
Note: Types of dry powder inhaler devices available include rotahaler, diskhaler, turbohaler, accuhaler and easyhaler.

2.2.3: Treatment of Chronic Asthma – Stepwise Approach

**Algorithm for Long Term Management of Childhood Asthma**

Intermittent β2 agonist

- Inhaled Corticosteroids (low dose)
- Inhaled Corticosteroids (moderate dose)
- Inhaled Corticosteroids (high dose)
- Inhaled Corticosteroids (very high dose)

Alternative §
- Leukotriene antagonist
- Cromones

Add on therapy
- Long acting β2 agonist #
- Leukotriene antagonist

Consider
- Prednisolone
- Theophylline

---

<table>
<thead>
<tr>
<th>STEP 1</th>
<th>STEP 2</th>
<th>STEP 3</th>
<th>STEP 4</th>
<th>STEP 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary health care provider (General Practice)</td>
<td>Refer to appropriate specialty care provider</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Inhaled corticosteroids recommended if symptoms persist despite alternative asthma treatment.

* Inhaled corticosteroids-
  - low dose: 100 – 200 mcg/day
  - moderate dose: 200 – 400 mcg/day
  - high dose: 400 – 800 mcg/day
  - very high dose: 800 – 1200 mcg/day

Long acting B2-agonists have the potential to mask the clinical effects of increasing eosinophilic airway inflammation when the steroid dose is insufficient.

Theophylline has a role in severe exacerbation of childhood asthma even though it has side effects. It should be considered prior to intubation.

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

### 2.3 Monitoring

Assessment during follow-up
1. Assess severity
2. Response to therapy
   - Interval symptoms
   - Frequency and severity of acute exacerbation
   - Morbidity secondary to asthma
   - Quality of life
   - PEF monitoring on each visit
3. Compliance
   - Frequency and technique
   - Reason and excuses
4. Education

Technique, factual information, written action plan, PEF monitoring may not be practical for all asthmatics but is essential especially for those have poor perception of symptoms and those with life threatening attacks.
Management of Acute Asthma

1. Assessment of Severity

A. Initial (Acute assessment)
   a) Diagnosis
      - Symptoms e.g. cough, wheezing, breathlessness, pneumonia
   b) Triggering factors
      - Food, weather, exercise, infection, emotion, drugs, aeroallergens
   c) Severity
      - Respiratory rate, colour, respiratory effort, conscious level

The initial assessment is the first step in the management of acute asthma

<table>
<thead>
<tr>
<th></th>
<th>Mild (admission unlikely)</th>
<th>Moderate (may need admission)</th>
<th>Severe (admission needed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>altered consciousness</td>
<td>No</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>physical exhaustion</td>
<td>No</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>pulsus paradoxus</td>
<td>sentences</td>
<td>phrases</td>
<td>words</td>
</tr>
<tr>
<td>central cyanosis</td>
<td>absent</td>
<td>absent</td>
<td>present</td>
</tr>
<tr>
<td>rhonchi</td>
<td>present</td>
<td>present</td>
<td>silent chest</td>
</tr>
<tr>
<td>use of accessory muscle</td>
<td>absent</td>
<td>moderate</td>
<td>marked</td>
</tr>
<tr>
<td>sternal retraction</td>
<td>absent</td>
<td>moderate</td>
<td>marked</td>
</tr>
<tr>
<td>initial PEF</td>
<td>&gt;60%</td>
<td>40-60%</td>
<td>&lt;40%</td>
</tr>
<tr>
<td>SaO2</td>
<td>&gt;93%</td>
<td>91-93%</td>
<td>&lt;90%</td>
</tr>
</tbody>
</table>

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.

2. Criteria for admission

- Failure to respond to standard home treatment.
- Failure of those with mild or moderate acute asthma to respond to nebulised β2 agonists.
- Relapse within 4 hours of nebulised β2 agonists.
- Severe acute asthma.
3. Acute Treatment

**Acute moderate/severe**

- Oxygen - mandatory to correct hypoxaemia. Maintain saturation >95%

1. Nebulised or subcutaneous β-agonist - continuous nebuliser if necessary.
2. First dose oral /IV steroids.

**No response**

Add 1. Nebulised Ipratropium bromide
2. ± IV β2 agonist or IV aminophylline

**If failing**

- Mechanical ventilation

**Note:**

1. Monitor pulse, colour, PEFR, ABG and O₂ Saturation (if available) 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.
4. Antibiotics indicated only if bacterial infection suspected.
5. Avoid sedatives and mucolytics.
6. Efficacy of prednisolone in the first year of life is poor.
7. On discharge, patients must be provided with an Action Plan to assist parents or patients to prevent/terminate asthma attacks. The plan must include on;
   a. how to recognize worsening asthma
   b. how to treat worsening asthma
   c. how & 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

- Aminophylline : No significant role but can be use in a control environment like ICU
### 4. Drug Dosages in Acute Asthma

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta2-agonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Salbutamol</td>
<td>Nebuliser solution</td>
<td>0.15 mg/kg/dose (max 5 mg) or &lt; 2 years old : 2.5 mg/dose&lt;br&gt; &gt; 2 years old : 5.0 mg/dose&lt;br&gt; Continuous : 500 mcg/kg/hr</td>
</tr>
<tr>
<td></td>
<td>Intravenous</td>
<td>Bolus: 5-10 mcg/kg over 10 min&lt;br&gt; Infusion: Start 0.5-1.0 mcg/kg/min&lt;br&gt; increased 1.0 mcg/kg/min&lt;br&gt; every 15 min to a maximum of 20 mcg/kg/min</td>
</tr>
<tr>
<td>- Terbutaline</td>
<td>Nebuliser solution</td>
<td>0.2-0.3 mg/kg/dose or &lt; 20 kg: 2.5 mg/dose&lt;br&gt; &gt; 20 kg: 5.0 mg/dose</td>
</tr>
<tr>
<td></td>
<td>Intravenous</td>
<td>5-10 mcg/kg/dose</td>
</tr>
<tr>
<td>- Fenoterol</td>
<td>Nebuliser solution</td>
<td>0.25-1.5 mg/dose</td>
</tr>
<tr>
<td></td>
<td>Parenteral</td>
<td></td>
</tr>
<tr>
<td><strong>Steroids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Prednisolone</td>
<td>Oral</td>
<td>1-2 mg/kg/day in divided doses (for 3-7 days)</td>
</tr>
<tr>
<td>- Hydrocortisone</td>
<td>Intravenous</td>
<td>4-5 mg/kg/dose 6 hourly</td>
</tr>
<tr>
<td>- Methylprednisolone</td>
<td>Intravenous</td>
<td>1-2 mg/kg/dose 6-12 hourly</td>
</tr>
<tr>
<td><strong>Ipratropium bromide</strong></td>
<td>Nebuliser solution (250 mcg/ml)</td>
<td>&lt; 5 years old : 250 mcg 4-6 hourly&lt;br&gt; &gt; 5 years old : 500 mcg 4-6 hourly</td>
</tr>
<tr>
<td><strong>Aminophylline</strong></td>
<td>Intravenous</td>
<td>6 mg/kg slow bolus (if not previously on theophylline) followed by infusion 0.5-1.0 mg/kg/hr</td>
</tr>
</tbody>
</table>

**References**
1) Guidelines for the Management of Childhood Asthma – Ministry of Health, Malaysia and Academy of Medicine, Malaysia
6) Jenkins et al. Salmeterol/Fluticasone propionate combination therapy 50/250ug bd is more effective than budesonide 800ug bd in treating moderate to severe asthma. Respiratory Medicine 2000. 94, 715-723.
VIRAL BRONCHIOLITIS

Aetiology and Epidemiology
Viral bronchiolitis is a common respiratory illness especially in infants between 1 to 6 months. 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
Viral bronchiolitis 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 have mild illness and about 1% of these children require hospital admission.

Table 1: Guideline for Hospital Admission in Viral Bronchiolitis

<table>
<thead>
<tr>
<th></th>
<th>Home Management</th>
<th>Hospital management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; than 3 months</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Toxic – looking</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Chest recession</td>
<td>Mild</td>
<td>Moderate/Severe</td>
</tr>
<tr>
<td>Central cyanosis</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Wheeze</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Crepitations on auscultation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Feeding</td>
<td>Well</td>
<td>Difficult</td>
</tr>
<tr>
<td>Apnoea</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxygen saturation</td>
<td>&gt;95%</td>
<td>&lt;93%</td>
</tr>
<tr>
<td>High risk group</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Chest x-ray
There is a wide range of radiological changes seen in viral bronchiolitis; hyperinflation is most commonly seen, segmental or lobar collapse/consolidation may be found. 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 and if intensive care is required.

Management
Careful assessment of the respiratory status and oxygenation are the most critical aspects of caring for children with viral bronchiolitis. Arterial oxygenation as ascertained by pulse oximetry (SaO₂) should be performed for all infants at presentation and maintained above 93%; with the administration of supplemental humidified oxygen if necessary.
Clinicians must monitor for signs of impending respiratory failure including inability to maintain satisfactory SpO$_2$ on inspired oxygen of more than 40% or a rising PCO$_2$. Very young infants are at risk of apnoea require greater vigilance.

**Nutrition and Fluid Therapy**

Infants admitted with viral bronchiolitis frequently have poor feeding, are at risk of aspiration and may be dehydrated. Small frequent feeds as tolerated can be allowed in children with moderate respiratory distress. Naso-gastric feeding, although not universally practiced, may be useful in these children who refuse to feed and also to empty the dilated stomach.

Intravenous fluids are given to children with severe respiratory distress, cyanosed and apnoea. Fluid therapy should be restricted to maintenance requirement of 100 ml/kg/day for infants, in the absence of dehydration.

Pooled data have indicated a modest clinical improvement with the use of β2-agonist. A trial of nebulised β2-agonist, given in oxygen, may be considered in infants with viral bronchiolitis. Vigilant and regular assessment of the child should be carried out if such a treatment is provided.

Randomised controlled trials of the use of inhaled steroids for treatment of viral bronchiolitis demonstrated no meaningful benefit

Antibiotics are recommended for all infants with

- recurrent apnoea and circulatory impairment,
- possibility of septicaemia
- acute clinical deterioration
- high white cell count
- progressive infiltrative changes on chest radiograph.

**References**

CROUP

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

The most common pathogen is parainfluenza virus (74%), (types 1, 2 and 3). The others are Respiratory Syncytial Virus, Influenza virus type A and B, Adenovirus, Enterovirus, Measles, Mumps and Rhinoviruses and rarely Mycoplasma pneumoniae and Corynebacterium Diphtheriae

Clinical Features
1. Low grade fever, cough and coryza for 12-72 hours followed by
2. Increasingly bark-like cough and hoarseness
3. Stridor that may occur when excited, at rest or both.
4. Respiratory distress of varying degree

Diagnosis
1. Croup is a clinical diagnosis. Studies show that it is safe to visualise the pharynx to exclude acute epiglotitis, retropharyngeal abscess etc. However, in severe croup, it is advisable to examine the pharynx under controlled conditions (ICU /O.T.)
2. 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)
1. Severity
   a. Mild: Stridor with excitement or at rest, with no respiratory distress.
   b. Moderate: Stridor at rest with intercostal, substernal or sternal recession.
   c. Severe: Stridor at rest with marked recession, decreased air entry and altered level of consciousness.
2. Pulse Oximetry is helpful but not essential
3. 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 of Viral Croup

Indications for hospital admission
1. Moderate and severe viral croup.
2. Toxic looking
3. Poor oral intake
4. Age less than 6 months
5. Unreliable caregivers at home
6. Family that lives a long distance from the hospital and lacks reliable transport
ALGORITHM FOR THE MANAGEMENT OF VIRAL CROUP

**MILD**
- Outpatient
  - Dexamethasone
    - Oral (1st choice) / Parenteral 0.15 kg/single dose
    - May repeat at 12 and 24 hours
  - Prednisolone
    - 1-2 mg/kg/stat
      - or if vomiting
  - Nebulised Budesonide
    - 2 mg single dose only

**MODERATE**
- In patient
  - Dexamethasone
    - Oral/parenteral 0.3-0.6 mg/kg single dose
    - and / or
  - Nebulised Budesonide
    - 2 mg stat and 1 mg 12 hrly

**SEVERE**
- In patient
  - Nebulised adrenaline
    - 0.5 mg/kg 1:1000
    - and
  - Dexamethasone
    - Parenteral 0.3-0.6 mg/kg
    - and
  - Nebulised Budesonide
    - 2 mg stat, 1 mg 12 hrly
    - and
  - Oxygen

- No improvement / deteriorate
  - Intubate and ventilate

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

The indications for oxygen therapy include:
1. severe viral croup
2. percutaneous SaO2 < 93%

Caution: With oxygen therapy, the SaO2 may be normal despite progressive respiratory failure and a high PaCO2. Hence clinical assessment is most important.
Antibiotics are not recommended unless bacterial super-infection is strongly suspected or the patient is very ill. Intravenous fluids are not usually necessary except for those unable to drink.

References

Pneumonia

There are two clinical definitions of pneumonia:

1) bronchopneumonia which is a febrile illness with cough, respiratory distress with evidence of localised or generalised patch infiltrates

2) lobar pneumonia which is similar to bronchopneumonia except that the physical findings and radiographs indicate lobar consolidation.

Aetiology
The specific aetiological agents cannot be identified in 40% to 60% of cases. Viral pneumonia cannot be distinguished from bacterial disease based on a combination of findings. One helpful indicator in predicting aetiological agents is the age group. The majority of lower respiratory tract infections that present for medical attention are viral in origin such as respiratory syncytial virus, influenza A and B, adenovirus and parainfluenza virus. The predominant bacterial pathogens that cause pneumonia in infants and children are shown in Table 1.

Table 1: Pathogens causing pneumonia

<table>
<thead>
<tr>
<th>Age</th>
<th>Bacterial Pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborns</td>
<td>Group B streptococcus, <em>Escherichia coli</em>, Klebsiella species, Enterobacteriaceae</td>
</tr>
<tr>
<td>1-3 months</td>
<td>Chlamydia trachomatis</td>
</tr>
<tr>
<td>Preschool</td>
<td>Streptococcus pneumoniae, Haemophilus influenzae type b, Staphylococcal aureus, Less common: group A streptococcus, Moraxella catarrhalis, Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>School</td>
<td>Mycoplasma pneumoniae, Chlamydia pneumoniae</td>
</tr>
</tbody>
</table>

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:

Table 2: Definition of Tachypnoea

<table>
<thead>
<tr>
<th>Age</th>
<th>Rate (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 2 months</td>
<td>&gt; 60</td>
</tr>
<tr>
<td>2-12 months</td>
<td>&gt; 50</td>
</tr>
<tr>
<td>12 months – 5 years</td>
<td>&gt; 40</td>
</tr>
</tbody>
</table>

Assessment of severity is essential for optimal management of pneumonia. Pneumonia may be categorized according to mild, severe, very severe based on the respiratory signs and symptoms as shown in Table 3 and Table 4.
Table 3: Assessment of severity of pneumonia in children age 2 months to 5 years old

<table>
<thead>
<tr>
<th>Mild Pneumonia</th>
<th>Fast breathing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe pneumonia</td>
<td>Chest indrawing</td>
</tr>
<tr>
<td>Very severe pneumonia</td>
<td>Not able to drink</td>
</tr>
<tr>
<td></td>
<td>Convulsions</td>
</tr>
<tr>
<td></td>
<td>Drowsiness</td>
</tr>
<tr>
<td></td>
<td>Malnutrition</td>
</tr>
</tbody>
</table>

Table 4: Assessment of severity of pneumonia in infants below two months old.

<table>
<thead>
<tr>
<th>Severe pneumonia</th>
<th>Severe chest indrawing or fast breathing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very severe pneumonia</td>
<td>Not feeding</td>
</tr>
<tr>
<td></td>
<td>Convulsions</td>
</tr>
<tr>
<td></td>
<td>Abnormally sleepy or difficult to wake</td>
</tr>
<tr>
<td></td>
<td>Fever/ low body temperature</td>
</tr>
<tr>
<td></td>
<td>Hypopnoea with slow irregular breathing</td>
</tr>
</tbody>
</table>

Adapted from WHO

Investigations
Children with bacterial pneumonia cannot be reliably distinguished from those with viral disease on the basis of any single parameter; clinical, laboratory or chest radiograph findings.

Chest radiograph is indicated when clinical criteria suggests pneumonia. It will not diagnose the aetiological agent. However the chest radiograph is not always necessary if facilities are not available or the pneumonia is mild.

Increased white blood count with predominance of polymorphonuclear cells may suggest bacterial cause. However, leucopenia can either suggest a viral cause or severe overwhelming infection.

Blood culture remains the non-invasive gold standard for determining the precise aetiology of pneumonia. However the sensitivity of this test is very low. Positive blood cultures are found only in 10% to 30% of patients with pneumonia. Blood culture should be performed in severe pneumonia or when there is poor response to the first line antibiotics.

Pleural fluid
If there is significant pleural effusion diagnostic pleural tap will be helpful.
Serology
*Mycoplasma pneumoniae, Chlamydia, Legionella and Moraxella catarrhalis* are difficult organisms to culture, and thus serology is performed in patients with suspected atypical pneumonia. Acute phase serum titre more than 1:160 or paired samples taken 2-4 weeks apart showing four fold rise is a good indicator of *Mycoplasma pneumoniae* infection. This test should be considered for children aged five years or older.

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

Criteria for hospitalization
Community acquired pneumonia can be treated at home. It is crucial to identify indicators of severity in children who may need admission. Failure to recognise the severity of pneumonia may lead to death. The following indicators can be used as a guide for admission.

- Children aged <3 months whatever the severity of pneumonia.
- Fever ( >38.5 °C ), refusal to feed and vomiting
- Fast breathing with or without cyanosis
- Associated systemic manifestation
- Failure of previous antibiotic therapy
- Recurrent pneumonia
- Severe underlying disorders ( i.e. immunodeficiency )

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

The majority of childhood infections are caused by viruses and do not require any antibiotic. However, it is also very important to remember that we should be vigilant to choose appropriate antibiotics especially in the initial treatment to reduce further mortality and morbidity.
Table 5: Predominant bacterial pathogens of children and the recommended antimicrobial agents to be used.

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Beta-lactam susceptible</th>
<th>Antimicrobial agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumonia</td>
<td></td>
<td>Penicillin, Cephalosporins</td>
</tr>
<tr>
<td>Haemophilus influenzae type b</td>
<td></td>
<td>Ampicillin, Chloramphenicol, Cephalosporins</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td></td>
<td>Cloxacillin</td>
</tr>
<tr>
<td>Group A Streptococcus</td>
<td></td>
<td>Penicillin, Cephalosporin</td>
</tr>
<tr>
<td>Mycoplasma pneumonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlamydia pneumonia</td>
<td></td>
<td>Macrolides such as erythromycin and azithromycin</td>
</tr>
<tr>
<td>Bordetella pertussis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**INPATIENT MANAGEMENT**

**Antibiotics**

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

<table>
<thead>
<tr>
<th></th>
<th>1st line</th>
<th>2nd line</th>
<th>3rd line</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-lactams drugs</strong></td>
<td>Benzylpenicillin, Amoxycillin, Ampicillin, Amoxycillin-Clavulanate</td>
<td>Cephalosporins: Cefotaxime, Cefuroxime, Ceftazidime</td>
<td>Carbapenem: Imipenem</td>
<td>Aminoglycosides: Gentamicin, Amikacin</td>
</tr>
</tbody>
</table>

If there are no signs of recovery, patients remain toxic and ill with spiking temperature for 48 - 72 hours, a second line antibiotics need to be considered. If Mycoplasma or Chlamydia species are the causative agents, a macrolide is more appropriate.

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 has been frequently reported in malnourished children.

**Staphylococcal infection**

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

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

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

**Cough Syrup**: It is not recommended as it causes suppression of cough and may interfere with airway clearance. Adverse effects and overdosage have been reported.

**Temperature Control**: The rationale to use paracetamol is only to reduce discomfort from symptoms. The paracetamol will not abolish the fever.

**Chest physiotherapy**
The function of chest physiotherapy in paediatric respiratory disease is to assist in the removal of tracheobronchial secretions. The intention is to remove airway obstruction, increase gas exchange and reduce the work of breathing. There is no evidence to suggest that chest physiotherapy should be routinely done in pneumonia.

OUTPATIENT MANAGEMENT

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

References

PAEDIATRIC ECG INTERPRETATION

Routine interpretation: Suggested sequence
1. Rhythm (sinus or non-sinus) by considering the P axis
2. Heart rate (atrial and ventricular rates, if different)
3. The QRS axis
4. Intervals: PR, QRS and QT
5. The P wave amplitude and duration
6. The QRS amplitude and R/S ratio, also abnormal Q waves
7. ST segment and T wave abnormalities

Rhythm:
Sinus rhythm is characterized by
• P waves preceding each QRS complex
• Normal P axis (0 to +90 degrees) i.e. upright P in I and aVF

Heart rate:
At usual paper speed of 25mm/sec, 1mm = 0.04s, 5mm = 0.2s
Methods used to calculate HR include
• Count the R-R cycle in 6 large divisions (1/50 min) and multiply by 50
• Count the number of large divisions between the two R waves and divide that into 300

When the ventricular and atrial rates are different, the atrial rate can be calculated using the P-P interval

QRS Axis:
RV dominance in infants gradually changes to LV dominance in adults
Hence, there is right axis deviation of QRS till 1 month, adult axis by 3 yr

Mean and ranges of Normal QRS Axes

<table>
<thead>
<tr>
<th>Age</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 wk-1mo</td>
<td>+110° (+30 to +180)</td>
</tr>
<tr>
<td>1-3mo</td>
<td>+70° (+10 to +125)</td>
</tr>
<tr>
<td>3mo-3yr</td>
<td>+60° (+10 to +110)</td>
</tr>
<tr>
<td>Older than 3yr</td>
<td>+60° (+20 to +120)</td>
</tr>
<tr>
<td>Adults</td>
<td>+50° (-30 to +105)</td>
</tr>
</tbody>
</table>

Intervals:
• PR interval varies with age and heart rate

<table>
<thead>
<tr>
<th>Age</th>
<th>Lower limit</th>
<th>Upper limit of norm</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3 yr.</td>
<td>0.08sec</td>
<td>0.15 (HR &lt; 100)</td>
</tr>
<tr>
<td>3 - 16 yr</td>
<td>0.10sec</td>
<td>0.16 (HR &lt; 100)</td>
</tr>
<tr>
<td>&gt; 16 yr.</td>
<td>0.12sec</td>
<td>0.18 (HR &lt; 100)</td>
</tr>
</tbody>
</table>
QRS duration | QT interval
---|---
Prem infants 0.04sec | QTc = \( \frac{QT \text{ measured (sec)}}{\sqrt{RR \text{ interval (sec)}}} \)
Full term 0.05sec
1 - 3 yr. 0.06sec
Child > 3 yr. 0.07sec
Adult 0.08sec

According to Bazett's formula, the QTc interval should not exceed 0.44 sec

P wave amplitude and duration:
- Mean P amplitude 1.5mm, max. 3mm.
- Normal P wave duration 0.06±0.02s.
- Max. P wave duration
  - <12mo 0.08sec
  - Child 0.10sec
- Right atrial enlargement - P > 3 mm peaked (P pulmonale)
- Left atrial enlargement - Bifid P > 0.10s (0.08s in infants) (P mitrale)
  P inversion >1mm in V1

Abnormal Q waves:
- Q wave commonly present in I, aVL and/or V5 and V6. May also be present in II, III and aVF.
- Presence of Q in V1 = RVH
- Deep Q waves suggest LVH
- Average Q wave duration is 0.02s and does not exceed 0.03s

ST segment and T waves
- ST segment horizontal, isoelectric shifts may be normal up to
  - 1mm in limb leads
  - 2mm in praecordial leads
- T wave amplitude usually less than the following:
  - in V5: < 1yr 11mm > 1yr 14mm
  - V6: < 1yr 7mm > 1yr 9mm
- Tall and peaked in hyperkalaemia

Criteria for RVH
- RV1 > 20mm at all ages
- SV6 > 14mm (0-7days); > 10mm (1wk-6mth); > 7mm (6mth-1yr); > 5mm (> 1yr)
- R/S V1 6.5 (0-3mth); 4.0 (3-6mth); 2.4 (6mth-3yr); 1.6 (3-5yr); 0.8 (6-15yr)
- T wave upright in V4R or V1 after 72 hrs.
- Presence of Q wave in V1.
RVH in the newborn
- S waves in lead I, ≥ 12mm
- R waves in aVR, ≥ 8mm
- Important abnormalities in V1 such as:
  - Pure R waves (without S) in V1, ≥ 10mm
  - R waves in V1, ≥ 25mm
  - QR pattern in V1 (also seen in 10% of normal newborns)
  - Upright T waves in V1 in newborns > 3 days old
- QRS axis greater than +180°

Criteria for LVH
- SV1 > 20mm
- RV6 > 20mm > 26mm in older child
- SV1 + RV6 > 40mm over 1yr of age; > 30mm if < 1yr
- Q wave of 4mm or more in V 5-6
- T wave inversion in V 5-6

Combined biventricular hypertrophy
- Direct evidence of RVH or LVH
- R + S in V4 > 70mm

Electrolyte changes affecting ECG

<table>
<thead>
<tr>
<th>Hypokalaemia &lt; 2.5 mmol/l</th>
<th>Hyperkalaemia &gt; 6 mmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>T Waves low, flat or inverted</td>
<td>Tall peaked T</td>
</tr>
<tr>
<td>ST Segment depressed</td>
<td>Widening QRS</td>
</tr>
<tr>
<td>QT interval increased</td>
<td>Prolonged PR, Lengthening QT</td>
</tr>
<tr>
<td>U Waves prominent</td>
<td>Diminishing size of P &amp; R waves</td>
</tr>
<tr>
<td></td>
<td>Depressed ST Segment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypocalcaemia</th>
<th>Hypercalcaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>QT prolonged.</td>
<td>QT shortened</td>
</tr>
<tr>
<td>ST Segment unchanged</td>
<td>Cardiac arrhythmias</td>
</tr>
<tr>
<td>Enhances effect of hypokalaemia</td>
<td></td>
</tr>
</tbody>
</table>

Diagram illustrating important intervals (or durations) and segments of an ECG cycle
Timing of Cardiac Surgery

A. Operative Timing in Left-to-Right Shunt Lesions

Patent Ductus Arteriosus

1. Transcatheter closure
   a) Majority of PDA’s
   b) Weight \( \geq 5\) kg

2. Surgical ligation.
   a) Large PDA with congestive cardiac failure
   b) Premature neonates with weight < 5kg, failed medical treatment, and in intractable
      congestive cardiac failure despite antifailure medications.

Ventricular Septal Defect (VSD)

1. Large shunt, congestive failure refractory to medical therapy.
   a) Repair at any age.
   b) Usually not necessary before 3-6m of age.

2. Moderate to large shunt, medical management successful.
   a) With significant pulmonary hypertension - repair by 12-18 m.
   b) Normal or minimal elevation of pulmonary artery pressure.
      i) Follow on medical management, may not require operation.
      ii) If Qp/Qs approximately > 2:1, repair at age 4-6 years.

3. VSD plus Aortic Insufficiency (AI)
   a) Early repair of ventricular defect is recommended.
   b) Probable aortic valvuloplasty with VSD closure in patients with significant aortic
      cusp prolapse and moderate AI.
   c) Trivial AI on colour Doppler or even significant prolapse with no AI is an indication
      for surgery

4. Small defects with small shunts - surgery not indicated
   - infective endocarditis prophylaxis vital

5. Prophylactic closure of small DCSA VSD remains unclear.

Atrial Septal Defect (Secundum)

1. Elective repair at ages 4-5 yr. in most patients.
   Transcatheter closure for defects < 20 mm

2. Rarely infants develop severe congestive failure in infancy and repair required.

3. Infants with large defects and minimal or no symptoms followed to age 4-5 yr.
   a) Defect may decrease in size and surgery not required.
   b) Delay in closure not detrimental for patients whose defects remain large

4. Small defects do not require closure, i.e. no evidence of RV volume overload on Echo.

Atrial Ventricular Septal Defect

1. Ostium primum
   a) Usually elective repair at 4-5 years.
   b) Earlier repair if severe CHF refractory to medical management or evidence of
      pulmonary hypertension.

2. Complete atrioventricular septal defect - repair in infancy.
   Operation can now be offered locally.
B. Operative Timing for Obstructive Lesions

Coarctation of the Aorta

1. Symptomatic Infant
   a) Simple - repair at time of presentation.
   b) With VSD
      i) Urgent coarctation repair + VSD closure
      ii) If PA banding not performed, early VSD repair if severe CHF.

2. Asymptomatic or minimal symptoms - repair is delayed until child is > 1 year old as the incidence of re-stenosis is then reduced.

3. Balloon Dilatation – alternative for those > 1 year with discreet native coarctation
   Restenosis of surgically repaired coarctation

Aortic Stenosis

1. Symptomatic Infant (Critical AS i.e. LV-Ao gradient 30 - 80 with CCF)
   a) Valvulotomy on an emergency.
   b) If left ventricle hypoplastic (approximately <60% of normal size) valvulotomy unlikely to be successful.

2. Symptomatic child with anginal-type chest pain or syncope unexplained by neurologic cause.
   a) Usually have LV strain pattern on ECG plus LV-Ao gradient > 50mmHg.
   b) Require urgent valvuloplasty or operation.

3. Asymptomatic Child
   a) LV-Ao gradient 11 - 25 mmHg (Mild) no intervention. (exception subvalvular membranous AS)
   b) LV-Ao gradient 25 - 49 mmHg (moderate) – no intervention unless symptomatic. No competitive sports.
   c) LV-Ao gradient 50 - 79mmHg (moderately severe) individualise. No competitive sports.
   d) LV-Ao gradient > 80 mmHg (severe) - usually elective valvulotomy / balloon dilatation. No competitive sports.

4. Valve Replacement
   a) Delay as long as possible - frequently required a second operation after initial valvulotomy.
   b) Delay if possible until adult-sized valve can be used.

Pulmonary Stenosis (PS)

1. Pressure Gradient
   - < 40 mmHg No intervention
   - > 60 mmHg Valvuloplasty
   - > 80 mm Hg Urgent referral for valvuloplasty
   - 40 - 60 mmHg Follow-up. Refer if symptomatic or RVH.

Mitral Stenosis

1. Valvulotomy usually not feasible.
2. Delay valve replacement until an adult-sized valve can be used.
C. Operative Timing for Valvular Insufficiency

Aortic Insufficiency

1. If possible, delay valve replacement until adult-sized prosthesis can be used.
2. Definite surgery for severe LV enlargement with congestive failure symptoms.
3. Individualise therapy with lesser signs and symptoms.

Mitral Insufficiency

1. Valve repair at any age, if suitable
2. Delay valve replacement until adult-sized prosthesis can be used, if possible.
3. Severe refractory atrial arrhythmia and significant symptoms refractory to medical management are indications for surgery.

Tricuspid Insufficiency

1. Infant: surgery almost never required.
2. Older patients: delay as long as medical management is reasonably effective.

Pulmonary Insufficiency

1. Occasionally needed in postoperative TOF.
2. Absent pulmonary valve syndrome - delay surgery as long as medical management is effective.

D. Operative Timing for Complex Conditions

Tetralogy of Fallot or Pulmonary Atresia with Ventricular Septal Defect

1. Delay repair until > 1 year in patients with minimal cyanosis and mild hypercyanotic spells that are easily controlled with propranolol.
2. No symptoms or minimal symptoms: elective repair at approximately 1 to 2 years.
3. Significant cyanosis in first 6 m.
   Palliative shunt in most patients, particularly with small pulmonary arteries and/or stenosis of major pulmonary artery branch.
   Elective repair at > 1 year.
4. Pulmonary Atresia plus VSD
   Required Blalock-Taussig shunt. Repair at 3-6 years, usually requiring right ventricular to pulmonary artery conduit.
Transposition of the Great Arteries

1. **Diagnosis < 2 months.** Require urgent referral for possible arterial switch.

2. **Diagnosis late.**

   **Intact Ventricular Septum**
   a) Atrial repair usually at 3-12 months.
   b) Senning or Mustard technique.
   c) Early severe cyanosis below 1-2 months: for arterial switch.

   **With Large Ventricular Septal Defect**
   a) Operation usually needed by 3-6 m.
      VSD closure plus arterial switch

   **With Ventricular Septal Defect plus Pulmonary Stenosis**
   a) Operation usually required in infancy and early childhood.
   b) Rastelli repair: VSD baffled such that left ventricle connected to aorta, right ventricle connected to pulmonary artery by conduit or homograft.
      i) Usually delayed until 4-6 years.
      ii) Multiple conduit replacements will be required.
   c) REV operation an alternative to (b); preferred choice as use of conduit is avoided

**Tricuspid Atresia**

   a) Usually shunt procedures required in infancy to increase pulmonary blood flow.
   b) Repair by Fontan procedure (connection of right atrium to pulmonary arteries) usually recommended at 4-6 years

**Single Ventricle**
If there is no stenosis in the pulmonary arteries then DO NOT refer as surgical outcome is poor at the moment.

**Pulmonary Atresia with Intact Ventricular Septum**

   a) Radiofrequency valvotomy + balloon dilatation ± PDA stenting in neonates with suitable anatomy.
   b) Diminutive right ventricle: shunt procedures with later Fontan-type repair at age 4-6 years.

**Truncus Arteriosus – Type I and II** - Rastelli operation (VSD closure + RV-PA conduit)

**Hypoplastic Left Heart Syndrome:** Multiple operation needed. Associated with high mortality. Currently low priority and for conservative management.

**References:**

Cardiac Failure

Cardiac failure results from the inability of the cardiac pump mechanism to supply the required cardiac output demanded by the body. Heart failure occurs more commonly in the first three months of life than in any other period of childhood; the earlier in life it occurs, the worse the prognosis.

1. Causes
The causes include both congenital and acquired conditions:

1. Left to right shunt
   - VSD
   - PDA
   - Truncus arteriosus
   - ASD
   - TAPVD

2. Obstructive lesion
   - Severe coarctation
   - Critical AS/PS
   - Hypoplastic Left Heart Syndrome

3. Regurgitant lesion
   - Ebstein's anomaly
   - Rheumatic carditis

4. Depressed ventricular contractility
   - Cardiomyopathy
   - Severe birth asphyxia/perinatal myocardial ischaemia

5. Abnormalities of cardiac rhythm
   - Congenital/complete heart block
   - Supraventricular tachycardia

6. Others
   - Large systemic AV malformation
   - Anaemia
   - Polycythaemia
   - Hypertension
   - Myocarditis

2. Symptoms and signs

Three Cardinal Signs of Cardiac Failure in Children:

1. Tachycardia
   - When the rate is greater than 180/min in infants and 150/min in older children, heart failure is usually present.
   * If HR > 220/min infants or > 180/min in older children do ECG and look for supraventricular tachycardia.

2. Cardiomegaly
   - displaced apex beat. AP chest X-ray CTR > 60%.

3. Hepatomegaly
   - More than 2 cm below the right costal margin in the midclavicular line.

Other Signs and Symptoms:

4. Tachypnoea and dyspnoea
   - Infant = > 60/min
   - 2 months to 12 months = > 50/min
   - 12 months – 5 years = > 40/min
   - Grunting and subcostal recession.

5. Restlessness

6. Gallop rhythm
   - A third heart sound is frequently heard at the cardiac apex in a normal heart in childhood but it is faint and not easy to hear. If there is a very obvious 3rd sound causing a gallop rhythm, heart failure is likely.

   - Signs of left ventricular failure (pulmonary oedema).
   - CXR - pulmonary venous congestion

8. Sweating and pallor at the end of feed, especially in infants with large left-to-right shunt such as VSD and PDA.

9. Feeding takes > 30 min per feed.
10. Failure to thrive

3. Treatment

3.1 General measures
a) Position of comfort: The baby should be propped up as comfortably as possible.
Fluid restriction to 3/4 maintenance (in the absence of dehydration or shock). Humidified oxygen if required.
b) Reducing metabolic requirement by tube feeding, keeping warm, and gentle handling.
c) Maximal caloric intake through N/G feeding of high caloric formula.
d) Correction of negative inotropic factors
   - Acidosis
   - Hypoglycaemia
   - Hypocalcaemia
   - Anaemia
e) Treat any associated respiratory infection

3.2 Drugs
4 groups: Diuretics, ACE inhibitors, inotropes, β-blockers

3.2.1 Diuretics
a) Loop diuretic - Frusemide
   Check serum electrolyte levels. If ↓ K⁺, potassium supplement is given orally KCl 2 mmol/kg/day.

b) Potassium sparing diuretic and aldosterone antagonist - Spironolactone
   Can be combined with a loop diuretic to prevent K⁺ loss. Beneficial in suppressing neurohormonal activities

c) Thiazides - Chlorothiazide or hydrochlorothiazide

3.2.2 ACE inhibitors (afterloading reducing agents)
ACE inhibitors –
   - Captopril: Test dose 0.01 mg/kg oral. 0.05-0.1mg/kg/dose (maximum 5 mg) 8H oral, increase if required to max 2mg/kg/dose (adult 50mg) 8 hourly.
   - Enalapril: 0.1 mg/kg (maximum 2.5 mg) daily oral, increase over 2 weeks if required to max. 0.5 mg/kg/dose (maximum 20 mg) 12H

Beware of first dose hypotension. Admit to introduce the medication. Beneficial in suppressing neurohormonal activities. Combination therapy is more effective in suppressing neurohormonal activation than monotherapy with aldosterone antagonist or ACE inhibitor.
3.2.3. **Inotropes**

a) Digoxin (do not give if bradycardic, caution in myocarditis)
   Effective in children with poor myocardial function.
   Less effective with volume overload (e.g. VSD, PDA, AV canal)

   Oral doses:

   | Age of patient | Digitalizing dose over 24 hr given in 3 doses | Maintenance dose over 24 hr given 12 hrly
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature</td>
<td>15 mcg/kg/day</td>
<td>5 mcg/kg/day</td>
</tr>
<tr>
<td>New-born &amp; older</td>
<td>40 mcg/kg/day</td>
<td>10 mcg/kg/day</td>
</tr>
</tbody>
</table>

   [Oral digoxin is usually satisfactory but if intravenous route is being used, the dose must be reduced to 3/4 of the oral dose.] Correct hypoxia, acidosis and hypokalaemia, which increase the tendency for digoxin toxicity.

   Maintenance dose is started 24 hours after initial digitalising dose.

b) **Inotropes**

   Infusion of dopamine or
dobutamine or
adrenaline or
milrinone

   In acute failure and in acute myocarditis.

3.2.4 **β-blockers – metoprolol, carvedilol**

β-blockers therapy should be reserved for patients with mild to moderate heart failure who are clinically stable on background medications consisting of diuretics, ACE inhibitors and digoxin.

*It must be stressed that in congenital cardiovascular malformation, the treatment of heart failure is only a first step in the management and the infant must be referred to a Paediatric Cardiologist to establish the diagnosis and to decide whether surgical treatment is indicated.*

*Heart failure in the first month of life can rarely be treated medically for any length of time. Simple lesions such as PDA and VSD rarely cause heart failure as early as the first month of life except in premature babies. It is usually caused by a lesion requiring surgery or is due to complex cardiac malformation.*

Ref: 1. MOH, Nat. Heart Ass. of M’sia & Academy of Medicine. Clinical Practise Guidelines on Heart Failure 2000
   2. O’Laughlin M.P. Congestive Heart Failure in Children. The Pediatric Clinics of North America 1999
Rheumatic Fever

Diagnosis: Modified Jones Criteria (1992 revision)
For diagnosis of Rheumatic Fever:
- 2 major criteria, OR 1 major and 2 minor
- PLUS evidence of recent infection with Group A beta haemolytic Streptococci.

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carditis **</td>
<td>Fever</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>Arthralgia</td>
</tr>
<tr>
<td>Chorea</td>
<td>Raised acute phase reactants (CRP or ESR)</td>
</tr>
<tr>
<td>Erythema Marginatum</td>
<td>Prolonged PR interval</td>
</tr>
<tr>
<td>Subcutaneous nodules</td>
<td></td>
</tr>
</tbody>
</table>

Evidence of preceding Streptococci infection
ASOT (>200 Todd U) or anti DNase B
Positive Throat Swab
Recent Scarlet Fever

** The following are evidence of Carditis:
- Cardiomegaly
- Cardiac Failure
- Pericarditis
- Tachycardia more than expected for fever esp. during sleep (>10 per °C)
- Significant murmurs of
  - Mitral Incompetence
  - Mitral Stenosis
  - Aortic Incompetence

Exceptions:
1. Chorea: May occur late and be only manifestation of RF
2. Indolent carditis: Patients presenting late to medical attention months after the onset of RF may have insufficient support to fulfil the criteria
3. In newly ill patients with a h/o RF, especially RHD, distinguishing recurrent carditis from pre-existing significant RHD may be impossible

Investigations
FBC, ESR, CRP, ASOT
Throat Culture
ECG, CXR
Echocardiogram
Blood culture to exclude SBE

Treatment
1. Bed rest while fever and acute manifestations persist, especially carditis.
   Gradual ambulation before returning to school.
   Do not allow full activity until acute phase reactants have returned to normal.

2. Eradication of Group A β haemolytic Streptococci.
   - Penicillin V 250mg 6 hourly x 10 days (children), 500mg 6 hourly (adolescents)
   - For patients with allergy to penicillin, erythromycin or 1st generation cephalosporin
3. Aspirin 80-100mg/kg/day in 4-6 doses. 
   Maintain anti-inflammatory dose for 6-8 weeks and until acute phase reactants (ESR, CRP) have returned to normal.

4. Prednisolone - used only in presence of moderate to severe carditis
   - reduces severity of acute illness but has NO effect on incidence or severity of subsequent valvular disease.
   
   Dose: 1-2 mg/kg/day for 2-4 weeks, tapering off over the last week of therapy.
   
   Aspirin may be discontinued during the administration of prednisolone but should be reintroduced when prednisolone is tapered off and maintained for an additional 2-4 weeks and until acute phase reactants have returned to normal.

5. Treat heart failure with diuretics and after-load agents.
   (Digoxin to be used only with caution)
   Consider surgery if heart failure persists or worsens during the acute phase despite aggressive medical therapy.

6. Prophylaxis:
   a) IM Benzathine penicillin 0.6 mega units (<25kg) or 1.2 mega units (>25kg)
      every 4 weekly.
      Administer the same dosage 3 weekly in patients with breakthrough Streptococcal pharyngitis.
      OR
      Oral Penicillin V 250mg bd
      IM route is preferable for compliance

   b) In patients who are allergic to penicillin,
      Erythromycin 250mg bd or Sulphadiazine 500mg daily

   Duration of prophylaxis:
   
   **Recommended for LIFE** especially in patients with carditis and valve disease.
   In patients with RF without carditis, at least until aged 21 years or 5 years after the last episode, whichever is longer.

7. Patients with rheumatic heart disease and valve damage require endocarditis prophylaxis before dental or surgical procedures.
Infective Endocarditis

Infective endocarditis is a microbial infection of the endothelium of the heart.

Diagnosis

1. Clinical features
2. Lab evaluation
   a. Blood cultures – Typical microorganism consistent with IE from two separate blood culture or 3 blood cultures over 24 hours period or daily cultures over several days (prior treatment with antibiotics may give intermittent negative cultures)
   b. Echocardiograph – presence of ‘oscillating mass’

Treatment

<table>
<thead>
<tr>
<th>Organism involved</th>
<th>Antibiotic of choice</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcal e.g Strep. viridan</td>
<td>i.v. penicillin ( or i.v. vancomycin if sensitive to penicillin ) + i.v. gentamicin¹</td>
<td>4 weeks</td>
</tr>
<tr>
<td></td>
<td>Or i.v./i.m. ceftriaxone</td>
<td></td>
</tr>
<tr>
<td>Enterococci e.g. Enterococcus faecalis</td>
<td>i.v. ampicillin ( or i.v. vancomycin if sensitive to penicillin ) + i.v. gentamicin¹</td>
<td>4 weeks²</td>
</tr>
<tr>
<td>Staphylococci e.g. Staph aureus or epidermidis</td>
<td>i.v. cloxacillin ( or penicillin if penicillin sensitive or vancomycin if penicillin-allergic/methicillin resistant staph ) + i.v. gentamicin ( or fusidic acid )</td>
<td>4 weeks³</td>
</tr>
<tr>
<td>Gram negative endocarditis</td>
<td>i.v. ampicillin Or i.v. cephalosporin ( e.g. ceftriaxone ) if resistant to Ampicillin</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Culture negative endocarditis</td>
<td>i.v. cloxacillin ( vancomycin if penicillin-allergic) + i.v. gentamicin</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Fungal endocarditis</td>
<td>amphotericin B</td>
<td>6-8 weeks⁴</td>
</tr>
</tbody>
</table>

¹ stop gentamicin after 2 weeks, monitor gentamicin level and renal function
² substitute streptomycin for gentamicin if resistant to gentamicin and treat for at least 6 weeks
³ stop gentamicin ( or fusidic acid ) after 1 week
⁴ surgical removal of infective tissue after 1-2 weeks medical treatment
### Cardiac Conditions Associated With Endocarditis

**Endocarditis prophylaxis recommended**

**High-risk category**
- Prosthetic cardiac valves, including bioprosthetic and homograft valves
- Previous bacterial endocarditis
- Complex cyanotic congenital heart disease (e.g., single ventricle states, transposition of the great arteries, tetralogy of Fallot)
- Surgically constructed systemic pulmonary shunts or conduits

**Moderate-risk category**
- Most other congenital cardiac malformations (other than above and below)
- Acquired valvar dysfunction (e.g., rheumatic heart disease)
- Hypertrophic cardiomyopathy
- Mitral valve prolapse with valvar regurgitation and/or thickened leaflets

**Endocarditis prophylaxis not recommended**

**Negligible-risk category (no greater risk than the general population)**
- Isolated secundum atrial septal defect
- Surgical repair of atrial septal defect, ventricular septal defect, or patent ductus arteriosus (without residua beyond 6 mo)
- Previous coronary artery bypass graft surgery
- Mitral valve prolapse without valvar regurgitation
- Physiologic, functional, or innocent heart murmurs
- Previous Kawasaki disease without valvar dysfunction
- Previous rheumatic fever without valvar dysfunction
- Cardiac pacemakers (intravascular and epicardial) and implanted defibrillators

### COMMON INVASIVE PROCEDURE THAT REQUIRE ANTIBIOTIC PROPHYLAXIS

**Oral, Dental procedures**
- Dental extractions
- Periodontal procedures
- Dental implant placement and reimplantation of avulsed teeth
- Root canal instrumentation
- Initial placement of orthodontic bands (but not brackets)
- Intraligamentary local anaesthetic injections
- Prophylactic cleaning of teeth or implants where bleeding is anticipated

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

**Gastrointestinal procedures,**
- Sclerotherapy for esophageal varices
- Esophageal stricture dilatation
- Endoscopic retrograde cholangiography with biliary obstruction
- Biliary tract surgery
- Surgical operations involving intestinal mucosa

**Genitourinary procedures**
- Cystoscopy
- Urethral dilatation

**- prophylaxis is recommended for high risk patients and is optional for medium-risk patients.**
<table>
<thead>
<tr>
<th>Situation</th>
<th>Agent</th>
<th>Regimen*</th>
</tr>
</thead>
</table>
| Standard general prophylaxis | Amoxicillin | Adults: 2 g  
Children: 50 mg per kg  
Taken orally one hour before the procedure |
| Patient is unable to take oral medications | Ampicillin | Adults: 2 g  
Children: 50 mg per kg  
Given IM or IV within 30 minutes before the procedure |
| Patient is allergic to penicillin | Clindamycin  
or Cefadroxil or cephalexin † | Adults: 2 g  
Children: 50 mg per kg  
Taken orally one hour before the procedure |
| Patient is allergic to penicillin and is unable to take oral medication | Clindamycin  
or Cefazolin | Adults: 600 mg  
Children: 20 mg per kg  
Given IV within 30 minutes before the procedure  
or Adults: 1 g  
Children: 25 mg per kg  
Given IM or IV within 30 minutes before the procedure |

IM=intramuscularly; IV=intravenously.

*--The total pediatric dose should not exceed the adult dose.
†--Cephalosporins should not be used in patients with an immediate-type hypersensitivity reaction (urticaria, angioedema or anaphylaxis) to penicillins
‡- The AHA no longer recommends erythromycin because of its gastrointestinal adverse effects and the complicated pharmacokinetics of the various formulations. Physicians and dentists who have successfully used erythromycin for prophylaxis in individual patients may choose to continue with this antibiotic.

A follow-up dose is no longer recommended.
## Endocarditis Prophylactic Regimens for Genitourinary and Gastrointestinal Procedures

<table>
<thead>
<tr>
<th>Situation</th>
<th>Agents</th>
<th>Regimen †</th>
</tr>
</thead>
</table>
| High-risk patients                 | Ampicillin plus gentamicin | Adults: ampicillin, 2 g IM or IV, plus gentamicin, 1.5 mg per kg IM or IV (gentamicin dose should not exceed 120 mg), given within 30 minutes of starting the procedure; six hours later, ampicillin, 1 g IM or IV, or amoxicillin, 1 g given orally ‡  
Children: ampicillin, 50 mg per kg IM or IV (dose not to exceed 2 g), plus gentamicin, 1.5 mg per kg IM, given within 30 minutes of starting the procedure; six hours later, ampicillin, 25 mg per kg IM or IV, or amoxicillin, 25 mg per kg given orally ‡ |
| High-risk patients who are allergic to ampicillin and amoxicillin | Vancomycin plus gentamicin | Adults: vancomycin, 1 g IV over one to two hours, plus gentamicin, 1.5 mg per kg IV or IM (gentamicin dose not to exceed 120 mg); injection or infusion should be completed within 30 minutes of starting the procedure ‡  
Children: vancomycin, 20 mg per kg IV over one to two hours, plus gentamicin, 1.5 mg per kg IV or IM; injection or infusion should be completed within 30 minutes of starting the procedure ‡ |
| Moderate-risk patients             | Amoxicillin or ampicillin  | Adults: amoxicillin, 2 g orally one hour before the procedure, or amoxicillin, 2 g IM or IV within 30 minutes of starting the procedure  
Children: amoxicillin, 50 mg per kg orally one hour before the procedure, or amoxicillin, 50 mg per kg IM or IV within 30 minutes of starting the procedure |
| Moderate-risk patients who are allergic to ampicillin and amoxicillin | Vancomycin                 | Adults: 1 g IV over one to two hours; infusion should be completed completed within 30 minutes of starting the procedure ‡  
Children: 20 mg per kg IV over one to two hours; infusion should be completed within 30 minutes of starting the procedure ‡ |

IM=intramuscularly; IV=intravenously.
*Excluding esophageal procedures.
†The total pediatric dose should not exceed the adult dose.
‡A second dose of vancomycin or gentamicin is not recommended.

### References
Kawasaki Disease

Kawasaki disease (also known as mucocutaneous lymph node syndrome) is a systemic febrile condition affecting children usually < 5 years old. It is one of the most common vasculitides of childhood. Aetiology remains unknown. Possible bacterial toxins or viral agents. Leading cause of acquired heart disease in the developed world.

**Diagnostic Criteria**

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

Other signs may be present including irritability, altered mental state, transient arthritis, diarrhoea, vomiting, abdominal pain, aseptic meningitis, hepatosplenomegaly.

Most important complication is coronary vasculitis occurring usually within 2 weeks of illness. Occurs in up to 35% of untreated children. Manifest as myocardial ischaemia, infarction, pericarditis, myocarditis, endocarditis, heart failure and arrhythmias.

**Treatment**

1) **IV Gammaglobulins**. 2 g/kg single infusion over 10 - 12 hours. Fever and systemic complaints resolve within 24-48 hours. Therapy within 10 days of onset of fever is effective in preventing coronary vascular damage.

2) **Salicylate**. 30 mg/kg/24 hours for 2 weeks or until patient is afebrile for 2-3 days. Then low dose 3-5 mg/kg OD for 6 - 8 weeks from onset or until ESR and platelet count returns to normal if no coronary artery abnormalities are observed on echocardiogram. If there is coronary aneurysm, low dose aspirin is continued until it resolves. Dipyridamole 3 - 5 mg/kg OD in place of aspirin especially in epidemics of influenza or varicella to avoid risk of Reyes syndrome.

3) **Corticosteroids**. Earlier concerns of possible detrimental effects of steroids are under increasing scrutiny. One recent (Prednisolone 2 mg/kg for 1 week then tail off over 2 weeks) study showed some benefit but will require more randomized controlled trials.

**Investigations**

- FBC - anaemia, leucocytosis, thrombocytosis.
- ESR and CRP elevated.
- ANA, RA factors negative.
- Liver enzymes ↑.
- CXR, ECG.
- Echocardiogram in the acute phase and repeat at 6-8 weeks or earlier if indicated.
**Vaccination**

Immunoglobulin administration may impair the efficacy of live-attenuated virus vaccines such as measles, mumps, rubella and varicella. Delay live-attenuated virus vaccination for at least 3 months.

**Prognosis.** Japanese studies show 1 - 2 % mortality from cardiac complications usually within 1 - 2 months of onset. Recovery is complete in children who do not have coronary artery involvement. 80% of aneurysm 3 - 5 mm in diameter resolve. 30% of 5 - 8 mm resolve. Prognosis worst for aneurysms > 8 mm in diameter.

**Atypical Kawasaki Disease**

Presence of coronary artery dilatation or aneurysm in children who do not fulfil the diagnostic criteria for KD. Tends to occur in infants and the youngest patients. High index of suspicion should be maintained for the diagnosis of atypical KD.

Echocardiography is therefore indicated in patients who have prolonged fever with:
- two other criteria,
- subsequent unexplained periungual desquamation,
- two criteria and thrombocytosis, or
- rash without any other explanation.

**Long term follow-up**

1. **No coronary artery changes at any stage of illness** – off antiplatelet dose of aspirin 6-8 weeks after the onset of illness. No restriction of physical activity after 6-8 weeks. Because the degree of future risk for ischaemic heart disease is still undetermined, periodic assessment and counselling about known cardiovascular risk factors every 5 years is suggested. Coronary angiography is not recommended.

2. **Transient coronary artery ectasia that disappears within 6-8 weeks after the onset of illness** - off aspirin after 6-8 weeks. No restriction of physical activity after 6-8 weeks. Risk assessment and counselling is recommended at 3-5 year intervals. Coronary angiography is not recommended.

3. **Small to medium (> 3mm but < 6mm) solitary coronary artery aneurysm in ≥ 1 coronary arteries.** – aspirin 3-5 mg/kg per day, at least until aneurysms regress. Annual follow-up with ECHO and ECG. Stress test every 2 years for patients > 10 years old. In the first decade of life, no restriction of physical activities beyond initial 6-8 weeks. In the second decade of life, physical activity is guided by stress testing every other year. No competitive sports. Angiography if myocardial ischaemia is demonstrated by stress tests.

4. **Multiple small to medium aneurysms, or one or more large aneurysms (≥ 6mm), including giant aneurysm without obstruction** – long term aspirin 3-5 mg/kg per day ± warfarin. Six monthly follow-up with ECHO and ECG. Stress tests with myocardial perfusion evaluation annually. In the first decade of life, no restriction of physical activities beyond initial 6-8 weeks. In the second decade of life, physical activity is guided by stress testing. No competitive sports. Angiography 6-12 months after recovery from the acute illness, or sooner if clinically indicated.
5. **Coronary artery obstruction confirmed by angiography** - long term aspirin 3-5 mg/kg per day ± warfarin ± β-adrenergic blocking drugs. Six monthly follow-up with ECHO and ECG. Annual stress testing and Holter. No contact sports, isometrics and weight training. Angiography when indicated.

**Reference:**
SHOCK

Shock is a state of inadequate tissue perfusion. Some causes include hypovolaemic, sepsis (distributive), neurogenic (distributive), anaphylaxis (distributive) and (cardiogenic).

Classification
1. hypovolaemic (e.g. acute gastroenteritis, haemorrhage)
2. distributive (e.g. sepsis, neurogenic)
3. cardiogenic (e.g. myocarditis, cardiac arrhythmias)

Assessment of shock

<table>
<thead>
<tr>
<th>Heart rate</th>
<th>Fast or slow. A very fast heart rate may be the cause of shock or may be a sign of stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>Assess systolic and diastolic pressure and calculate pulse pressure</td>
</tr>
<tr>
<td>Systemic perfusion</td>
<td><em>Pulse location:</em> palpable peripherally and centrally? If absent peripherally, decompensated shock is present</td>
</tr>
<tr>
<td></td>
<td><em>Pulse volume:</em> thready, normal or bounding</td>
</tr>
<tr>
<td></td>
<td><em>Skin perfusion:</em> temperature, colour, capillary refill time (normal &lt; 2 secs)</td>
</tr>
<tr>
<td></td>
<td><em>CNS function:</em> evaluate response to environment</td>
</tr>
<tr>
<td></td>
<td><em>Urine output:</em> reflects renal perfusion and often reflects splanchnic perfusion (normal 1 - 2 mls/kg/hr)</td>
</tr>
</tbody>
</table>

Management

Refer to appendix for management of shock due to arrhythmias. Management for the other causes of shock is dealt with in the relevant chapters.
FEBRILE CONVULSIONS

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

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

Febrile convulsions are classified as either simple or complex.

### Simple Febrile Convulsions
- Duration < 15 minutes
- Generalised seizure.
- Does not recur during the febrile episode.

### Complex Febrile Convulsions
- Duration > 15 minutes
- Focal features
- > 1 seizure during the febrile episode
- Residual neurological deficit post-ictally, such as Todd's paralysis.

**Management**

1. Not all children need to be admitted. The main reasons for admission are:
   - To exclude intracranial pathology especially infection
   - Fear of recurrent fits
   - To investigate and treat the cause of fever besides meningitis or encephalitis
   - To allay parental anxiety, especially if they are staying far from the hospital.

2. **Investigation**
   - The need for blood counts, lumbar puncture, urinalysis, chest X-ray, blood culture etc., will depend on clinical assessment of the individual case.
   - **Lumbar puncture**
     a. Must be done (unless contraindicated – see chapter on "Meningitis")
        - Any signs suspicious of intracranial infection
        - Prior antibiotic therapy
        - Persistent lethargy and not fully interactive 6-8 hours after the seizure
     b. Strongly recommended:
        - < 12 months old
        - First complex febrile convolution
        - In district hospital without paediatrician
        - If parents have a problem with bringing the child again to hospital in event of deterioration at home.
   - Measurement of serum calcium and electrolytes are rarely necessary in children with febrile convulsions.
   - **EEG is not indicated** even for those with multiple recurrences or with complex febrile convulsions.

3. Parents should be counselled on the benign nature of this condition.
**Prognosis**

Febrile convulsions are benign events with excellent prognosis:
- 3% of population have febrile convulsions.
- 30% recurrence after 1st attack
- 48% recurrence after 2nd attack
- 2 – 7% develop subsequent afebrile seizure or epilepsy
- No evidence of permanent neurological deficits following febrile convulsions or even febrile status epilepticus
- No deaths were reported from simple febrile convulsions.

4. **Control fever**
   - Take off clothing and tepid sponging.
   - Antipyretic e.g. syrup or rectal Paracetamol 15 mg/kg 6 hourly.
   - Antipyretic is indicated for patient’s comfort, but it has not been shown to reduce the recurrence rate of febrile convolution.

5. **Parents should also be advised on first aid measures during a convulsion, if this were to recur namely:**
   - Do not panic, remain calm. Note time of onset of the fit.
   - Loosen the child’s clothing especially around the neck.
   - Place the child in the left lateral position with the head lower than the body.
   - Wipe any vomitus or secretion from the mouth.
   - Do not insert any object into the mouth even if the teeth are clenched.
   - Do not give any fluids or drugs orally.
   - Stay near the child until the convulsion is over and comfort the child as he/she is recovering.

6. **Rectal Diazepam**
   - Parents of children with high risk of recurrent febrile convolution should be supplied with rectal diazepam.
   - They should be advised on how to administer it in case the convulsion lasts more than 5 minutes.
   - Dose: 0.5 mg / kg

**Risk Factors for Recurrent Febrile Convulsions**

- Family history of febrile convulsion
- Age < 18 months
- Low degree of fever (< 40°C) during 1st febrile convulsion
- Brief duration (< 1 hr) between onset of fever and convulsion

* No risk factor < 15% recurrence
Two or > risk factors > 30% recurrence
Three or > risk factors > 60% recurrence
7. Prevention of Recurrent Febrile Convulsions

The following are effective in preventing recurrent febrile convulsions:
- Phenobarbitone
- Sodium valproate
- Intermittent oral diazepam during febrile illness

However, these modalities are NOT RECOMMENDED because:

- The risks and potential side effects of these medications outweigh the benefits.
- No medication has been shown to prevent the future onset of epilepsy.
- Febrile convulsions have an excellent outcome with no neurological deficit nor any effect on intelligence.

<table>
<thead>
<tr>
<th>Risk Factors for Subsequent Epilepsy³</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Neurodevelopmental abnormality</td>
</tr>
<tr>
<td>- Complex febrile convulsion</td>
</tr>
<tr>
<td>- Family history of epilepsy</td>
</tr>
<tr>
<td>- Brief duration between onset of fever and initial convulsion</td>
</tr>
</tbody>
</table>

References:


Epilepsy

A. Management of Acute Seizure.

a. General Measures

1. a. Rapid cardiopulmonary assessment.
   b. Lie child on side with head to side and head slightly lower than trunk to aid drainage of secretion from oral cavity.
   c. Clear airway and give oxygen via high flow mask.
   d. Do not restraint seizure movement but protect child from injury from surrounding hard object.
   e. Do not put anything between teeth.
   f. Establish intravenous or intraosseous assess.

2. Initial investigations - Bedside glucose levels, RBS, ABG, Renal Profile, Ca, Mg, FBC ± Drug Levels.

b. Stop the Seizure.
(80% will stop spontaneously. However if persists and lasts > 5 minutes, approach should be the same as in established status)

i) Pre Status (< 30 min.)

DIAZEPAM - 0.3 mg/kg IV or 0.5 mg/kg rectal. (Maximum 10 - 15 mg)

(Onset of action 1-2 min (IV) 3 min (rectal). Watch out for respiratory depression especially if phenobarbitone has been given. Flumazenil 10 mcg/kg is antagonist.)

- REPEAT DIAZEPAM if seizure does not stop after 10 minutes or
- RECTAL PARALDEHYDE 0.4 ml/kg if available (give with same volume of olive oil)

PHENYTOIN - 18 mg/kg IV infused over 20 minutes

(Dilute with 0.9% saline. Monitor HR, BP and ECG)

Or

PHENOBARBITONE - 20 mg/kg IV over 10 minutes (Maximum 600 mg)

if less than 1 year old or if patient was on oral phenytoin

(Give the above through intraosseous route if still cannot get IV access)
ii) Established Status (> 30 min.)

(Definition of Status epilepticus: Any seizure lasting or repeating itself without recovering of consciousness in between seizure lasting > 30 minutes.)

If the above measures do not stop the seizure arrange transfer to HDU/ PICU

MIDAZOLAM INFUSION -  IV 0.15 mg/kg bolus then infusion at 1 ug/kg/min increasing to 4 ug/kg/min over 60 minutes if necessary. (Doses up to 18 ug/kg/min has been reported in literature)\(^1\).

Paralyse and ventilate (Get help from anaesthetist on-call if appropriate)

THIOPENTONE INFUSION -  4 mg/kg slowly IV bolus (beware of hypotension), then 1 – 5 mg/kg/hr infusion.

Consider pressor support

iii) Refractory Status

(> 60 - 90 minutes and seizures still not controlled with (I) and (ii) )

Consult a paediatric intensivist or neurologist if appropriate.
Consider EEG monitoring

Options available:

- IV Phenobarbitone 10 mg/kg every 30 minutes up to 100 mg/kg in 24 hours to achieve burst-suppression pattern on EEG
- IV Sodium Valproate 30 mg/kg bolus followed by 1-5 mg/kg/hr for 6 – 12 hours.
- IV Lignocaine infusion
- Consider IV pyridoxine if patient is < 2 year old

**Prognosis**

- < 1 hour 3.7% mortality
- > 1 hour 34.8% mortality.

c) Look for underlying cause.

d) Taper off anticonvulsant.

Taper the anticonvulsant over 2 weeks and then take off. No grounds for prophylactic anticonvulsant unless 2 fits per year. (as > 30% will have only a single seizure).
B. Further Management and Investigations

a. History of the seizure in detail. Also ask for birth history, developmental milestones and family history.

b. Look for dysmorphism, neurocutaneous signs and complete CNS examination.

c. **Investigations** are recommended only if a second afebrile seizure occurs. This is because the risk of recurrence is 42% (27-81%) and treatment is recommended only after 2\textsuperscript{nd} episode of seizure and is frequent. Furthermore there is no evidence that treatment after single episode influences prognosis

- Routine biochemical tests are not indicated except if the clinical features suggest a biochemical disorder such as hypoglycaemia or hypocalcaemia.

- Role of EEG
  - Support the clinical diagnosis of epileptic seizures
  - Distinguish partial vs generalized epilepsies
  - Identify specific epilepsy syndromes, hence choice of AED.
  - Localization of seizures foci in intractable epilepsy
  - Help to predict recurrence risk after first unprovoked seizure
  - Rarely, monitor anti-epileptic therapy

- MRI (preferred) or CT scan is indicated for any child with
  - A single episode of seizure if there is focal neurological signs or a history suggestive of space occupying lesions.
  - Epilepsy occurring in the 1st year of life except febrile seizures
  - Partial epilepsy except benign rolandic epilepsy
  - Developmental delay or regression

- Specific investigations (e.g. Metabolic screen, CSF for amino acid, lactate and neurotransmitter, muscle and skin biopsy, trial of pyridoxine or folinic acids, etc) must be individualised and ordered judiciously with specific aetiology in mind
C. Principles of Anticonvulsant Therapy for Epilepsy.

Monotherapy as far as possible. Increase dose gradually until epilepsy is controlled or until maximum recommended dose is reached or side effects occur. Monitor drug levels only to check compliance or in situations of polypharmacy where drug interaction is suspected. Please read up on the potential side effects of all these drugs, some of which (e.g. Steven-Johnson syndrome) may be life threatening.

Choice of Anticonvulsants:

<table>
<thead>
<tr>
<th>Seizure type</th>
<th>First line</th>
<th>Second line</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Partial Seizures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple partial</td>
<td>Carbamazepine</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>Complex partial</td>
<td>Valproate</td>
<td>Topiramate</td>
</tr>
<tr>
<td>Secondly generalized</td>
<td>Phenytoin</td>
<td>Phenobarbitone</td>
</tr>
<tr>
<td></td>
<td>Phenobarbitone</td>
<td>Clonazepam</td>
</tr>
<tr>
<td>B. Generalized Seizures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonic-clonic</td>
<td>Valproate</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>Clonic</td>
<td></td>
<td>Topiramate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clonazepam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carbamazepine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenobarbitone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenobarbitone</td>
</tr>
<tr>
<td>Absence</td>
<td>Valproate</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td></td>
<td>Ethosuximide</td>
<td>Clonazepam</td>
</tr>
<tr>
<td>Atypical absences</td>
<td>Valproate</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>Atonic, tonic</td>
<td></td>
<td>Topiramate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clonazepam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carbamazepine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenobarbitone</td>
</tr>
<tr>
<td>Myoclonic</td>
<td>Valproate</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td></td>
<td>Clonazepam</td>
<td>Topiramate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenobarbitone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Piracetam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lamotrigine*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(* May cause seizure aggravation in SMEI and JME)</td>
</tr>
<tr>
<td>Infantile Spasm</td>
<td>ACTH or Prednisolone</td>
<td>Nitrazepam / Clonazepam</td>
</tr>
<tr>
<td></td>
<td>Vigabatrin (in TS)</td>
<td>Valproate</td>
</tr>
</tbody>
</table>
## Side Effects, and Toxicities of Anticonvulsants

<table>
<thead>
<tr>
<th>AED</th>
<th>Side Effects</th>
<th>Serious Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Drowsiness, dizziness, ataxia, diplopia, Rashes</td>
<td>Agranulocytosis</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Drowsiness, hypotonia, salivary and Bronchial hypersecretion</td>
<td>-</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Dizziness, somnolence, rash</td>
<td>Steven-Johnson Syndrome</td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>Behavioural disturbance, drowsiness Ataxia, rash</td>
<td>-</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Ataxia, diplopia, dizziness, hirsutism Gum hypertrophy, sedation</td>
<td>Megaloblastic anemia</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>Nausea, epigastric pain, tremor, alopecia Weight gain, thrombocytopenaenia</td>
<td>Encephalopathy Hepatitis, pancreatitis</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Weight loss, somnolence, mental slowing and word-finding difficulty, renal calculi</td>
<td>-</td>
</tr>
</tbody>
</table>

### D. Advice for Parents

- a. Need to be compliant if on anticonvulsant. **Need to treat for at least 2 years seizure-free period and then to taper off over 3 - 6 months.** Do not stop the medication by themselves. Sudden withdrawal of drugs may precipitate breakthrough seizures.
- b. If epilepsy is photosensitive, to watch TV in a brightly lit room. Avoid sleep deprivation and alcohol.
- c. Better to shower than use a bath. Do not lock bathroom.
- d. No cycling in traffic, climbing sports or swimming alone.
- e. Allow driving only in well-controlled epilepsy, seizure-free for at least 1 year, off or on treatment, or purely nocturnal seizures.
- f. Know emergency treatment for a seizure.
- g. Inform school.

### References:

5. Nelson’s Textbook of Paediatrics
**E. Miscellaneous Information**

**ILAE 1981 Classification**  
*(based on seizure type and accompanying EEG)*

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial - Simple Complex</td>
<td>Partial seizure with secondary generalization</td>
</tr>
<tr>
<td>Generalized - Absence</td>
<td>Atypical absences, Myoclonic, Tonic-clonic, Tonic or Clonic, Atonic</td>
</tr>
<tr>
<td>Unclassified</td>
<td></td>
</tr>
</tbody>
</table>

**Differential Diagnosis of Seizures**

<table>
<thead>
<tr>
<th>Age</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates and infants</td>
<td>Jitteriness and benign myoclonus, Apnoea, Gastro-oesophageal reflux, Shuddering attacks, Benign paroxymal torticollis, Hyperekplexia</td>
</tr>
<tr>
<td>Young children</td>
<td>Breath holding spells, Reflex anoxic seizures, Parasomnias, Benign paroxysmal vertigo, Paroxysmal choreoathetosis, Tics and ritualistic movements, Rage attacks</td>
</tr>
<tr>
<td>Childhood and Adolescents</td>
<td>Vasovagal syncope, Migraine, Narcolepsy, Panic attacks, Pseudoseizures</td>
</tr>
<tr>
<td>Any Age</td>
<td>Endocrine, metabolic and toxic causes, Drug-induced dystonia, Cardiac dysrhythmias</td>
</tr>
</tbody>
</table>

**Classification of Epilepsies and Epileptic syndromes (ILAE 1989)**

**Localization-related (focal, partial) epilepsies & syndromes**

- **Idiopathic**
  - Benign childhood epilepsy with centrotemporal spikes
  - Childhood epilepsy with occipital paroxysm
  - Primary reading epilepsy
- **Symptomatic**
  - Characterised by simple partial seizures
  - Characterised by complex partial seizures
  - Characterised by secondarily generalised seizures
- **Unknown as to whether the syndrome is idiopathic or symptomatic**

**Generalized epilepsies and syndromes**

- **Idiopathic**
  - Benign neonatal familial convulsions
  - Benign neonatal convulsions
  - Benign myoclonic epilepsy in infancy
  - Childhood absence epilepsy
  - Juvenile absence epilepsy
  - Juvenile myoclonic epilepsy
  - Epilepsy with grand mal seizures on awakening
- **Cryptogenic or symptomatic**
  - West syndrome
  - Lennox-Gastaut syndrome
  - Epilepsy with myoclonic astatic seizures
  - Epilepsy with myoclonic absences
- **Symptomatic**
  - Early myoclonic encephalopathy
  - Early infantile epileptic encephalopathy
  - Specific syndrome

**Epilepsies and syndromes undetermined, whether focal or generalised**

- Neonatal seizures
- Severe myoclonic epilepsy in infancy
- Epilepsy with continuous spike and wave EEG during slow-wave sleep
- Acquired epileptic aphasia (Landau-Kleffner syndrome)

**Special syndromes; situation-related seizures**

- Febrile convulsions
- Isolated seizures or isolated status epilepticus
- Seizures occurring only when there is an acute metabolic or toxic event
1. Meningitis is still a major and sometimes fatal problem in Paediatrics. Morbidity is also high. About 30% of survivors have some sequelae of their disease\(^1\). However, these complications can be reduced if meningitis is treated early.

2. **Approach to children with Fever & Signs/Symptom of Bacterial Meningitis**

   **When NOT to do Lumbar Puncture?**
   - Haemodynamically unstable
   - Consciousness impaired
   - Abnormal ‘doll’s eye’ reflexes / pupils
   - Lateralized signs / abnormal posturing
   - Immediately after a seizure
   - Papilloedema

   **Fever & Signs/Symptoms of Bacterial Meningitis**
   
   Is Lumbar Puncture contraindicated?
   
   - No  
   - Yes
   
   **LP**  
   - Withhold LP

   Blood and Urine C&S
   
   Start antibiotics ± Dexamethasone

   Abnormal CSF
   
   Positive
   
   Negative

   Normal CSF wait for CSF culture and Latex agglutination.

   Improve
   
   No improvement

   Complete Course of Treatment
   
   (7 days to 14 days depending on organism)

   Persistent fever for 72 hrs
   
   (rule out the various causes)

   & neurological deficit

   Repeat LP if no evidence of raised ICP

   Change antibiotics

   No response

   Response

   Think of TB, fungus or encephalitis

   Complete course of antibiotics

   N.B. In cases of aseptic meningitis or encephalitis please send CSF and serum for viral serology e.g. for Japanese encephalitis.
3. CSF results

Table 1: Cerebrospinal Fluid Findings in Various CNS Disorder with Fever

<table>
<thead>
<tr>
<th>Condition</th>
<th>Leukocytes</th>
<th>Protein  mg/dl</th>
<th>Glucose  mmol/l</th>
<th>Pressure</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Bacterial Meningitis</td>
<td>100 - &gt;50,000</td>
<td>100 - 500</td>
<td>&lt;0.5-1.5</td>
<td>↑</td>
<td>Gram stain may be positive</td>
</tr>
<tr>
<td>Partially Treated Bacterial Meningitis</td>
<td>1 - 10,000 usually ↑ PMN but may have lymphocytes</td>
<td>100+</td>
<td>↓</td>
<td>N/↑</td>
<td>CSF C&amp;S may be sterile in case of pneumococcal &amp; meningococcus</td>
</tr>
<tr>
<td>Tuberculosis Meningitis</td>
<td>10 - 500 Early PMN, later ↑ Lymphocytes</td>
<td>100 - 500</td>
<td>0 - 2.0</td>
<td>May be low due to block</td>
<td>Smear for AFB positive in CSF. Chloride ↓. ESR↑</td>
</tr>
<tr>
<td>Fungal Meningitis</td>
<td>50 – 500 (Lymphocytes)</td>
<td>50 - 200</td>
<td>N↓</td>
<td>N/slight ↑</td>
<td>CSF for Indian ink / cryptococcal antigen</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>10 - 1,000 N/50-100</td>
<td>N</td>
<td>N/↑</td>
<td>Send for CSF Virology*</td>
<td></td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>&lt;10 lymphocyte</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>May not be febrile</td>
</tr>
</tbody>
</table>

4. Prompt treatment with antibiotic essential

Remember to use the correct dosage of antibiotic that will penetrate the CSF.

Table 2: Likely organism and type of antibiotics according to age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Initial Antibiotic</th>
<th>Likely Organism</th>
<th>Duration (if uncomplicated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 month</td>
<td>C Penicillin + Cefotaxime</td>
<td>Group B Streptococcus E. coli</td>
<td>21 days</td>
</tr>
<tr>
<td>1 - 3 months</td>
<td>C Penicillin + Cefotaxime</td>
<td>All of the above &amp; H. influenzae Strep. pneumoniae</td>
<td>10 – 21 days</td>
</tr>
<tr>
<td>&gt; 3 months</td>
<td>C Penicillin + Cefotaxime or Ceftriaxone</td>
<td>H. influenzae</td>
<td>7 – 10 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. pneumoniae</td>
<td>10 – 14 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N. meningitides</td>
<td>4 – 7 days</td>
</tr>
</tbody>
</table>

N.B.
1. Terminate inappropriate antibiotics when infective organism has been identified.
2. Ceftriazone has resulted in more rapid sterilisation of the CSF than either Cefotaxime and Cefuroxime. Furthermore in one study the incidence of deafness was reduced in Ceftriazone compared with those treated with Cefuroxime (Achieves of Disease in Childhood 1992 and Clinical Paediatric 1991)
3. Ideally, MIC of the antibiotics used for the susceptible organism especially S. pneumoniae is required to decide on the antibiotic of choice. Example:-
   Drug of choice
   - MIC < 0.1 mg/L Penicillin – sensitive strain
   - MIC 0.1-< 2 mg/L Ceftriaxone or Cefotaxime (relatively resistant)
   - MIC > 2 mg/L Vancomycin (resistant strain)
4. Resistance to penicillin in community acquired S. pneumoniae in HKL is 16.9 %.
5. Duration of treatment may need to be extended as a result of complication e.g. subdural empyema or brain abscess.
5. **Use of Steroids** to decrease the sequelae of bacterial meningitis\(^{3,5}\).
   a. There is evidence that use of steroids can reduce the sequelae of meningitis especially sensorineural deafness in H. influenzae meningitis. There may also be of benefit in S. pneumonia meningitis. There has been no benefit shown for meningococcal or neonatal meningitis.
   b. The best effect is achieved if the steroid is given before or with the first antibiotic dose.
   c. Dosage: Dexamethasone 0.15 mg/kg 6 hourly for 4 days or 0.4 mg/kg 12 hourly for 2 days
   d. Our recommendation is to give steroid if the CSF at LP is turbid and the patient has not been given any prior antibiotics.

6. **Supportive Measures**
   - Monitor temperature, pulse, B/P and respiration 4 hourly and input/output.
   - Nil by mouth if unconscious.
   - Careful fluid balance required. Usually a maintenance IV fluid is sufficient. Only if SIADH occurs, reduce to 2/3 maintenance for the initial 24 hours. Patient may need more fluid if dehydrated.
   - If fontanel hasn’t close, note daily head circumference. Ultrasound ± CT scan (if effusion or hydrocephalus is suspected).
   - Fit chart.
   - Daily CNS assessment is essential.
   - Patient must be observed for 24 hours after stopping therapy and if there is no complication, they can be discharged.

### Table 3: Normal CSF Value

<table>
<thead>
<tr>
<th></th>
<th>Neonates</th>
<th>Infants</th>
<th>Thereafter</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cells/mm(^3)</strong></td>
<td>&lt; 30</td>
<td>&lt; 10</td>
<td>&lt; 5</td>
</tr>
<tr>
<td><strong>Glucose mmol/l</strong></td>
<td>1.1 – 3.3</td>
<td>3.9 – 5.0</td>
<td>2.8 – 4.4</td>
</tr>
<tr>
<td><strong>Protein mg/dl</strong></td>
<td>20 - 150*</td>
<td>15 - 45</td>
<td>20 - 40</td>
</tr>
<tr>
<td><strong>Pressure mm H(_2)O</strong></td>
<td>50 - 80</td>
<td>40 - 150</td>
<td>70 - 200</td>
</tr>
<tr>
<td><strong>Chloride mg/dl</strong></td>
<td>700 - 750</td>
<td>700 - 750</td>
<td></td>
</tr>
</tbody>
</table>

* RBS must be taken at same time and CSF glucose at least less than 2/3 of Random blood sugar to be considered abnormal.

** CSF protein : values up to 3g/l (300 mg %) may be found in prem.

### Table 4: Gram Staining

<table>
<thead>
<tr>
<th></th>
<th>Pneumococcus</th>
<th>Meningococcus</th>
<th>Haemophilus influenzae</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>gram positive extracellular diplococci.</td>
<td>gram negative intracellular diplococci.</td>
<td>gram negative coccobacilli</td>
</tr>
</tbody>
</table>

### Indications for CT Scan in Meningitis
(Mainly useful to detect complications)
- Prolonged depression of consciousness
- Prolonged focal or late seizures
- Focal neurological abnormalities
- Enlarging head circumference
- Suspicious of subdural effusion or empyema

### Indications to treat Subdural Effusion
- Rapid ↑ in OFC with no hydrocephalus
- Focal CNS sign or ↑ ICP
- Suspected subdural empyema

Most do not need treatment.
7. Persistent Fever in a Patient on Treatment with Meningitis
   a. Thrombophlebitis and injection sites e.g. intramuscular abscess.
   b. Intercurrent infection e.g. pneumonia, UTI or nosocomial infection.
   c. Resistant organisms. Inappropriate antibiotics or inadequate dosage.
   d. Subdural effusion / empyema or brain abscess.
   e. Antibiotic fever.

8. Management of increased intracranial pressure
   a. During the first 18 to 24 hours, there is cerebral hyperaemia, therefore cerebral protection may be indicated.
   b. 30° bed head elevation
   c. Antipyretic agents if febrile
   d. Avoid frequent and vigorous tracheal suction
   e. Correction of hyponatraemia / SIADH
   f. Use i/v Mannitol judiciously

9. Follow-up (Long term follow-up is essential)
   a. Note development of child at home and in school.
   b. Note head circumference.
   c. Ask for any occurrence of fits or any behavioural abnormalities.
   d. Assess vision, hearing and speech (if necessary, do an audiometry in assessment of hearing especially in those with speech delay)
   e. Follow-up until child speak normally or intelligible to others (usually need to follow-up until 4 years old).

10. Prognosis depends on:-
    a. Age - worse in younger patients.
    b. Duration of illness prior to effective antibiotics treatment.
    c. Specific organism causing disease - more complication noted with Haemophilus influenzae and S. pneumoniae.
    d. Presence of focal signs.

---

1 Hussain IH, Sofiah A, Ong LC, Ng HP et al. Haemophilus influenzae meningitis in Malaysia. Pediatr Infect Dis J. 1998 Sep;17(9 Suppl):S189-90
2 Nelson’s Textbook of Pediatrics
6 Antibiotic Guidelines 2000 / 2001, Hospital Kuala Lumpur
CHILD WITH ALTERED CONSCIOUSNESS

Initial management of a child with altered consciousness.

1. Do a rapid cardiopulmonary assessment and initiate resuscitation

**Airway**

**Breathing** (O2, intubate & ventilate if needed)

**Circulation** (chest compression, IV / IO access, volume expansion & inotropes if needed)

**Dextrostix** (correct immediately after sending blood for RBS and storing a sample for later investigation)

2. Assess level of consciousness using modified Glasgow Coma Scale:

<table>
<thead>
<tr>
<th></th>
<th>&gt;5 years</th>
<th>&lt;5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye</td>
<td></td>
<td></td>
</tr>
<tr>
<td>opening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Spontaneous</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>To voice</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>To pain</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Verbal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Orientated</td>
<td>Alert, babbles, coos words or sentences- normal</td>
</tr>
<tr>
<td>4</td>
<td>Confused</td>
<td>Less than usual ability, irritable cry</td>
</tr>
<tr>
<td>3</td>
<td>Inappropriate words</td>
<td>Cries to pain</td>
</tr>
<tr>
<td>2</td>
<td>Incomprehensible sounds</td>
<td>Moans to pain</td>
</tr>
<tr>
<td>1</td>
<td>No response to pain</td>
<td>No response to pain</td>
</tr>
<tr>
<td>Motor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Obeys command</td>
<td>Normal spontaneous movement</td>
</tr>
<tr>
<td>5</td>
<td>Localise to supraocular pain (&gt;9 Months)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Withdraws from nailbed pressure</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Flexion to supraocular pain</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Extension to supraocular pain</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>No response to supraocular pain</td>
<td></td>
</tr>
</tbody>
</table>

3. If the child’s score is 12 or less give intravenous Mannitol 0.25-.5g/kg.

This initial dose is **contraindicated** if patient is hypotensive or having renal failure. Meanwhile arrange for admission into PICU/HDU for possible ventilation if the condition deteriorates. Ventilation will also be immediately necessary if the child has evidence of imminent herniation based on examination of brainstem reflexes.
### 4. Herniation syndromes

<table>
<thead>
<tr>
<th>Uncal (one temporal lobe)</th>
<th>Unilateral fixed dilated pupil, unilateral ptosis, minimal deviation of eyes on oculocephalic or oculovestibular testing, hemiparesis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diencephalic (both temporal lobes)</td>
<td>Small or midpoint pupils reactive to light, full deviation of eyes on oculocephalic or oculovestibular testing, flexor response to pain with decorticate posturing, hypertonia with hypereflexia and upgoing plantars; Cheynes-Stokes respiration.</td>
</tr>
<tr>
<td>Midbrain Upper pontine</td>
<td>Midpoint pupils fixed to light, minimal deviation to light on oculocephalic or oculovestibular testing, extensor response to pain with decerebrate posturing. Hyperventilation.</td>
</tr>
</tbody>
</table>

If there is no papillary response to light, no eye deviation to oculocephalic or oculovestibular testing, no response to pain and flaccidity with extensor plantars, with shallow or ataxic breathing, this usually means that there has been herniation through the foramen magnum and prognosis is guarded.

A child that does not have evidence of a herniation syndrome, has a coma scale score of >12 and who responds to mannitol may not need ventilation.

### Clinical Assessment of Coma

#### General Examination
- Skin: rash, anemia, cyanosis, jaundice, petechiae
- Temperature: fever- infection, drugs/toxin; hypothermia-circulatory failure, drugs/toxins.
- Blood pressure: Septicemia, Addison’s; Hypertensive crisis
- Breath: Poison (e.g. LMS), Fetor hepaticus, Inborn Errors of Metabolism
- Pulse: Arrhythmia.
- Abdomen: organomegaly

#### Neurological
- Head, neck and ear drum (trauma)
- Meningitis-infection/bleed
- Fundoscopy
- Motor function (Tone, Reflexes, Plantars, Clonus)

#### Brainstem reflexes
- Pupillary responses
- Spontaneous eye movements
- Oculocephalic if no suspicion of cervical instability
- Caloric (cold - both eyes towards ear irrigated)
- Corneal

#### Coma Scale: see table

#### Respiratory Pattern: Cheynes stokes, hyperventilation, apneustic
- ( Hemisphere, Midbrain, Pons )

5. All children with an encephalopathy will need an urgent CT scan unless they are known to have a metabolic disorder or have diabetes. If a parainfectious cause or a brain tumour is suspected it is best to proceed straight to an MRI scan.
Once the child has been stabilized, subsequent management should be directed to establishing the cause of the encephalopathy and acute complications.

### Differential Diagnosis of Coma

<table>
<thead>
<tr>
<th>No focal or lateralizing signs</th>
<th>No focal or lateralizing signs, Meningismus present:</th>
</tr>
</thead>
<tbody>
<tr>
<td>No meningismus:</td>
<td>Meningitis</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
</tr>
<tr>
<td>Hypoxic-ischaemic</td>
<td>Subarachnoid hemorrhage</td>
</tr>
<tr>
<td>Metabolic/toxic</td>
<td>Encephalitis</td>
</tr>
<tr>
<td>Epilepsy</td>
<td></td>
</tr>
<tr>
<td>Hypo/hyperthermia</td>
<td></td>
</tr>
</tbody>
</table>

**Focal Brainstem or lateralizing cerebral signs**

- Cerebral tumour
- Cerebral hemorrhage / infarction
- Cerebral abscess

### Aetiology

- **Infection** – bacterial meningitis or abscess, viral, mycoplasma, malaria, fungal, rickettsial
- **Parainfectious** – Cortical thrombosis, Acute disseminated encephalomyelitis
- **Metabolic** – hypoglycemia, inborn errors of metabolism, hyper/hyponatremia, diabetes, hypopituitarism,
- **Toxic** – drug overdose, accidental or intentional, environmental toxins- insecticides, intussusception
- **Hypoxic-ischemic** – near drowning, postictal, post cardiac arrest, thrombo-embolic.
- **Hemorrhagic** – ruptured aneurysms, A-V malformations, arteriovenous occlusion
- **Traumatic** – accidental or nonaccidental
- **Epilepsy** – nonconvulsive status

In Malaysia 2/3 of cases are infective and all child with encephalopathy and fever should be treated with antibiotics until they are stable enough for a lumbar puncture. The others are metabolic (13%) hypoxic-ischemic(5%), intracranial hemorrhage (4%) and the rest miscellaneous including intussusception-2.5%.

### Laboratory Investigations

All children will need the following tests:

- FBC
- BUSE
- ABG
- LFT
- Coagulation profile
- 4 hourly dextrostix
Infective screen – blood & urine culture, viral studies, Mycoplasma titres, lumbar puncture.

Selected patients depending on history and initial laboratory results may need
- Full metabolic workout – collect and store acute samples of urine and plasma
- Toxicology screen
- Drug levels of suspected agents
- EEG
- ECG monitoring
- Special studies for malaria, rickettsia, leptospirosis, mycobacterium.

8. Management

a. Treatment of infection – as this is the most common cause of encephalopathy in Malaysia, unless the underlying cause is obvious, all cases should receive antibiotic cover.

Broad spectrum antibiotics e.g. Ceftriaxone/Cefotaxime should be initiated. Although Herpes encephalitis is uncommon in Malaysia, acyclovir should still be started in a child suspected of acute encephalitis until the etiology becomes more definite. Anti-tuberculous and anti-fungal drugs are rarely needed.

b. Control of convulsions: this is common in any encephalopathy. See status epilepticus protocol.

c. Detect and treat raised intracranial pressure

Intracranial pressure (ICP) should be monitored either clinically by repeated neurological examinations or preferably via intracranial pressure transducers.

Treatment of Raised ICP
- Nurse the child with the head end of the bed elevated up to 30 degrees, in a quite environment. Avoid unnecessary suction/procedures.
- Carefully monitor fluid balance. Do not use hypo-osmolar solutions or plain dextrose. Fluid restriction is generally harmful except in the rare case of SIADH, which must be proven by serum and urine osmolality tests.
- Mannitol in small doses of 0.25-0.5g/kg can be repeated up to 4 times daily. A CT scan should be done after the first dose to exclude intracranial hemorrhage.
- Hyperventilation may be harmful as too low a PaCO₂ will reduce cerebral blood flow. Hence the child should be ventilated to maintain adequate oxygenation and normocapnoea (PaCO₂ 4.0 – 4.6 kPa)
- When medical measures fail, the child will require surgical decompression usually in the form of an external ventricular drain. The need for this may be obvious after seeing the CT scan.
- Maintenance of cerebral blood flow via an adequate cerebral perfusion pressure is essential in the management of all cases.

Cerebral Perfusion Pressure = Mean Arterial Pressure – Intracranial Pressure. Beyond the neonatal period this figure must be maintained at >40 mmHg.
If the child has high BP do not lower the blood pressure except in cases of hypertensive encephalopathy e.g. Acute Glomerulonephritis/Lupus.

d. General Measures
- Regular change of position to avoid bedsores
- Eye protection with eye pads and methyl cellulose eye drops
- Care of bowel and bladder
- Nutrition
- Mobilisation with the help of physiotherapists
- Chest drainage to prevent hypostatic pneumonia.

9. Outcome
This depends on the underlying cause. It is worse for hypoxic-ischaemic and infection and best for metabolic. Overall 1/3 die, 1/3 recover with deficit and 1/3 recover fully. All patients will need long term follow until they are stabilized. Many acute complications e.g. cortical blindness and motor deficits improve with time. Anticonvulsants started during the acute illness should be tailed off by 6 weeks unless the child continues to experience fits on follow up. Cognitive and behavioural sequelae may only become obvious after a few months. Cases suspected of a metabolic cause may need long term dietary management.

Ref.:  
CHILD WITH ALTERED CONSCIOUSNESS

Initial management of a child with altered consciousness.

1. Do a rapid cardiopulmonary assessment and initiate resuscitation

Airway
Breathing (O2, intubate & ventilate if needed)
Circulation (chest compression, IV / IO access, volume expansion & inotropes if needed)
Dextrostix (correct immediately after sending blood for RBS and storing a sample for later investigation)

2. Assess level of consciousness using modified Glasgow Coma Scale:

<table>
<thead>
<tr>
<th></th>
<th>&gt;5 years</th>
<th>&lt;5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye opening</td>
<td>Spontaneous</td>
<td>To voice</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>To pain</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal</td>
<td>Orientated</td>
<td>Alert, babbles, coos words or sentences- normal</td>
</tr>
<tr>
<td>5</td>
<td>Confused</td>
<td>Less than usual ability, irritable cry</td>
</tr>
<tr>
<td>4</td>
<td>Inappropriate words</td>
<td>Cries to pain</td>
</tr>
<tr>
<td>3</td>
<td>Incomprehensible sounds</td>
<td>Moans to pain</td>
</tr>
<tr>
<td>2</td>
<td>No response to pain</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor</td>
<td>Obeys command</td>
<td>Normal spontaneous movement</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Localise to supraocular pain (&gt;9 Months)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Withdraws from nailbed pressure</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Flexion to supraocular pain</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Extension to supraocular pain</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>No response to supraocular pain</td>
<td></td>
</tr>
</tbody>
</table>

3. If the child’s score is 12 or less give intravenous Mannitol 0.25-.5g/kg.

This initial dose is contraindicated if patient is hypotensive or having renal failure. Meanwhile arrange for admission into PICU/HDU for possible ventilation if the condition deteriorates. Ventilation will also be immediately necessary if the child has evidence of imminent herniation based of examination of brainstem reflexes.
4. Herniation syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Uncal</strong></td>
<td>Unilateral fixed dilated pupil, unilateral ptosis, minimal deviation of eyes on oculocephalic or oculovestibular testing, hemiparesis.</td>
</tr>
<tr>
<td><em>(one temporal lobe)</em></td>
<td></td>
</tr>
<tr>
<td><strong>Diencephalic</strong></td>
<td>Small or midpoint pupils reactive to light, full deviation of eyes on oculocephalic or oculovestibular testing, flexor response to pain with decorticate posturing, hypertonia with hypereflexia and upgoing plantars; Cheynes-Stokes respiration.</td>
</tr>
<tr>
<td><em>(both temporal lobes)</em></td>
<td></td>
</tr>
<tr>
<td><strong>Midbrain</strong></td>
<td>Midpoint pupils fixed to light, minimal deviation to light on oculocephalic or oculovestibular testing, extensor response to pain with decerebrate posturing. Hyperventilation.</td>
</tr>
<tr>
<td><strong>Upper pontine</strong></td>
<td></td>
</tr>
</tbody>
</table>

If there is no papillary response to light, no eye deviation to oculocephalic or oculovestibular testing, no response to pain and flaccidity with extensor plantars, with shallow or ataxic breathing, this usually means that there has been herniation through the foramen magnum and prognosis is guarded.

A child that does not have evidence of a herniation syndrome, has a coma scale score of >12 and who responds to mannitol may not need ventilation.

Clinical Assessment of Coma

**General Examination**
Skin: rash, anemia, cyanosis, jaundice, petechiae
Temperature: fever- infection, drugs/toxin; hypothermia-circulatory failure, drugs/toxins.
Blood pressure: Septicemia, Addison’s; Hypertensive crisis
Breath: Poison (e.g. LMS), Fetor hepaticus, Inborn Errors of Metabolism
Pulse: Arrhythmia.
Abdomen: organomegaly

**Neurological**
Head, neck and ear drum (trauma)
Meningism-infection/bleed
Fundoscopy
Motor function
( Tone, Reflexes, Plantars, Clonus )

**Brainstem reflexes**
Pupillary responses
Spontaneous eye movements
Oculocephalic if no suspicion of cervical instability
Caloric (cold - both eyes towards ear irrigated)
Corneal

**Coma Scale**: see table

**Respiratory Pattern**: Cheynes stokes, hyperventilation, apneustic
( Hemisphere, Midbrain, Pons )

5. All children with an encephalopathy will need an urgent CT scan unless they are known to have a metabolic disorder or have diabetes. If a parainfectious cause or a brain tumour is suspected it is best to proceed straight to an MRI scan.
Once the child has been stabilized, subsequent management should be directed to establishing the cause of the encephalopathy and acute complications.

6. Aetiology

**Infection** – bacterial meningitis or abscess, viral, mycoplasma, malaria, fungal, rickettsial

**Parainfectious** – Cortical thrombosis, Acute disseminated encephalomyelitis

**Metabolic** – hypoglycemia, inborn errors of metabolism, hyper/hyponatremia, diabetes, hypopituitarism,

**Toxic** – drug overdose, accidental or intentional, environmental toxins- insecticides, intussusception

**Hypoxic-ischemic** – near drowning, postictal, post cardiac arrest, thrombo-embolic.

**Hemorrhagic** – ruptured aneurysms, A-V malformations, arteriovenous occlusion

**Traumatic** – accidental or nonaccidental

**Epilepsy** – nonconvulsive status

In Malaysia 2/3 of cases are infective and all child with encephalopathy and fever should be treated with antibiotics until they are stable enough for a lumbar puncture. The others are metabolic (13%) hypoxic-ischemic(5%), intracranial hemorrhage (4%) and the rest miscellaneous including intussusception-2.5%.

7. Laboratory Investigations

All children will need the following tests:

- FBC
- BUSE
- ABG
- LFT
- Coagulation profile
- 4 hourly dextrostix
Infective screen – blood & urine culture, viral studies, Mycoplasma titres, lumbar puncture.

Selected patients depending on history and initial laboratory results may need
- Full metabolic workout – collect and store acute samples of urine and plasma
- Toxicology screen
- Drug levels of suspected agents
- EEG
- ECG monitoring
- Special studies for malaria, rickettsia, leptospirosis, mycobacterium.

8. Management

a. Treatment of infection – as this is the most common cause of encephalopathy in Malaysia, unless the underlying cause is obvious, all cases should receive antibiotic cover.

Broad spectrum antibiotics e.g. Ceftriaxone/Cefotaxime should be initiated. Although Herpes encephalitis is uncommon in Malaysia, acyclovir should still be started in a child suspected of acute encephalitis until the etiology becomes more definite. Anti-tuberculous and anti-fungal drugs are rarely needed.

b. Control of convulsions: this is common in any encephalopathy.

See status epilepticus protocol.

c. Detect and treat raised intracranial pressure

Intracranial pressure (ICP) should be monitored either clinically by repeated neurological examinations or preferably via intracranial pressure transducers

**Treatment of Raised ICP**

- Nurse the child with the head end of the bed elevated up to 30 degrees, in a quite environment. Avoid unnecessary suction/procedures.
- Carefully monitor fluid balance. Do not use hypo-osmolar solutions or plain dextrose. Fluid restriction is generally harmful except in the rare case of SIADH, which must be proven by serum and urine osmolality tests.
- Mannitol in small doses of 0.25- 0.5g/kg can be repeated up to 4 times daily. A CT scan should be done after the first dose to exclude intracranial hemorrhage.
- Hyperventilation may be harmful as too low a PaCO\textsubscript{2} will reduce cerebral blood flow. Hence the child should be ventilated to maintain adequate oxygenation and normocapnoea (PaCO\textsubscript{2} 4.0 – 4.6 kPa)
- When medical measures fail, the child will require surgical decompression usually in the form of an external ventricular drain. The need for this may be obvious after seeing the CT scan.
- Maintenance of cerebral blood flow via an adequate cerebral perfusion pressure is essential in the management of all cases.

Cerebral Perfusion Pressure = Mean Arterial Pressure – Intracranial Pressure. Beyond the neonatal period this figure must be maintained at >40 mmHg.
If the child has high BP do not lower the blood pressure except in cases of hypertensive encephalopathy e.g. Acute Glomerulonephritis/Lupus.

d. General Measures
- Regular change of position to avoid bedsores
- Eye protection with eye pads and methyl cellulose eye drops
- Care of bowel and bladder
- Nutrition
- Mobilisation with the help of physiotherapists
- Chest drainage to prevent hypostatic pneumonia.

9. Outcome
This depends on the underlying cause. It is worse for hypoxic-ischaemic and infection and best for metabolic. Overall 1/3 die, 1/3 recover with deficit and 1/3 recover fully. All patients will need long term follow until they are stabilized. Many acute complications e.g. cortical blindness and motor deficits improve with time. Anticonvulsants started during the acute illness should be tailed off by 6 weeks unless the child continues to experience fits on follow up. Cognitive and behavioural sequelae may only become obvious after a few months. Cases suspected of a metabolic cause may need long term dietary management.

Ref.:  
BRAIN DEATH

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

Need for brain death concept
The reasons for the need to recognize brain death are
• Ethical – Brain death is a definite clinical state. Adults with brain death will develop asystole within a week regardless of what treatments are given. In over 2,000 well-documented cases of brain death, nobody has survived. It is therefore a matter of good medical practice to recognize brain death.
• Human – Every man has a right to dignity and respect at death, and the pronouncement of death should not be unduly delayed.
• Utilitarian – Treating patients in ICU is costly. It is morally and economically unjustifiable to keep ventilating brain dead patient, thus depriving others with better prognosis to these facilities.
• Organ transplantation – Acceptance of brain death will be an important step for cadaveric organ transplantation program.

Diagnosis of brain death (All to be fulfilled)

A. Preconditions:

(i). Patient is in deep coma, apnoeic and on ventilator, for at least 12 hours.
(ii). Cause of coma fully established and sufficient to explain the status of patient.
(iii). There is irremediable structural brain damage.

B. Exclusions:

(i). Coma due to metabolic or endocrine disturbance, drug intoxication and primary hypothermia (defined as a core temperature of 32 ºC or lower).
(iii). Coma of undetermined cause.
(iv) Preterm neonates.

C. Diagnostic Criteria: (All to be fulfilled )

(i). Deep coma, unresponsive and unreceptive, Glasgow coma scale 3 / 15.
(ii). Apnoea, confirmed by apnoea test.
(iii ) Absent brain stem reflexes confirmed by the following tests:-
    1. Pupillary light reflex
    2. Oculo-cephalic reflex
    3. Motor response in cranial nerve distribution
    4. Corneal reflex
    5. Vestibulo-ocular reflex (Caloric Test)
    6. Oro-pharyngeal reflex
    7. Tracheo-bronchial reflex
Test
(All conditions and exclusions must be 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) is absent. 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 is seen when pressure stimulus is applied to the supraorbital nerve, deep pressure on both condyles at the level of the temporo-mandibular joint or on the nail bed.
5. **Vestibulo-ocular reflex** (Caloric test). The test should not be performed if there is a perforated tympanic membrane. Caloric testing is done with head 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 directed to the cold caloric stimulus is absent.
6. **Oropharyngeal reflex.** Absent gag response when the posterior pharynx is stimulated.
7. **Tracheo-bronchial reflex.** A suction catheter is passed down through the endotracheal tube to the level of the carina or beyond. Lack of cough response to bronchial suctioning should be demonstrated.
8. **Apnoea test.**
   - Prerequisites: The patient must be in stable cardiovascular and respiratory state.
   - Adjust ventilator to maintain Pa CO$_2$ 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 Pa CO$_2$ after 5 minutes and again after ~ 8 min. if Pa CO$_2$ has not exceeded 60 mm Hg.
   - Re-connect to ventilator after test.
   - The disconnection of the ventilator shall not exceed 10 minutes at any one time.
   - The apnoea test is positive when there is no respiratory effort with a Pa CO$_2$ 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 Pa CO$_2$ < 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.
   (For patient 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.

<table>
<thead>
<tr>
<th>Age</th>
<th>Hours between 2 examinations</th>
<th>Recommended no. of EEGs</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 days - 2 months</td>
<td>48</td>
<td>2</td>
</tr>
<tr>
<td>2 months - 1 year</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>&gt; 1 year*</td>
<td>12</td>
<td>Not needed</td>
</tr>
</tbody>
</table>

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

Assessment and Certification

1. 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.
2. 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.
3. 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 (Doctors C and D) or Doctor A and B if the same doctors are performing the repeat test. The time of death will be declared by the doctors performing the repeat test.
4. 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.
5. Brain death certification must only be done in areas of the hospital with full facilities for intensive cardiopulmonary care of comatose patients.

Pitfalls in diagnosis

1. May occur in patients with
   - Severe facial trauma
   - Pre-existing papillary abnormalities
   - Sleep apnoea or severe pulmonary disease resulting in chronic retention of CO₂
   - Toxic levels of any sedative drugs, aminoglycosides, tricyclic antidepressants, anticonvulsants, chemotherapeutic drugs, neuromuscular blocking agents.
2. Drug levels are useful if they can be quantified. If the drug level is below the therapeutic range, brain death can be declared.

3. 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.

4. When the drug is not known 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 a ancillary test (EEG) for brain death.

5. 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.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Elimination T ½(hours)</th>
<th>Therapeutic range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>2 - 5</td>
<td>50 - 150 ng/ml</td>
</tr>
<tr>
<td>Diazepam</td>
<td>40</td>
<td>0.2 – 0.8 ug/ml</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>10 - 60</td>
<td>2 – 10 ug/ml</td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>100</td>
<td>20 – 40 ug/ml</td>
</tr>
<tr>
<td>Pentobarbitone</td>
<td>10</td>
<td>1 – 5 ug/ml</td>
</tr>
<tr>
<td>Thiopentone</td>
<td>10</td>
<td>6 – 35 ug/ml</td>
</tr>
<tr>
<td>Morphine</td>
<td>2 – 3</td>
<td>70 – 450 ng/ml</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>10 – 24</td>
<td>75 – 200 ng/ml</td>
</tr>
</tbody>
</table>

6. 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.

References:
DIABETES MELLITUS

Diabetes in children is almost invariably type I diabetes mellitus. The incidence of type II diabetes mellitus is on the increasing trend among young people due to obesity.

A. Signs and Symptoms

<table>
<thead>
<tr>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polydipsia</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Polyuria</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Enuresis (secondary)</td>
<td>Hyperventilation due to acidosis</td>
</tr>
<tr>
<td></td>
<td>Drowsiness</td>
</tr>
<tr>
<td></td>
<td>Coma</td>
</tr>
</tbody>
</table>

B. Diagnosis

- Symptomatic child
- Random plasma glucose level >11.0 mmol/L
- Fasting plasma sugar (>7.0 mmol/L)

A glucose tolerance test is rarely needed in children.

C. Diabetic Ketoacidosis (DKA)

DKA can be defined as decompensated diabetes with:-

- Hyperglycaemia (blood glucose >11.0 mmol/L)
- Metabolic acidosis (venous pH <7.3 and or HCO3 <15 mmol/L)
- Heavy glycosuria (55 mmol/L) and ketonuria

And who are: ≥ 5% dehydrated, ± vomiting, ± drowsy

Management of DKA

- Assess severity of dehydration

- Immediate investigations
  - Weigh the child or obtain recording of recent visit
  - Capillary blood glucose (often inaccurate in the presence of poor peripheral circulation and severe acidosis)
  - Venous blood glucose, electrolytes and urea
  - Blood gas: capillary, venous or arterial
  - As indicated: FBC, HbA1c, urine FEME & culture, blood culture, CXR.
  - Height measurement for calculation of body surface area (BSA)
• **Resuscitation**
  In shock with poor peripheral pulses, or coma:-
  - Oxygen 100% by face mask
  - Nasogastric tube to drain stomach if there is vomiting ± impaired consciousness.
  - Normal saline, the volume is 10-20 ml/kg over 1-2 hours, repeated if necessary.

• **Correction of dehydration**

Total fluid required = Deficit + Maintenance

Use either: **Fluid calculation (model 1)**

Calculate DEFICIT = estimated % dehydration x body weight (kg & equivalent in ml)
Calculate MAINTENANCE (ml)

Calculation of maintenance fluid volumes for different ages

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>Maintenance fluid (ml/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>3 – 9</td>
<td>80</td>
</tr>
<tr>
<td>1 - 5</td>
<td>10 – 19</td>
<td>70</td>
</tr>
<tr>
<td>6 - 9</td>
<td>20 – 29</td>
<td>60</td>
</tr>
<tr>
<td>10 - 14</td>
<td>30 – 50</td>
<td>50</td>
</tr>
<tr>
<td>15</td>
<td>&gt;50</td>
<td>35</td>
</tr>
</tbody>
</table>

Fluid maintenance according to BSA: 1500 ml/m²/day

Then add DEFICIT to 48 hours MAINTENANCE. Replace this volume evenly over 48 hours as normal saline.

Or use: **Fluid calculation (model 2)**

Covers MAINTENANCE + 10% DEFICIT given evenly over 48 hours in children of all sizes.

3 – 9 kg : 6 ml/kg/h
10 – 19 kg : 5 ml/kg/h
>20 kg : 4 ml/kg/h for children weighing (up to a maximum of 250 ml/h)

IV or oral fluids that may have been given before the child presents for treatment and prior to assessment should be factored into calculation of deficit and repair.

Initial IV fluid administration and, if needed, volume expansion, should begin immediately with an isotonic saline, 0.9% N/S or balanced salt solutions as Ringer’s lactate.

Subsequent fluid management should be with a solution with a tonicity equal to or greater than 0.45% saline.
- This can be achieved by administering 0.9% saline or, balanced salt solution (Ringer’s lactate or 0.45% saline with added potassium).
- Rate of IV fluid should be calculated to rehydrate evenly over at least 48 hours.
As the severity of dehydration may be difficult to determine and can be overestimated, infuse fluid each day at a rate rarely in excess of 1.5 - 2 times the usual daily requirement based on age, weight or BSA. Urinary losses should not be added to the calculation of replacement fluids.

If serum sodium is >150 mmol/L: Use NaCl 0.45%

When blood glucose has fallen below 14 mmol/L, the fluid should be changed to 0.45% or 0.9% N/S + 5% dextrose.

**Oral fluids**

- In severe dehydration and acidosis, only allow sips of cold water or ice to suck.
- Oral fluids (fruit juice/ORS) should only be offered after substantial improvement and no vomiting.
- Oral fluid volume should be subtracted from the IV calculations.

**Correct Electrolyte Imbalance**

**Potassium (K)**
Total body K is always substantially depleted in DKA.
Serum/plasma K may be low, normal or high.
Replacement therapy should be based on serum potassium measurements.

Start potassium replacement immediately if the patient is hypokalaemic; otherwise, start potassium concurrent with starting insulin therapy. If the patient is hyperkalaemic, defer potassium until urine output is documented.

If serum K is not available before the completion of resuscitation, ECG monitoring is recommended before K is added to the infusion fluid.

Starting potassium concentration in the infusate should be 40 mmol/L and potassium replacement should continue throughout IV fluid therapy. Repeat serum K 2 hours after fluids begin.

Maintenance K: 35 mmol/m^2/24 hr

**Correction of Acid Base**

Criteria: Arterial pH < 6.9

Verify pH 1 hour after completion of HCO₃ perfusion and repeat if necessary.

Potential hazards of bicarbonate therapy:-
- Exacerbation of CNS acidosis
- Hypokalaemia and altered calcium ionization
- Excessive osmolar load
- Tissue hypoxia
- **Insulin**
  - Dose: 0.1 units/kg/hour
  - Route of administration: IV

Dilute 50 units actrapid in 50 ml of NS, run at 1 ml/hr. (Note: 1ml = 1 unit)
Continue at this rate until resolution of ketoacidosis.

The expected drop of glycaemia with this rate is 4 – 5 mmol/L/hr.

**To prevent a rapid decrease in plasma glucose and hypoglycaemia, add glucose to the IV fluid when the plasma glucose falls to 14-17 mmol/L.**

Use 0.45% or 0.9% NS with glucose 5%.
Maintain blood glucose in the desired range of 8-12 mmol/L.

If blood glucose rises again >15 mmol/L, increase the insulin infusion by 25%.

If blood glucose falls to < 8 mmol/L, or falls too rapidly, increase the concentration of glucose to ≥10% with added saline.

The insulin rate should only be decreased if the blood glucose level remains below the target range despite glucose supplementation.

If ketoacidosis do not improve:-
- Reassess the patient
- Review insulin therapy
- Consider other causes of impaired response to insulin; e.g infection, errors in insulin preparation.

Consider stopping IV insulin therapy when:-
- Glycaemia is normal between 5.5 – 8 mmol/L
- Correction of ketoacidosis (pH >7.35, HCO₃ >14 mmol/L)
- Patient is fully conscious

Immediately after stopping IV insulin, commence insulin SC. Calculate the total units of insulin utilized in 24 hours and divide it into 6 hourly doses.

- **Monitoring**
  With respect to the severity of the patient, hourly observation is required.

**Clinically:-**
- Vital signs: respiration, BP, PR, temperature.
- Consciousness: hypoglycaemia, intracranial hypertension
- Fluid input and output*
- Daily weight

*Urine Output
If this is inadequate (<1.5 ml/kg/h), causes include acute renal failure, continuing shock, urinary obstruction, bladder retention.
Investigations:-

a) Capillary blood sugar hourly. Cross-check every 2 or 4 hours against laboratory venous glucose.
b) Urea, electrolytes, and blood gases: should be repeated every 2-4 h until acidosis is reversed.
c) Creatinine: minimum is 24 hours, 72 hours and 7 days after admission.
d) Urine: sugar and ketones every time patient micturates
e) ECG: with respect to the initial finding

- When patient is fully conscious with normal peripheral perfusion, start oral feeds.
- During hospitalization and before discharge
  a) Adjust insulin dose
  b) Diabetic education
  c) Refer to a dietitian

D. Complications

- Cerebral Oedema

It most commonly occurs in the first 24 hours after starting rehydration when the general condition of the patient seems to be improving. Vigilant observation is required.

A fluid input >4 litres/m² per 24 h is a risk factor in cerebral oedema. Too rapid reduction in intravascular osmolality may aggravate the process.

Warning signs/symptoms of cerebral oedema:-
- Headache and slowing of the heart rate
- Recurrence of vomiting
- Change in neurological status (restlessness, irritability, increased drowsiness, incontinence) or specific neurological signs (e.g. cranial nerve palsies).
- Rising blood pressure
- Decreased oxygen saturation.
- A fall in serum sodium has been noted as one of the few laboratory correlates of impending cerebral oedema.

Late signs: convulsions, papilloedema, respiratory arrest

Action
- Exclude hypoglycaemia
- If warning signs occur at any time of the day or night, give immediate IV mannitol 1 g/kg over 20 min (i.e. 5 ml/kg 20% solution).
- Halve rehydration rate until situation is improved
- Nurse with the child’s head elevated
- Move to ICU as soon as possible
- Alert anaesthetic and senior paediatric staff (if assisted ventilation is required, maintain PCO₂ above 3.5 kPa)
- Consider continuation of mannitol infusion 0.25 g/kg/h to prevent rebound increase in ICP (or repeat bolus doses every 4-6 h).
- Cranial imaging should be considered after child has been stabilized. Intracranial events as haemorrhage, thrombosis and infarction may occur.

- Hypoglycaemia and hypokalaemia
  Avoid by careful monitoring and adjustment of infusion rates.

- Aspiration pneumonia
  Avoid by nasogastric tube in a vomiting child with impaired consciousness.

- Other associations with DKA: require specific management e.g. continuing abdominal pain (due to liver swelling/gastritis/bladder retention – but beware appendicitis), pneumothorax ± pneumomediastinum, interstitial pulmonary oedema, unusual infections (e.g. TB, fungal infections), hyperosmolar hyperglycaemic non-ketotic coma, ketosis in type 2 diabetes.

E. Diabetes Care in Children

1. Insulin therapy.
   Average dosage requirements are as follows:-
   - Preadolescent: 1.0 unit/kg/day
   - Adolescent: 1.0 – 1.5 units/kg/day (increase during pubertal growth spurt)

   In young children, insulin is usually given twice a day, before breakfast and dinner, utilizing combinations of short and intermediate-acting insulin. Generally, 2/3 of the total insulin dose is given in the morning and 1/3 in the evening. On each occasion, 2/3 is given as intermediate-acting insulin and 1/3 is given as short-acting insulin.

   Older children may use a 3 or 4 injections a day regime that allow greater flexibility.

2. Home blood glucose monitoring (HBGM)
   Two blood glucose level per day (e.g.: prebreakfast and predinner) is recommended. The patient/parents can choose the time to monitor the blood glucose and the next day they can choose a different time e.g. prelunch and prebed time). The goals are for a preprandial or fasting level of 4.0 – 10.0 mmol/L for younger children and 4.0 – 7.0 mmol/L for adolescents and older children.

3. Diet: A balance and healthy diet for age is required with dietician involvement.

4. Exercise: No restriction but it may be necessary during strenuous exercise to have fast-acting carbohydrates frequently. Plan the injection sites according to the activity e.g. inject insulin in the arm if one plans to go cycling.

5. Adequate education of patient and parents by doctors and diabetic educators e.g. group teaching sessions, diabetes camps.
   a) Hypoglycemia: recognition and treatment
   b) Keep a diary of the HBGM
c) Technique of insulin injections
d) Sites of insulin injections
e) Adjustment of insulin dosage with respect to HBGM results
f) Specific direction to parents to seek medical assistance early at times of illness.
g) At times of sickness, check urine for ketones once upon awakening and when blood glucose is >14 mmol/L. Checking for blood ketones is preferable to urine ketones. If positive to seek for medical advice.

6. Serum TSH and blood lipid profile at time of diagnosis – when stable clinically and biochemically. Subsequently a serum TSH should be done once a year and if it is elevated, then a serum T4 and antithyroid antibodies should be done.

7. HbA1c: 4-6 measurements/year in younger children and 3-4 measurements/year in older children. Target control is <7.6% according to Diabetes Control and Complication Trial (DCCT)

8. Medic alert, which may be life-saving in an emergency situation.

9. After 5 years of onset of diabetes, particularly in the post-adolescent patient, careful evaluation for complications, on annual basis, including:
   a) Fundoscopic examination (retinopathy)
   b) Neurological evaluation
   c) Cardiovascular system evaluation
   d) Renal function test, test for microalbuminuria

10. Diabetes support group – Persatuan Diabetes Malaysia (PDM) or Malaysian Diabetes Association, Diabetes Resource Centre at the regional center or the respective hospital. Encourage patient and family members to enroll as members of PDM and participate in their activities.

F. Diabetes and Illness

Illness associated with fever tends to raise blood glucose because of higher levels of stress hormones, gluconeogenesis and insulin resistance.

Illness associated with vomiting and diarrhoea (e.g. gastroenteritis) may lower blood glucose, with the possibility of hypoglycaemia.

Guidance should include advice on the following:-

- Never stop insulin
  But advice should be available on alterations of insulin dose.

- More frequent monitoring
  Frequent blood glucose testing facilitates optimal management.
  Urinary ketone tests will guide management.
• Loss of appetite: Replacing meals with easily digestible food and sugar-containing fluids.

• Maintaining hydration: Hyperglycaemia, fever and excessive glycosuria increase fluid losses.

• Specific medical advice: Treating fever, malaise and headache with antipyretics.

**Infections associated with hyperglycaemia with or without ketosis**

Recommend additional doses of short or rapid-acting insulin with careful monitoring to reduce blood glucose, prevent ketoacidosis and avoid hospital admission.

The dose and frequency of injection will depend on the age of the child, the level and duration of hyperglycaemia, the severity of ketosis and previous experience with alterations of insulin.

e.g. Sick child, blood glucose 15-20 mmol/L (± ketosis) : Advise 10-20% of total daily dose (or 0.1 u/kg) as short or rapid-acting insulin every 2-4 hr until blood glucose falls to <15 mmol/L. Thereafter any additional doses might be 5 -10% of the total daily dose.

**Infections associated with hypoglycaemia**

These infections are often associated with nausea, vomiting ± diarrhoea. Advise replacing meals with frequent small volumes of sugary drinks and careful blood glucose monitoring.

Reduction of insulin dose by 20-50% may be required

If hypoglycaemia (and nausea or food refusal) persists, an injection of glucagon may reverse the hypoglycaemia and enable oral fluids to be reestablished.

**References**

5. ISPAD Consensus Guidelines for the Management of Type 1 Diabetes Mellitus in Children and Adolescents 2000. NB : ISPAD is the abbreviation for International Society For Pediatric and Adolescent Diabetes.
7. Diabetes Care 2003; 26 (suppl 1): S1
Congenital Hypothyroidism

The incidence of congenital hypothyroidism worldwide is 1 in 2500 - 4000 live births. In Malaysia, it is reported as 1 in 4000 - 5000. It is the commonest preventable cause of mental retardation in children.

Thyroid hormones are crucial for:-

- Normal growth and development of the brain and intellectual function, during prenatal and early postnatal period.
- Maturation of the foetal lungs and bones.

Causes :-

- Thyroid dysgenesis (85%)
  - athyreosis (30%)
  - hypoplasia (10%)
  - ectopic thyroid (60%)

- Inborn error of thyroid hormone synthesis (1 in 30,000)
- Hypothalamopituitary defect (1 in 100,000)
- Peripheral resistance to thyroid hormone (very rare)
- Transient neonatal hypothyroidism (1 in 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, 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.
SCREENING FOR CONGENITAL HYPOTHYROIDISM

Cord blood sample collected at birth

- **TSH <25 mU/L** (NORMAL)
- **TSH 25 – 60 mU/L** (BORDERLINE)
- **TSH > 60 mU/L** (HIGH)

  *Total T4 analysis (on cord blood)*

  - **T4 >100 nmol/L** (NORMAL)
  - **T4 <100 nmol/L** (LOW)

**CLINICAL EVALUATION**
Venous *T4 & TSH*

- **TSH↑**
  - **T4↓**
  - 1° hypothyroidism
- **TSH↑**
  - **T4 NI**
  - 1° hypothyroidism compensated
- **TSH NI**
  - **T4 ↓**
  - 1° hypothyroidism, delayed TSH rise
- **TSH NI**
  - **T4 NI**
  - Normal

Interpretation of the results should take into account the physiological variations of the hormone levels during the neonatal period.
*Free thyroxine level if available is preferable to total thyroxine level. NI : normal*
Treatment:-

**Timing:** Should begin immediately after diagnosis is established. If features of hypothyroidism are present, treatment is started urgently pending T4/TSH results.

**Duration:** It is lifelong except in children suspected of having transient hypothyroidism where re-evaluation is done at 2 - 3 years of age.

**Preparation:** Only T4 tablets should be used. There are currently no approved liquid preparations, and thyroid suspensions prepared by the individual pharmacists may result in unreliable dosing. The T4 tablet should be crushed, mixed with breast milk, formula, or water and fed to the infant. The tablets should not be mixed with soy formulas or any preparation containing iron (formulas or vitamins), both of which reduce the absorption of T4.

**General doses of L-thyroxine by age:-**

<table>
<thead>
<tr>
<th>Age</th>
<th>mcg/kg/dose, daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 3 months</td>
<td>10 – 15</td>
</tr>
<tr>
<td>3 – 6 months</td>
<td>8 – 10</td>
</tr>
<tr>
<td>6 – 12 months</td>
<td>6 – 8</td>
</tr>
<tr>
<td>1 – 5 yr</td>
<td>5 – 6</td>
</tr>
<tr>
<td>6 – 12 yr</td>
<td>4 – 5</td>
</tr>
<tr>
<td>&gt; 12 yr</td>
<td>2 – 3</td>
</tr>
</tbody>
</table>

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. For example, if the dose of T4 has to be stepped up from 50 to 75 mcg and the doctor thinks it is a bit too much, he/she can prescribe 50 mcg on even days and 75 mcg on odd days of the calendar month. This will give an average dose of 62.5 mcg. Please ensure that parents/patient understand the regime of treatment to ensure compliance.

**Goal of Therapy:-**

In the 1\(^{st}\) year of life :-

<table>
<thead>
<tr>
<th>Adequate Treatment</th>
<th>Inadequate treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4 10 -16 mcg/dL (130 - 206 nmol/L)</td>
<td>T4 &lt; 10 mcg/dL (&lt;103 nmol/L)</td>
</tr>
<tr>
<td>FT4 1.4 – 2.3 ng/dL (18 - 30 pmol/L)</td>
<td>TSH &gt; 5 mU/L</td>
</tr>
<tr>
<td>TSH &lt; 5 mU/L</td>
<td>TSH &gt;15 mU/L more than once during first year</td>
</tr>
</tbody>
</table>

1) The goal of therapy is to restore the euthyroid state by maintaining a normal serum T4/free T4 level at the upper half of the normal range for age rather than to suppress the TSH to normal values for age.

2) After initiation of T4 therapy, serum thyroid hormone concentrations increase first (should be normal within 1-2 weeks), and then TSH secretion begins to fall (should be normal after 1 month of treatment) because of the negative feedback action of T4 on the pituitary and hypothalamus.

3) The dose can be increased in 3 weeks in patients who continue to have symptoms and have a low serum T4 concentration, but it should be recognized that serum T4 and TSH at this time are not steady-state values. Given the one-week plasma half-life of T4, it takes about 6 weeks (six half-lives) before a steady state is attained after therapy is initiated or the dose is changed.
4) Some infants may have a high serum TSH concentration (10 - 20 mU/L) despite serum T4 values in the upper half of the normal range. This is the result of resetting of the pituitary-thyroid feedback threshold due to intrauterine hypothyroidism.

**Follow-up:**

- Monitor T4 / TSH at regular intervals
- Monitor growth (weight / height / OFC)
- Development assessment

The American Academy of Pediatrics recommends measurement of serum T4 or free T4 and TSH according to the following schedule:-

- At 2 and 4 weeks after initiation of T4 treatment.
- Every 1 to 2 months during the first year of life.
- Every 2 to 3 months between 1 and 3 years of age.
- Every 3 to 12 months thereafter until growth is complete
- Two weeks after any change in dosage.
- At more frequent intervals when compliance is questioned or abnormal results are obtained.

**Transient Hypothyroidism:**

Some 10 to 20% of patients with congenital hypothyroidism have transient hypothyroidism.

**Causes**

- Iodine deficiency particularly in preterm infants
- Transfer of blocking antibodies or antithyroid drugs in infants of mothers with autoimmune thyroid disease
- Gestational hyperthyroidism
- Iodine exposure

**Re-evaluation**

Most thyroid dependent brain growth is completed by 3 years so that the test is safer at this age than earlier.

- Stop L-thyroxine for 2 - 4 weeks
- Repeat thyroid function test : T4/FT4, TSH
- Thyroid scan
- KIV re-start L-thyroxine if confirmed hypothyroid.
Maternal Hyperthyroidism

1. T3, T4 does not cross the placenta. Antithyroid drugs as propylthiouracil (PTU), carbimazole and TSH receptor stimulating antibody crosses the placenta.

2. Maternal hypothyroidism is poorly tolerated by foetus. Mothers should be kept mildly thyrotoxic. Babies must have their thyroid function tested at birth to detect a hyper or hypothyroid state.

3. PTU is preferred to carbimazole during pregnancy. Carbimazole use has been associated with cutis aplasia in the neonate. The dose should be kept as low as possible to reduce the risk of foetal goitre.

4. Irrespective of what drug the mother received, her baby must have a thyroid function test done.

5. Breastfeeding: PTU is preferred to carbimazole during breastfeeding. Breastfeeding is not advisable for mothers taking large doses of antithyroid drugs (PTU >100 mg or carbimazole >10 mg) as these are secreted in the breast milk. The thyroid function of the baby should be checked regularly.

References

- Endocrine update (Lecture by Professor Wu Loo Ling).
- Clinical features and detection of congenital hypothyroidism. Stephen LaFranchi 2004. UpToDate (www.uptodate.com)
- Treatment and prognosis of congenital hypothyroidism. Stephen LaFranchi. 2004. UpToDate (www.uptodate.com)