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<td>Septic Arthritis</td>
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<td>Growing Pains</td>
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<td>Systemic Lupus Erythematosus (SLE)</td>
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<td>Vasculitides</td>
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<td>Kawasaki Disease</td>
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# Pediatric Quick Reference Values

## Table 1. Average Vitals at Various Ages

<table>
<thead>
<tr>
<th>Age</th>
<th>Pulse (bpm)</th>
<th>Resp. Rate (br/min)</th>
<th>sBP (mmHg)</th>
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<tr>
<td>Birth</td>
<td>120 - 160</td>
<td>35 - 50</td>
<td>70</td>
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<tr>
<td>Preschool</td>
<td>70 - 140</td>
<td>20 - 30</td>
<td>80 - 90</td>
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<tr>
<td>Adolescent</td>
<td>60 - 120</td>
<td>15 - 20</td>
<td>90 - 120</td>
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## Table 2. Average Blood Chemistry at Various Ages

<table>
<thead>
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<th>Test</th>
<th>Birth</th>
<th>Preschool</th>
<th>Adolescent</th>
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<tbody>
<tr>
<td>Sodium (mmol/L)</td>
<td>133 - 142</td>
<td>135 - 143</td>
<td>135 - 145</td>
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<tr>
<td>Potassium (mmol/L)</td>
<td>4.5 - 6.5</td>
<td>3.5 - 5.2</td>
<td>3.5 - 5.2</td>
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<tr>
<td>Chloride (mmol/L)</td>
<td>96 - 106</td>
<td>99 - 111</td>
<td>98 - 106</td>
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<tr>
<td>Serum Creatinine (μmol/L)</td>
<td>&lt;125</td>
<td>&lt;44</td>
<td>&lt;106</td>
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<tr>
<td>BUN (mmol/L)</td>
<td>2.9 - 10</td>
<td>1.8 - 5.4</td>
<td>2.9 - 7.1</td>
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<tr>
<td>Glucose (fasting; mmol/L)</td>
<td>&gt;2.5</td>
<td>2.8 - 6.1</td>
<td>3.3 - 6.1</td>
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<tr>
<td>Glucose (fasting; mg/dL)</td>
<td>&gt;45</td>
<td>50 - 110</td>
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<tr>
<td>pH (arterial)</td>
<td>7.30 - 7.40</td>
<td>7.35 - 7.45</td>
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<td>pCO₂ (mmHg)</td>
<td>30 - 50</td>
<td>30 - 42</td>
<td>33 - 46</td>
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<tr>
<td>pO₂ (mmHg)</td>
<td>50 - 60</td>
<td>80 - 100</td>
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<td>Bicarbonate (mmol/L)</td>
<td>16 - 22</td>
<td>18 - 24</td>
<td>20 - 28</td>
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<td>ALT (U/L)</td>
<td>&lt;60</td>
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<td>AST (U/L)</td>
<td>&lt;110</td>
<td>&lt;45</td>
<td>&lt;36</td>
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## Table 3. Average Hematological Labs at Various Ages

<table>
<thead>
<tr>
<th>Test</th>
<th>2 Days</th>
<th>1 Week</th>
<th>1 Month</th>
<th>1-5 Yrs</th>
<th>6-14 Yrs</th>
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<tbody>
<tr>
<td>Hemoglobin (g/L)</td>
<td>150 - 250</td>
<td>115 - 180</td>
<td>110 - 140</td>
<td>120 - 160</td>
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<tr>
<td>Hemoglobin (g/dL)</td>
<td>15 - 20</td>
<td>11.5 - 18</td>
<td>11 - 14</td>
<td>12 - 16</td>
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<tr>
<td>Hematocrit</td>
<td>0.46 - 0.74</td>
<td>0.35 - 0.54</td>
<td>0.33 - 0.42</td>
<td>0.36 - 0.48</td>
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<tr>
<td>RBC count (x 10¹²/L)</td>
<td>3.5 - 6.0</td>
<td>3.5 - 5.5</td>
<td>4.0 - 5.0</td>
<td>4.5 - 5.5</td>
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<tr>
<td>Reticulocytes (x 10⁹/L)</td>
<td>&lt;5.0</td>
<td>&lt;5.0</td>
<td>10.0 - 100.0</td>
<td>10.0 - 100.0</td>
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<td>MCV (fL)</td>
<td>110</td>
<td>90</td>
<td>80 - 94</td>
<td>90 - 94</td>
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<td>MCH (pg)</td>
<td>24 - 34</td>
<td>24 - 31</td>
<td>24 - 31</td>
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<td>MCHC (g/L)</td>
<td>320 - 360</td>
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<td>WBC (x 10⁹/L)</td>
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<td>5 - 21</td>
<td>5 - 12</td>
<td>4 - 10</td>
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<td>Polymorphs (x 10⁹/L)</td>
<td>6 - 26</td>
<td>1.5 - 10</td>
<td>1.5 - 8.5</td>
<td>1.5 - 7.5</td>
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<tr>
<td>Bands (x 10⁹/L)</td>
<td>0 - 4.5</td>
<td>0 - 4.5</td>
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<tr>
<td>Lymphocytes (x 10⁹/L)</td>
<td>2.0 - 11.0</td>
<td>2.0 - 11.0</td>
<td>2.0 - 8.0</td>
<td>1.5 - 7.0</td>
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<td>Platelets (x 10⁹/L)</td>
<td>150 - 450</td>
<td>150 - 450</td>
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<td>INR</td>
<td>0.9 - 2.7</td>
<td>0.9 - 2.7</td>
<td>0.8 - 1.2</td>
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<td>PTT (s)</td>
<td>25 - 60</td>
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<tr>
<td>TSH (mU/L)</td>
<td>1.38 - 3.25</td>
<td>1.7 - 6.1</td>
<td>0.7 - 6.4</td>
<td>0.7 - 6.4</td>
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</table>

**Pediatric Quick Formula Reference**

- **Mid Parental Height:**
  - Boy = [father height (cm) + mother height (cm) + 13 cm] / 2
  - Girl = [father height (cm) + mother height (cm) - 13 cm] / 2

- **BMI:** weight (kg) / height (m²)

- **Energy Requirements:**
  - 0-10 kg: 100 cal/kg/day
  - 0-20 kg: 1,000 cal + 50 cal/kg/day for each kg >10
  - >20 kg: 1,500 cal + 20 cal/kg/day for each kg >20
Regular Visits

- usual schedule: newborn, within 1 week post-discharge, 1, 2, 4, 6, 9, 12, 15, 18, 24 months
  - yearly until age 6, then every other year
  - yearly again after age 11
- history
- physical exam
- immunization (see Immunization, P5)
- counselling/anticipatory guidance (see Nutrition P7, Colic P10, Sudden Infant Death Syndrome (SIDS) P11, and Injury Prevention Counselling P11 sections)

Developmental Milestones

Table 4. Developmental Milestones

<table>
<thead>
<tr>
<th>Age</th>
<th>Gross Motor</th>
<th>Fine Motor</th>
<th>Speech and Language</th>
<th>Adaptive and Social Skills</th>
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<tbody>
<tr>
<td>6 weeks</td>
<td>Prone-lifts chin intermittently</td>
<td>—</td>
<td>—</td>
<td>Social smile</td>
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<tr>
<td>2 months</td>
<td>Prone-arms extended forward</td>
<td>Pulls at clothes</td>
<td>Responds to voice, laughs</td>
<td>Recognizes parents</td>
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<tr>
<td>4 months</td>
<td>Prone-raises head + chest, rolls over, no head lag</td>
<td>Reach and grasp, objects to mouth</td>
<td>Begins to babble, responds to name</td>
<td>Stranger anxiety during object permanence</td>
</tr>
<tr>
<td>6 months</td>
<td>Prone-weight on hands, tripod sit</td>
<td>Ulnar grasp, transfers objects from hand to hand</td>
<td>Drinks with cup, waves bye-bye</td>
<td></td>
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<tr>
<td>9 months</td>
<td>Pulls to stand, crawls</td>
<td>Finger-thumb grasp</td>
<td>2 words, follows 1-step command</td>
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<tr>
<td>12 months</td>
<td>Walks with support</td>
<td>Finger grasp, throws</td>
<td>Drinks with cup, waves bye-bye</td>
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<td>15 months</td>
<td>Walks without support</td>
<td>Draws a line</td>
<td>Drinks with cup, waves bye-bye</td>
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<td>18 months</td>
<td>Up steps with help</td>
<td>Tower of 3 cubes, scribbling</td>
<td>Drinks with cup, waves bye-bye</td>
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<tr>
<td>24 months</td>
<td>Up 2 feet/step, run, kicks</td>
<td>Tower of 6 cubes, undresses</td>
<td>Drinks with cup, waves bye-bye</td>
<td></td>
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<tr>
<td>3 years</td>
<td>Tri-cycle, up 1 foot/step, down 2 feet/step, stands on one foot, jumps</td>
<td>Copies a circle and a cross, puts on shoes</td>
<td>Drinks with cup, waves bye-bye</td>
<td></td>
</tr>
<tr>
<td>4 years</td>
<td>Hops on 1 foot, down 1 foot</td>
<td>Copies a circle, uses scissors</td>
<td>Drinks with cup, waves bye-bye</td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td>Skips; rides bicycle</td>
<td>Copy a triangle, prints name, ties shoe laces</td>
<td>Drinks with cup, waves bye-bye</td>
<td></td>
</tr>
</tbody>
</table>

Primitive Reflexes

- reflexes seen in normal newborns; may indicate abnormality (e.g. cerebral palsy) if persist after 4-6 months
- Moro reflex
  - infant is placed semi-upright, head supported by examiner’s hand, sudden withdrawal of supported head with immediate resupport elicits reflex
  - reflex consists of abduction and extension of the arms, opening of the hands, followed by flexion and adduction of arms
  - absence of Moro suggests CNS injury; asymmetry suggests focal motor lesions (e.g. brachial plexus injury)
- Galant reflex
  - infant is held in ventral suspension and one side of the back is stroked along paravertebral line; the pelvis will move in the direction of stimulated side
  - grasp reflex: flexion of fingers with the placement of a finger in the infant’s palm
  - tonic neck reflex: turning the head results in the “fencing” posture (extension of ipsilateral leg and arm)
  - placing and stepping reflex (“primitive walking”): infant places feet on a surface when it is brought into contact with it
• rooting reflex: infant pursues tactile stimuli near the mouth
• parachute reflex: tilting the infant to the side while in a sitting position results in ipsilateral arm extension (appears by 6-8 months)
• upgoing plantar reflexes (Babinski sign) is normal in infants (i.e. <2 yrs)

## Routine Immunization

### Table 5. Routine Immunization Schedule

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Schedule</th>
<th>Route</th>
<th>Reaction</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP/IPV</td>
<td>2, 4, 6, 18 mos</td>
<td>IM</td>
<td>At 24-48 hrs&lt;br&gt;• Minor: fever, local redness, swelling, irritability&lt;br&gt;• Major: prolonged crying (1%), hypotonic unresponsive state (1:1750), seizure (1:1950) on day of vaccine&lt;br&gt;• Prophylaxis: acetaminophen 10-15 mg/kg given 4 hrs prior to injection and q4h afterwards</td>
<td>Previous anaphylactic reaction to vaccine; evolving untoward neurologic disease; hypersensitive/hypotonic following previous vaccine; anaphylactic reaction to neomycin or streptomycin</td>
</tr>
<tr>
<td>Hib</td>
<td>2, 4, 6, 18 mos</td>
<td>IM</td>
<td>Minor: fever, local redness, swelling, irritability</td>
<td></td>
</tr>
<tr>
<td>Pneu-C</td>
<td>2, 4, 6, 15 mos</td>
<td>IM</td>
<td>Minor: fever, local redness, swelling, irritability</td>
<td></td>
</tr>
<tr>
<td>MMR*</td>
<td>12, 18 mos</td>
<td>SC</td>
<td>At 7-14 days&lt;br&gt;• Fever, measles-like rash&lt;br&gt;• Lymphadenopathy, arthralgia, arthritis, parotitis (rare)</td>
<td></td>
</tr>
<tr>
<td>Men-C</td>
<td>2, 4, 6 mos</td>
<td>OR 12 mos</td>
<td>IM</td>
<td>Redness/swelling (&lt;50%), fever (9%), irritability (&lt;38°), rash (0.1%)</td>
</tr>
<tr>
<td>Var*</td>
<td>15 mos</td>
<td>SC</td>
<td>Mild local reaction (20% but higher in immunocompromised)&lt;br&gt;Mild varicella-like papules or vesicles (5%)&lt;br&gt;Low-grade fever (15%)</td>
<td>Pregnant or planning to get pregnant within next 3 months; anaphylactic reaction to gelatin</td>
</tr>
<tr>
<td>Hep B</td>
<td>3 doses: 0, 1, 6 mos; administered in some provinces in grade 7 (can be given at birth or in school)</td>
<td>IM</td>
<td>Local redness, swelling</td>
<td>Anaphylactic reaction to Baker's yeast</td>
</tr>
<tr>
<td>dTpa</td>
<td>Start at 14-16 yrs</td>
<td>IM</td>
<td>Anaphylaxis (very rare)</td>
<td>Pregnancy (1st trimester)</td>
</tr>
<tr>
<td>Td</td>
<td>Adult yrs, q10 yrs</td>
<td>IM</td>
<td>Local anodynia and swelling (70%)</td>
<td></td>
</tr>
<tr>
<td>Flu**</td>
<td>Every autumn 6-23 mos</td>
<td>IM</td>
<td>Local tenderness at injection site&lt;br&gt;Fever, malaise, myalgia, rash, febrile seizures&lt;br&gt;Hyperosmolarity reactions</td>
<td>Anaphylactic reaction to eggs, &lt;6 mos of age</td>
</tr>
<tr>
<td>Gardasil™</td>
<td>Given in grades 3-9 in some provinces; 3 doses at 0, 2, 6 months for females between 9-26</td>
<td>IM</td>
<td>Local tenderness, redness, itching, swelling at injection site.</td>
<td></td>
</tr>
</tbody>
</table>

*Safety of MMR Vaccine<br>According to the CDC, the weight of currently available scientific evidence does not support the hypothesis that MMR vaccine causes either autism or IDI.<br>http://www.cdc.gov/vlp/vacconcerns/autism/nip/vacsa/autisnmrmv@2 (see website for more details)

### Administration of Vaccines
- injection site<br>  - infants (<12 months old): anterolateral thigh<br>  - children: deltoid<br>  - DTaP+IPV+Hib (Pentacel™, Pentavax®): 5 vaccines given as 1 IM injection<br>  - two live vaccines (varicella, MMR) must be given subcutaneously either at the same visit or separated by 4 weeks or more

### Contraindications to Any Vaccine
- moderate to severe illness ± fever (no need to delay vaccination for mild URTI)
- allergy to vaccine component
Possible Adverse Reactions
- any vaccine
  - local: induration or tenderness (MMR is especially painful)
  - systemic: fever, rash
  - allergic: urticaria, rhinitis, anaphylaxis
- specific vaccine reactions (see Table 5)

Other Vaccines

Hepatitis A
- inactivated monovalent hepatitis A vaccine (Havrix™, Vaqta™, Avaxim™, Epaxal Berna™)
- given as a series of 2 vaccinations 4-6 months apart (cost ~$50 total)
- recommended as pre-exposure prophylaxis for individuals at increased risk of infection
  (e.g. travel to endemic countries, residents of communities with high endemic rates, IV
drug use, etc.)
- can also be given as a combination vaccine with Hep B (Twinrix™)
- immunoglobulin can be used for short-term protection in infants and immunocompromised patients

Hepatitis B
- set of 3 vaccinations given in infancy (0, 1, 6 months) if at increased risk of infection (born
to mother with Hep B, belonging to an area with high endemic rates), or mid-childhood to
early teens (in Ontario, given in grade 7)
- if mother is HBsAg +ve, give HBIG at birth and Hep B vaccine at birth, 1 mo, 6 mos

BCG Vaccine
- infants of parents with infectious TB at time of delivery
- groups/communities with high rates of disease/infection (offered to aboriginal children
  on reserves), health care workers at risk
- only given if patient has a negative TB skin test
- side effects: erythema, papule formation 3-6 weeks after intradermal injection,
enlargement of regional lymph nodes

TB Skin Test (Mantoux)
- screen high risk populations only (family history, HIV, immigrants from countries with
  increased incidence, substance abuse in family, homeless, aboriginal)
- intradermal injection of 5TU (0.1 ml) of tuberculous antigen (purified protein derivative).
  read result at 48-72 hrs
- TB test should be postponed for 4-6 weeks after administration of live BCG vaccine due to
  risk of false negative result
- test interpretation
  - check area of raised INDURATION (not just area of erythema) at 48-72 hours
  - positive result if:
    - >15 mm: children >4 years with no risk factors
    - >10 mm: children <4 years, or at risk for environmental exposure
    - >5 mm: children with close TB contact, immunosuppressed
  - BCG history irrelevant – does not usually give positive response (unless <6 weeks
    previously)
  - positive reaction means active disease or previous contact with TB

Human Papillomavirus Vaccine (Gardasil™) – see Gynecology
- given in grades 7-8 in some provinces

Quadrivalent Meningococcal Vaccine (Menactra™)
- given in some provinces in Grade 9
- protects against Neisseria meningitidis strains A, C, W-135, and Y
- in Canada, currently recommended for patients with asplenia, travelers to endemic areas
  (such as the Hajj in Mecca), laboratory workers, and military recruits

Rotavirus Vaccine (RotaTeq™)
- oral vaccine given in 3 doses with first at age 6-12 weeks
- shown to reduce viral gastroenteritis in infants
- not currently covered in Canada
**Nutrition**

**Breast Feeding**
- colostrum for first few days – clear fluid with nutrients (high protein, low fat) and immunoglobulins
- full milk production by 3-7 days; mature milk by 15-45 days
- support for mothers who want to breast feed should start while in hospital
- signs of inadequate intake: <6 wet diapers per day after first week, sleepy or lethargic, <7 feeds per day, sleeping throughout the night, weight loss >10% of birth weight, jaundice
- rule of thumb: ~ 1 stool/day of age for first week
- feeding schedule (newborn baby needs 120 kcal/kg/day)
  - premature infants: q2-3 hours
  - term infants: q3-5 hours, q5 hours at night until about 2-3 months of age
- breast-fed babies require the following supplements
  - vitamin K (given IM at birth)
  - vitamin D 400 IU/day (Tri-Vi-Sol™ or Di-Vi-Sol™); especially during winter months
  - fluoride (after 6 months if not sufficient in water supply)
  - iron: from 4 months to 12 months (iron fortified cereals or ferrous sulphate solution)
- contraindications to breast feeding
  - mother receiving chemotherapy or radioactive compounds
  - mother with HIV/AIDS, active untreated TB, herpes in breast region
  - mother using >0.5 g/kg/day alcohol and/or illicit drugs (decrease milk production and/or directly toxic to baby)
  - mother taking certain medications e.g. antimetabolites, bromocriptine, chloramphenicol, high dose diazepam, ergots, gold, metronidazole, tetracycline, lithium, cyclophosphamide
- Note: oral contraceptive pills (OCP) not a contraindication to breast feeding (estrogen may decrease lactation but is not dangerous to infant)

**Advantages of Breast Feeding**
- “Breast is Best” – exclusive breastfeeding during the first 4 months of life is recommended by Health Canada, the Dietitians of Canada, and the Canadian Pediatric Society
- breast milk is easily digested and has a low renal solute load
- immunologic
  - IgA, macrophages, active lymphocytes, lysozymes, lactoferrin (lactoferrin inhibits E.coli growth in intestine)
  - protection is greatest during early months, but is cumulative with increased duration of breastfeeding
  - lower allergenicity than cow’s milk protein (decreased cow’s milk protein allergy and eczema)
  - lower pH promotes growth of lactobacillus in the gastrointestinal tract (protective against pathogenic intestinal bacteria)
- parent-child bonding, economical, convenient

**Complications of Breast Feeding**
- mother
  - sore/cracked nipples: treat with warm compresses, massage, frequent feeds, soothing barrier creams (Desitin™, Vaseline®), proper latching technique
  - breast engorgement (usually in first week): continue breast feeding and/or pumping
  - mastitis (usually due to S. aureus): treat with cold compresses between feeds, cloxacillin for mother, continue nursing, ± incision and drainage
- infant
  - breast feeding jaundice (first 1-2 weeks): due to lack of milk production and subsequent dehydration (see Jaundice)
  - breast milk jaundice: rare (0.5% of newborns); due to substances in breast milk that inhibit conjugation of bilirubin (persists up to 4-6 months)
  - poor weight gain: consider dehydration or failure to thrive
  - oral candidiasis (thrush); check baby’s mouth for white cheesy material that does not scrape off; treat baby with antifungal such as nystatin (Mycostatin™) (treat mother topically to prevent transmission)

**Alternatives to Breast Feeding**

<table>
<thead>
<tr>
<th>Table 6. Infant Formulas</th>
<th>Indication(s)</th>
<th>Content (compared to breast milk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast milk</td>
<td>Most babies</td>
<td>70:30 whey/protein ratio</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fat from dietary butterfat</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carbohydrate from lactose</td>
</tr>
<tr>
<td>Cow’s milk based</td>
<td>Premature babies</td>
<td>Plant fats instead of dietary butterfat</td>
</tr>
<tr>
<td>(Enfamil™, Similac™)</td>
<td>Transitional</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Contraindication to breastfeeding</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower whey/protein ratio</td>
</tr>
</tbody>
</table>
Table 6. Infant Formulas (continued)

<table>
<thead>
<tr>
<th>Type of Formula</th>
<th>Indication(s)</th>
<th>Content (compared to breast milk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fortified formula</td>
<td>Low birth weight, Premature babies</td>
<td>More calories</td>
</tr>
<tr>
<td>Soy protein</td>
<td>Galactosemia</td>
<td>Corn syrup solids or sucrose instead of lactose</td>
</tr>
<tr>
<td>(Isomil™, Prosobee™)</td>
<td>Lactase intolerance</td>
<td></td>
</tr>
<tr>
<td>Partially hydrolyzed</td>
<td>Delayed gastric emptying, Risk of cow’s milk allergy</td>
<td>Protein is 100% whey with no casein</td>
</tr>
<tr>
<td>proteins (Good Start™)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein hydrolysate</td>
<td>Malabsorption</td>
<td>Corn syrup solids, sucrose, OR tapioca starch instead of lactose</td>
</tr>
<tr>
<td>(Nutramigen™, Alimentum™,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pegestimil™, Poragen™)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amino acid</td>
<td>Food allergy</td>
<td>No proteins, just free amino acids</td>
</tr>
<tr>
<td>(Neocate™)</td>
<td>Short gut</td>
<td>Corn syrup solids instead of lactate</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Inborn errors of metabolism</td>
<td>Various different compositions for children with galactosaemia, proionic acidemia, etc.</td>
</tr>
</tbody>
</table>

Most formulas contain 680 calories per liter; fortified formulas for premature babies may contain more calories. Formula may also be supplemented with specific nutrients in babies with malabsorption syndromes. True lactase intolerance is extremely rare in children under age 5.

Infant Feeding

Table 7. Dietary Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Food</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 4-6 months</td>
<td>Breast milk, formula</td>
<td>Rice cereals first because less allergenic</td>
</tr>
<tr>
<td>6 to 9 months</td>
<td>Iron enriched cereals, Pureed vegetables</td>
<td>Yellow/orange vegetables first and green last (more bulky)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Avoid vegetables with high nitrate content (beets, spinach, turnips)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Introduce vegetables before fruit (alternate yellow and green vegetables daily)</td>
</tr>
<tr>
<td></td>
<td>Pureed fruits and juices, Pureed meats, fish, poultry, egg yolk</td>
<td>No egg white until 12 months (risk of allergy)</td>
</tr>
<tr>
<td>9 to 12 months</td>
<td>Finger foods, peeled fruit, cheese, and cooked vegetables, homo milk</td>
<td>No honey until &gt;12 months (risk of botulism)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No peanuts or raw, hard vegetables until age 3 to 4 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No added sugar, salt, fat, or seasonings</td>
</tr>
</tbody>
</table>

- do not delay introduction of solid foods beyond 9 months
- introduce 2-3 new foods per week (easier to identify adverse reactions) and allow a few days between each introduction
- avoid excessive milk/juice intake when >1 year

Normal Physical Growth

- newborn size influenced by maternal factors (placenta, in utero environment)
- premature infants (<37 weeks): use corrected gestational age until 2 years
- not linear; most rapid growth during first two years; growth spurt at puberty
- different tissue growth at different times
  - first two years: CNS
  - mid-childhood: lymphoid tissue
  - puberty: gonadal maturation (testes, breast tissue)
- body proportions: upper/lower segment ratio – midpoint is symphysis pubis
  - newborn 1.7; adult male 0.97; adult female 1.0
- poor correlation between birth weight and adult weight

Table 8. Average Growth Parameters

<table>
<thead>
<tr>
<th>Normal</th>
<th>Growth</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight</td>
<td>3.25 kg</td>
<td>2 x birth wt by 4-5 mos, 3 x birth wt by 1 year, 4 x birth wt by 2 years</td>
</tr>
<tr>
<td>Length/Height</td>
<td>50 cm</td>
<td>25 cm in 1st year, 12 cm in 2nd year, 6 cm in 3rd year then 4.7 cm/year until puberty, 1/2 adult height at 2 years</td>
</tr>
<tr>
<td>Head Circumference</td>
<td>35 cm</td>
<td>2 cm/month for first 3 mos, 1 cm/month at 3-6 mos, 0.5 cm/month at 6-12 mos</td>
</tr>
</tbody>
</table>

Scoliosis Screening

Despite mass school screening implemented in parts of the USA and Canada in the 1970s-80s, the Canadian (1994) and American (2004) Task Forces on Preventive Health Care do NOT currently recommend routine screening using the Forward Bend Test (FBT). Cohort studies indicate the forward bend test has poor sensitivity for identifying pathologic curves (Karachalios et al. 1999, Yawn et al. 1999, Puijs et al. 1996). Furthermore, there is no evidence to suggest that screening and increased bracing lead to better outcomes.

Term newborn should gain 20-30 g/day "1 oz. per day except on Sunday"

To estimate weight of child >1 year (kg) = Age x 2 + 8
Dentition

- primary dentition (20 teeth)
  - first tooth at 5-9 months (lower incisor), then 1 per month until 20 teeth
  - 6-8 central teeth by 1 year
- secondary dentition (32 teeth)
  - first adult tooth is 1st molar at 6 years, then lower incisors
  - 2nd molars at 12 years, 3rd molars at 18 years

Failure to Thrive (FTT)

Table 9. Failure to Thrive Patterns

<table>
<thead>
<tr>
<th>Growth Parameters</th>
<th>Suggestive Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>decreased Wt</td>
<td>Normal Ht</td>
</tr>
<tr>
<td></td>
<td>Normal HC</td>
</tr>
<tr>
<td></td>
<td>Caloric insufficiency</td>
</tr>
<tr>
<td></td>
<td>Decreased intake</td>
</tr>
<tr>
<td></td>
<td>Increased losses</td>
</tr>
<tr>
<td>decreased Wt</td>
<td>Decreased Ht</td>
</tr>
<tr>
<td></td>
<td>Normal HC</td>
</tr>
<tr>
<td></td>
<td>Structural dysplasias</td>
</tr>
<tr>
<td></td>
<td>Constitutional growth delay</td>
</tr>
<tr>
<td>decreased Wt</td>
<td>Decreased Ht</td>
</tr>
<tr>
<td></td>
<td>Decreased HC</td>
</tr>
<tr>
<td></td>
<td>Intrauterine insult</td>
</tr>
<tr>
<td></td>
<td>Genetic abnormality</td>
</tr>
</tbody>
</table>

(HC = head circumference; Ht = height; Wt = weight)

Definition

- weight <3<sup>rd</sup> percentile, or falls across two major percentile curves, or <80% of expected weight for height and age
- inadequate caloric intake most common factor in poor weight gain
- may have other nutritional deficiencies (e.g. protein, iron, vitamin D)

History

- duration of problem and growth history
- detailed dietary and feeding history, appetite, behaviour before and after feeds, bowel habits
- pregnancy, birth, and postpartum history; developmental and medical history (including medications); social and family history (parental height, weight, growth pattern)
- assess 4 areas of functioning: child's temperament, child-parent interaction, feeding behaviour and parental psychosocial stressors

Physical exam

- height (Ht), weight (Wt), head circumference (HC), arm span, upper-to-lower (U/L) segment ratio
- assessment of nutritional status, dysmorphism, Tanner stage, evidence of chronic disease
- observation of a feeding session and parent-child interaction
- signs of abuse or neglect

Investigations (as indicated by clinical presentation)

- CBC, blood smear; electrolytes, urea, ESR, T4, TSH, urinalysis
- bone age x-ray (left wrist – compared to standardized wrist x-rays)
- karyotype in all short girls and in short boys where appropriate
- any other tests indicated from history and physical exam: renal or liver function tests, venous blood gases, ferritin, immunoglobulins, sweat chloride, fecal fat

Causes of FTT

Organic FTT

- inability to feed
  - insufficient breast milk production
  - poor retention (GERD, vomiting)
  - CNS, neuromuscular, mechanical problems with swallowing, sucking
  - anorexia (associated with chronic disease)
- inadequate absorption (see Pediatric Gastroenterology, P34)
  - malabsorption: celiac disease, cystic fibrosis (CF), pancreatic insufficiency
  - loss from the GI tract: chronic diarrhea, vomiting

Non-Organic

- Malnutrition
- Inadequate absorption
- Inappropriate utilization of nutrients
- Increased energy requirements
- Errors in making formula

Energy Requirements

- 0-10 kg: 100 cal/kg/day
- 0-20 kg: 1,000 cal + 50 cal/kg/day for each kg > 10
- +20 kg: 1,500 cal + 20 cal/kg/day for each kg > 20

Clinical signs of FTT

- SMALL KID
  - Subcutaneous fat loss
  - Muscle atrophy
  - Alopecia
  - Lethargy
  - Lagging behind normal
  - Kwashiorkor
  - Infection (recurrent)
  - Dermatitis
• inappropriate utilization of nutrients
  • renal loss: e.g. tubular disorders
  • inborn errors of metabolism
  • endocrine: type 1 diabetes, diabetes insipidus (DI), hypopituitarism, congenital hypothyroidism
• increased energy requirements
  • pulmonary disease: CF
  • cardiac disease
  • endocrine: hyperthyroidism, DI, hypopituitarism
  • malignancies
  • chronic infections
• inflammatory: systemic lupus erythematosus (SLE)
• decreased growth potential
  • specific syndromes, chromosomal abnormalities, GH deficiency
• intrauterine insults: fetal alcohol syndrome (FAS), TORCH infections
• treatment: cause-specific

Non-Organic FTT
• often due to malnutrition, inadequate nutrition, poor feeding technique, errors in making formula
• these children may present as picky eaters, with poor emotional support at home or poor temperamental “fit” with caregiver
• may have delayed psychomotor, language, and personal/social development
• emotional deprivation, poor parent-child interaction, dysfunctional home
• child abuse and/or neglect
• parental psychosocial stress, personal history of suffering abuse or neglect
• treatment: most are managed as outpatients with multidisciplinary approach
  • primary care physician, dietitian, psychologist, social work, child protection services

**Obesity**

• prevalence of childhood obesity in Canada has tripled (1981-1996)

**Definition**

• weight >95th percentile for age and height, or BMI >30, or weight >20% greater than expected for age and height
• caused by a chronically positive energy balance (intake exceeds expenditure)

**Risk Factors**

• genetic predisposition:
  • if 1 parent is obese - 40% chance of obese child
  • if both parents are obese - 80% chance of obese child
• genetic heritability accounts for 25-40% of juvenile obesity

**Clinical Presentation**

• history: diet, activity, family heights and weights, growth curves
• physical examination: may suggest secondary cause, e.g. Cushing syndrome
• organic causes are rare (<5%)
  • genetic: e.g. Prader-Willi, Carpenter, Turner syndromes
  • endocrine: e.g. Cushing syndrome, hypothyroidism
• complications
  • childhood obesity is an unreliable predictor of adult obesity
  • unless >180% of ideal body weight
  • however, 70% of obese adolescents become obese adults
  • association with: hypertension, dyslipidemia, slipped capital femoral epiphysis, type 2 diabetes, asthma, obstructive sleep apnoea
  • boys: gynecomastia
  • girls: polycystic ovarian disease, early menarche, irregular menses
  • psychological: teasing, decreased self-esteem, unhealthy coping mechanisms, depression
• management
  • encouragement and reassurance; engagement of entire family
  • diet: qualitative changes; do not encourage weight loss but allow for linear growth to catch up with weight; special diets used by adults are not encouraged
  • evidence against very low calorie diets for preadolescents
  • behaviour modification: increase activity, change eating habits/meal patterns
  • insufficient evidence for or against exercise, family programs for obese children
• education: multidisciplinary approach, dietitian, counselling
• surgery and pharmacotherapy are not used in children

**Colic**

• rule of 3's: unexplained paroxysms of irritability and crying for >3 hours/day and >3 days/week for >3 weeks in an otherwise healthy, well-fed baby
• occurs in 10% of infants
etiology: generally regarded as a lag in the development of normal peristaltic movement in gastrointestinal tract, other theories suggest a lack of self-soothing mechanisms
other reasons why babies cry: wet, hunger or gas pains, too hot or cold, overstimulated, need to suck or be held
timing: onset 10 days to 3 months of age; peak 6-8 weeks
child cries, pulls up legs and passes gas soon after feeding
management
  • parental relief, rest and reassurance
  • hold baby, soothe, car ride, music, vacuum, check diaper
  • medications (Oval^®
     drops, gripe water) of no proven benefit
  • if breast feeding, elimination of cow’s milk protein from mother’s diet (effective in very small percentage of cases)
  • try casein hydrolysates formula (Nutramigen^®)

Milk Caries

• decay of superior front teeth and back molars in first 4 years of life
• often occur in children put to bed with a bottle of milk or juice
• can also be caused by breast-feeding (especially prolonged night feeds)
• prevention
  • no bottle at bedtime (unless plain water)
  • use water as thirst quenchers during the day, do not sweeten pacifier
  • can clean teeth with soft damp cloth or toothbrush and water
  • avoid fluoridated toothpaste until able to spit (>3 years) because of fluorosis risk (stains teeth)
  • Canadian Dental Association recommends assessment by dentist 6 months after eruption of first tooth, or by 1 year of age

Injury Prevention Counselling

• injuries are the leading cause of death in children >1 year of age
• main causes: motor vehicle crashes, burns, drowning, falls, choking, infanticide

Table 10. Injury Prevention Counselling

<table>
<thead>
<tr>
<th>0-6 months</th>
<th>6-12 months</th>
<th>1-2 years</th>
<th>2-5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not leave infant alone on bed, on change table or in tub</td>
<td>Install stair barriers</td>
<td>Never leave unattended</td>
<td>Bicycle helmet</td>
</tr>
<tr>
<td>Keep crib rails up</td>
<td>Discourage use of walkers</td>
<td>Keep pet handles turned to back of stove</td>
<td>Never leave unattended at home, driveway or pool</td>
</tr>
<tr>
<td>Check water temp before bathing</td>
<td>Avoid play areas with sharp-edged tables and corners</td>
<td>No nuts, raw carrots, etc., due to choking hazard</td>
<td>Teach bike safety, stronger safety, and street safety</td>
</tr>
<tr>
<td>Do not hold hot liquid and infant at the same time</td>
<td>Cover electrical outlets</td>
<td>No running while eating</td>
<td>Swimming lessons, sunscreen, toddler seats in the car, fences around pools, dentist by age 3</td>
</tr>
<tr>
<td>Turn down hot water heater</td>
<td>Unplug appliances when not in use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Check milk temp before feeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have appropriate car seats – required before allowed to leave hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• &lt; 9 kg; rear-facing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 10-18 kg; front-facing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 18-36.4 kg; booster seat</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* always have Poison Control number by telephone
* have smoke and carbon monoxide detectors in the house and check yearly

Poison Prevention

• keep all types of medicines, vitamins, and chemicals locked up in a secure container
• potentially dangerous: drugs, drain cleaners, furniture polish, insecticides, cosmetics, nail polish remover, automotive products
• do not store any chemicals in juice, soft drink, or water bottles
• keep alcoholic beverages out of a child’s reach: as little as 3 ounces of hard liquor can kill a 2-year-old
• always read the label before administering medicine to ensure it is the right drug and correct dose
• always keep the telephone number of Poison Control near your phone

Sudden Infant Death Syndrome (SIDS)

Definition

• sudden and unexpected death of an infant <12 months of age in which the cause of death cannot be found by history, examination or a thorough postmortem and death scene investigation
Epidemiology
- 0.5/1,000 (leading cause of death between 1-12 months of age); M:F = 3:2
- more common in children placed in prone position
- in full term infants, peak incidence is 2-4 months, 95% of cases occur by 6 months
- increase in deaths during peak respiratory syncytial virus (RSV) season
- most deaths occur between midnight and 8 AM

Risk Factors
- more common in prematurity, if smoking in household, minorities (higher incidence in aboriginals and African Americans), socially disadvantaged
- risk of SIDS is increased 3-5 times in siblings of infants who have died of SIDS

Prevention – "Back to Sleep, Front to Play"
- place infant on back, NOT in prone position when sleeping
- allow supervised play time daily in prone position
- alarms/other monitors not recommended – increase anxiety and do not prevent life-threatening events
- avoid overheating and overdressing
- appropriate infant bedding (use firm mattress, avoid loose bedding, do not use crib bumper pads)
- no smoking
- pacifiers appear to have a protective effect; do not reinsert if falls out

Circumcision
- elective procedure to be performed only in healthy, stable infants
- contraindicated when genital abnormalities present (hypospadias, etc.) or known bleeding disorder
- usually performed for social or religious reasons (not covered by OHIP)
- complications (<1%): local infection, bleeding, urethral injury
- medical benefits include prevention of phimosis, slightly reduced incidence of UTI, balanitis, cancer of the penis
- 2 recent RCTs (Lancet 369, Feb 2007) suggested that routine circumcision significantly reduced HIV transmission (studies conducted in high endemic areas, i.e. Africa);
  circumcision also appears to reduce HPV transmission
- routine circumcision is not currently recommended by the CPS or AAP

Toilet Training
- 90% of kids attain bowel control before bladder control
- generally females train earlier than males
- 25% by 2 years old (in North America), 98% by 3 years old have daytime bladder control
- signs of toilet readiness
  - ambulating independently, stable on potty, desire to be independent or to please caregivers (i.e. motivation), sufficient expressive and receptive language skills
    (2-step command level), can stay dry for several hours (large enough bladder)

Approach to the Crying/Fussing Child

History
- description of infant’s baseline feeding, sleeping, crying patterns
- infectious symptoms – fever, tachypnea, rhinorrhea, ill contacts
- feeding intolerance – gastroesophageal reflux with esophagitis
- nausea, vomiting, diarrhea, constipation
- trauma
- recent immunizations (vaccine reaction) or medications (drug reactions), including maternal drugs taken during pregnancy (neonatal withdrawal syndrome), and drugs that may be transferred via breast milk
- inconsistent history; pattern of numerous emergency department (ED) visits, high-risk social situations all raise concern of abuse

Physical Examination
- perform a thorough head-to-toe exam with the child completely undressed
Table 11. The Physical Examination of the Crying/Fussing Child

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Examination Findings</th>
<th>Possible Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEENT</td>
<td>Bulging fontanelle</td>
<td>Meningitis</td>
</tr>
<tr>
<td></td>
<td>Blepharospasm, tearing</td>
<td>Corneal abrasion</td>
</tr>
<tr>
<td></td>
<td>Retinal hemorrhage</td>
<td>Shaken baby syndrome</td>
</tr>
<tr>
<td></td>
<td>Oropharyngeal infections</td>
<td>Thrush</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Irritability or lethargy</td>
<td>Meningitis</td>
</tr>
<tr>
<td></td>
<td>Sepsis</td>
<td>Anomalous coronary artery</td>
</tr>
<tr>
<td></td>
<td>Congestive Heart Failure (CHF)</td>
<td>Myocarditis</td>
</tr>
<tr>
<td></td>
<td>Supraventricular tachycardia</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Poor perfusion</td>
<td>Pneumonia</td>
</tr>
<tr>
<td></td>
<td>Tachycardia</td>
<td>CHF</td>
</tr>
<tr>
<td></td>
<td>Tachypnea</td>
<td>Respiratory disease</td>
</tr>
<tr>
<td></td>
<td>Gagging</td>
<td>Response to pain</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Mass, empty RLQ</td>
<td>Intussusception</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Scrotal swelling</td>
<td>Incarcerated hernia</td>
</tr>
<tr>
<td></td>
<td>Perineal/ctitoral swelling</td>
<td>Hair tourniquet</td>
</tr>
<tr>
<td></td>
<td>Anal fissure</td>
<td>Constipation or diarrhea</td>
</tr>
<tr>
<td></td>
<td>Hemorrhoidal positive stool</td>
<td>Intussusception</td>
</tr>
<tr>
<td></td>
<td>Rectal</td>
<td>Volvulus</td>
</tr>
<tr>
<td>Genitourinary</td>
<td></td>
<td>Necrotizing enterocolitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Point tenderness or decreased movement</td>
<td>Fracture</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Osteomyelitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Toe/finger hair tourniquet</td>
</tr>
</tbody>
</table>

Abnormal Child Behaviours

Elimination Disorders

ENURESIS
- involuntary urinary incontinence by day and/or night (typically by 5-6 years old)
- wetting at least twice a week for at least 3 consecutive months or causes significant distress to the child
- treatment should not be considered until 6 years of age; high rate of spontaneous cure
- should be evaluated if >6 years old; dysuria; change in gross colour, odour, stream; secondary or diurnal

Primary Nocturnal Enuresis
- wet only at night during sleep, can be normal up to age 6
- prevalence: 10% of 6-year olds, 5% of 12-year olds, 1% of 18-year olds
- developmental disorder or maturational lag in bladder control while asleep
- more common in boys, family history common
- treatment:
  - time and reassurance (~20% resolve spontaneously each year), behaviour modification (limiting nighttime fluids, voiding prior to sleep), engaging child using rewards, bladder retention exercises, scheduled toileting
  - conditioning: “wet” alarm wakes child upon voiding (70% success rate)
  - medications (considered second line therapy): DDAVP by nasal spray or oral tablets (high relapse rate, costly), oxybutynin (Ditropan™), imipramine (Tofranil™) (rarely used, lethal if overdose, cholinergic side effects)

Secondary Enuresis
- develops after child has sustained period of bladder control (6 months or more)
- nonspecific regression in the face of stress or anxiety (e.g. birth of sibling, significant loss, family discord)
- may also be secondary to urinary tract infection (UTI), diabetes mellitus (DM), diabetes insipidus (DI), neurogenic bladder, cerebral palsy (CP), sickle cell disease, seizures, pinworms
- may occur if engrossed in other activities
- treatment depends on cause

Diurnal Enuresis
- daytime wetting (60-80% also wet at night)
- timid, shy, temperament problems
- may result from psychosocial stressors, rule out structural anomalies (e.g. ectopic ureteral site, neurogenic bladder), UTI, constipation, CNS disorders; most common cause is micturition deferral
- treatment: depends on cause; behavioural (scheduled toileting, double voiding, good bowel program), pharmacotherapy
ENCOPRESIS
- Fecal incontinence in a child > 4 years old, at least once per month for 3 months
- Prevalence: 1-1.5% of school-aged children (rare in adolescence); M:F = 6:1 in school-aged children
- Usually associated with chronic constipation
- Must exclude medical causes (e.g., Hirschsprung disease, hypothyroidism, hypercalcemia, spinal cord lesions, anorectal malformations)

Retentive Encopresis
- Causes
  - Physical: anal fissure (painful stooling)
  - Emotional: disturbed parent-child relationship, coercive toilet training, social stressors
- History
  - Child withholds bowel movement, develops constipation, leading to fecal impaction and seepage of soft or liquid stool (overflow incontinence)
  - Crosses legs or stands on toes to resist urge to defecate
  - Distressed by symptoms, soiling of clothes
  - Toilet training coercive or lacking in motivation
  - May show oppositional behaviour
- Physical exam
  - Digital rectal exam: large fecal mass in rectal vault
  - Anal fissures (result from passage of hard stools)
- Treatment
  - Complete clean-out of bowel
    - Enemas and suppositories
  - Maintenance of regular bowel movements - compliance is crucial
    - Stool softeners (e.g., Colace™, Lactulose™, Lansoy™, mineral oil regularly)
    - Diet modification (see Pediatric Gastroenterology, P34)
    - Toilet schedule and positive reinforcement
    - Assessment and guidance regarding psychosocial stressors
    - Behavioural modification
- Complications: continuing cycle, toxic megacolon (requires >3-12 months to treat), bowel perforation

Sleep Disturbances

Daily Sleep Requirement
- <6 months: 16 hours
- 6 months: 14.5 hours
- 12 months: 13.5 hours
- 2 years: 13 hours
- 4 years: 11.5 hours
- 6 years: 9.5 hours
- 12 years: 8.5 hours
- 18 years: 8 hours

Nap Patterns
- 2/day at 1 year
- 1/day at 2 years: 2-3 hours
- 0.5/day at 5 years: 1.7 hours

Types of Sleep Disturbances
- Insufficient sleep quantity
  - Difficulty falling asleep
    - e.g., Limit Setting Sleep Disorder
    - Preschool and older children
    - Bedtime resistance
    - Due to caregiver’s inability to set consistent bedtime rules and routines
    - Often exacerbated by child’s oppositional behaviours
- Poor sleep quality
  - Frequent arousals
    - e.g., Sleep Onset Association Disorder
    - Infants and toddlers
    - Child learns to fall asleep only under certain conditions or associations (with parent, with light on, in front of TV)
    - Child loses ability to self soothe
    - During the normal brief arousal periods of sleep (~90-120 min), child cannot fall back asleep because same conditions are not present
- Parasomnias
  - Episodic nocturnal behaviours
  - Often involves cognitive disorientation and autonomic/skeletal muscle disturbance
  - E.g., Sleepwalking, sleep terrors, nightmares

Management of Sleep Disturbances
- Set strict bedtimes and “wind-down” routines
- Do not send child to bed hungry
- Always sleep in bed, dark and quiet and comfortable room, without “associations”
- do not use bedroom for timeouts
- systematic ignoring and gradual extinction for sleep onset association disorder
- positive reinforcement for limit setting sleep disorder

**Nightmares**
- prevalence: common in boys, 4-7 years old
- associated with REM sleep (anytime during night)
- upon awakening, child is alert and clearly recalls frightening dream
- may be associated with daytime stress/anxiety
- treatment: reassurance

**Night Terrors**
- prevalence: 15% of children have occasional episodes
- abrupt sitting up, eyes open, screaming
- panic and signs of autonomic arousal
- occurs in early hours of sleep, non-REM, stage 4 of sleep
- no memory of event, parents unable to calm child
- stress/anxiety can aggravate them
- course: remits spontaneously at puberty
- treatment: reassurance

**Breath-Holding Spells**
- occur in 0.1-5% of healthy children 6 months-4 years of age
- spells usually start during first year of life
  - 2 types
    - cyanotic (more common), usually associated with anger/frustration
    - pallid, usually associated with pain/surprise
- child is provoked (usually by anger, injury or fear), starts to cry and then becomes silent
- spell resolves spontaneously or the child may lose consciousness; rarely progresses to seizures
- treatment
  - behavioural – help child control response to frustration and avoid drawing attention to spell
  - avoid being too permissive in fear of precipitating a spell

**Child Abuse and Neglect**

**Definition**
- an act of commission (abuse – physical, sexual, or psychological) or omission (neglect) by a caregiver that harms a child

**Legal Duty to Report**
- upon reasonable grounds to suspect abuse and/or neglect, physicians are required by law to contact the Children's Aid Society (CAS) personally to disclose all information
- duty to report overrides patient confidentiality; physician is protected against liability
- ongoing duty to report: if there are additional reasonable grounds to suspect abuse and/or neglect, a further report to the CAS must be made

**Risk Factors**
- environmental factors
  - social isolation
  - poverty
  - domestic violence
- caregiver factors
  - parents were abused as children
  - psychiatric illness
  - substance abuse
  - single parent family
  - poor social and vocational skills, below average intelligence
- child factors
  - difficult temperament
  - disability, special needs (e.g. developmental delay)
  - premature

**Presentation of Physical Abuse**
- history inconsistent with physical findings, or history not reproducible
- delay in seeking medical attention
- injuries of varied ages, recurrent or multiple injuries
- distinctive marks: belt buckle, cigarette burns, hand prints
- patterns of injury: bruises on the face, abdomen, buttocks, genitalia, upper back, posterior rib fractures; immersion burns (i.e. hot water)
- altered mental status: head injury, poisoning
- physical findings not consistent with any underlying medical condition
- shaken baby syndrome
  - violent shaking of infant resulting in intracranial hemorrhages, retinal hemorrhages, and posterior rib fractures
  - diagnosis confirmed by head CT or MRI, ophthalmologic exam, skeletal survey/bone scan
  - head trauma is the leading cause of death in child maltreatment

**Sexual Abuse**
- prevalence: 1 in 4 females, 1 in 10 males
- peak ages at 2-6 and 12-16 years
- most perpetrators are male and known to child
  - in decreasing order: family member, non-relative known to victim, stranger
- presentation
  - disclosure: diagnosis usually depends on child telling someone
  - psychosocial: specific or generalized fears, depression, nightmares, social withdrawal, lack of trust, low self-esteem, school failure, sexually aggressive behaviour, advanced sexual knowledge, sexual preoccupation or play
  - physical signs: recurrent UTIs, pregnancy, STIs, vaginitis, vaginal bleeding, pain, genital injury, enuresis
- investigations depend on presentation, age, sex, and maturity of child
  - sexual assault examination kit within 24 hours if prepubertal, within 72 hours if pubertal
  - rule out STI, UTI, pregnancy (consider STI prophylaxis or morning after pill)
  - rule out other injuries (vaginal/anal/oral penetration, fractures, head trauma)

**Management of Child Abuse and Neglect**
- history
  - from child and each caregiver separately (if possible)
- physical exam
  - head to toe (do not force)
  - emotional state
  - development
  - document and/or photograph all injuries: type, location, size, shape, colour, pattern
    - be aware of “red herrings” (e.g. Mongolian blue spots vs. bruises)
- investigations
  - blood tests to rule out medical causes (e.g. thrombocytopenia or coagulopathy)
  - STI work-up
  - skeletal survey/bone scan
  - CT/MRI
  - ophthalmology exam
- report all suspicions to Children’s Aid Society; request emergency visit if imminent risk to child or any siblings in the home
- acute medical care: hospitalize if indicated or if concerns about further or ongoing abuse
- arrange consultation to social work and appropriate follow-up
- may need to discharge child directly to CAS or to responsible guardian under CAS supervision

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**Adolescent Medicine**

**Normal Sexual Development**
- puberty occurs with the maturation of the hypothalamic–pituitary–gonadal axis
- increases in the pulsatile release of gonadotrophin hormone (GnRH) → increased release of LH and FSH → maturation of gonads and release of sex steroids → secondary sexual characteristics
- also requires adrenal production of androgens

**Females**
- occurs between age 7-13 years (may start early as 6 years in African-American girls)
- usual sequence
  - thelarche: breast budding (breast asymmetry may occur as one breast may grow faster than the other; becomes less noticeable as maturation continues)
  - adrenarche: axillary hair, body odour, mild acne
  - growth spurt
  - menarche: mean age 13 years; occurs 2 years after breast development and indicates that growth spurt is almost complete (Tanner Stage 4)
- early puberty is common and often constitutional, late puberty is rare
Males
• occurs between age 9-14 years (starts 2 years later than in girls)
• usual sequence
  • testicular enlargement
  • penile enlargement: occurs at Tanner Stage 4
  • adrenarche: axillary and facial hair, body odour, mild acne
  • growth spurt: occurs later in boys (Tanner Stage 4)
• early puberty is uncommon (need to rule out organic disease) but late puberty is common and often constitutional

<table>
<thead>
<tr>
<th>Table 12. Tanner Staging (Sexual Maturity Rating)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
</tbody>
</table>

Normal Variation in Puberty

Premature Thelarche
• isolated breast tissue development in girls 6 months to 2 years
• requires careful history and physical to ensure no other estrogen effects or other signs of puberty (e.g. growth spurt)
• may be due to increased sensitivity to estrogen
• requires observation and periodic examinations every 6-12 months to ensure no further signs of puberty

Physiologic Leukorrhea
• occurs in the 6 months prior to menarche; scant mucoid, clear to milky vaginal discharge, not associated with pruritis or foul odour
• due to stimulation of endometrial glands by estrogen

Irregular Menstruation
• menses may be irregular in duration and length of cycle
• on average it takes 18 months to go through the first 12 periods
• birth control pills should be avoided as treatment

Premature Adrenarche
• usually develops in boys and girls before the age of 6, benign self-limiting condition
• adrenal production of DHEAS (precursor of androstenedione, testosterone and estrogen) reaches pubertal levels at an earlier age
• pubic and axillary hair, body odour, mild acne
• determine whether other signs of puberty are present (girls – thelarche; boys – testicular enlargement)
• exclude androgen secreting tumours (investigations: DHEAS levels, androstenedione, testosterone, bone age)

Gynecomastia
• transient development of breast tissue in boys
• common self-limited condition seen in 50% of male adolescents during puberty
• must distinguish true breast tissue from fat: 1-3 cm round, mobile, sometimes tender, firm mass under areola
• discharge from nipple or fixed mass should be investigated

Other Adolescent Medicine Topics
• Substance Abuse – see Psychiatry
• Eating Disorders – see Psychiatry
• Depression/Suicide – see Psychiatry
• Sexually Transmitted Infections – see Gynecology
Heart Murmurs

- 50-80% of children have audible heart murmurs at some point in their childhood
- most childhood murmurs are functional (e.g. “innocent”) without associated structural abnormalities and have normal ECG and radiologic findings
- in general, murmurs can become audible or accentuated in high output states, e.g. fever, anemia

Table 13. Differentiating Innocent and Pathological Heart Murmurs

<table>
<thead>
<tr>
<th></th>
<th>Innocent</th>
<th>Pathological</th>
</tr>
</thead>
<tbody>
<tr>
<td>History and Physical</td>
<td>Asymptomatic</td>
<td>Symptoms and signs of cardiac disease (FTT, exercise intolerance)</td>
</tr>
<tr>
<td>Timing</td>
<td>Systolic ejection murmur (SEM)</td>
<td>All diastolic, pansystolic, or continuous (except venous hum)</td>
</tr>
<tr>
<td>Grade</td>
<td>&lt;3/6</td>
<td>3/6 (palpable thrill)</td>
</tr>
<tr>
<td>Splitting</td>
<td>Physiologic S2</td>
<td>May have fixed split or single S2</td>
</tr>
<tr>
<td>Extra sounds/Clicks</td>
<td>None</td>
<td>May be present</td>
</tr>
<tr>
<td>Change of Position</td>
<td>Murmur varies</td>
<td>Unchanged</td>
</tr>
</tbody>
</table>

Table 14. Five Innocent Heart Murmurs

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Age</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral Pulmonic Stenosis</td>
<td>Neonates, low-pitched, radiates to axilla and back</td>
<td>neonates, usually disappears by 3-6 mos</td>
<td>Patent Ductus Arteriosus (PDA)</td>
</tr>
<tr>
<td>Stills Murmur</td>
<td>Vibratory, lower left sternal border (ULSB) or apex, SEM</td>
<td>3-6 yrs</td>
<td>Subaortic stenosis</td>
</tr>
<tr>
<td>Venous Hum</td>
<td>Infraclavicular hum, continuous, R&gt;L</td>
<td>3-6 yrs</td>
<td>Patent Ductus Arteriosus (PDA)</td>
</tr>
<tr>
<td>Pulmonary Ejection</td>
<td>Soft, blowing, upper left sternal border (ULSB), SEM</td>
<td>8-14 yrs</td>
<td>Patent Ductus Arteriosus (PDA)</td>
</tr>
<tr>
<td>Supraclavicular Arterial Bruit</td>
<td>Low intensity, above clavies</td>
<td>any age</td>
<td>Patent Ductus Arteriosus (PDA)</td>
</tr>
</tbody>
</table>

Congenital Heart Disease (CHD)

PRENATAL CIRCULATION

Before Birth
- fetal lungs bypassed by flow through fetal shunts:
  - shunting deoxygenated blood
    - ductus arteriosus: connection between pulmonary artery and aorta
  - shunting oxygenated blood
    - foramen ovale: connection between R and L atria
    - ductus venosus: connecting between umbilical vein and IVC
- circulation:
  - placenta (deoxygenated blood) > umbilical vein > ductus venosus > IVC > R atrium > oxygenated blood shunted through foramen ovale > L atrium > L ventricle > aorta > brain/myocardium/upper extremities
  - deoxygenated blood returns via SVC to R atrium > 1/3 of blood entering R atrium does not flow through foramen ovale and flows to the R ventricle > pulmonary arteries > ductus arteriosus > aorta > systemic circulation > placenta for reoxygenation

At Birth
- with first breath, lungs open up and pulmonary resistance decreases allowing pulmonic blood flow
- with separation of low resistance placenta, systemic circulation becomes a high resistance system
- with closure of the fetal shunts and changes in pulmonic/systemic resistance, infant circulation assumes normal adult flow
- increasing pulmonic flow increases left atrial pressures leading to foramen ovale closure
- increased oxygen concentration in blood after first breath leads to decreased prostaglandins leading to closure of the ductus arteriosus
- as the umbilical cord is clamped, the umbilical vein closes, systemic vascular resistance increases and the ductus venosus closes
Embryologic Development
- Most critical period of fetal heart development is between 3-8 weeks gestation
- Single heart tube grows rapidly forcing it to bend back upon itself and begin to assume the shape of a 4 chambered heart
- Insults at this time are most likely to lead to CHD

Epidemiology
- 8/1,000 live births can present with heart murmur, heart failure, or cyanosis
- Ventricular septal defect is the most common lesion

Table 15. Risk Factors for Common CHD

<table>
<thead>
<tr>
<th>INFANT FACTORS/GENETIC CONDITIONS</th>
<th>Abnormality (%)</th>
<th>MATERNAL FACTORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormality</td>
<td>Dominant cardiac defect</td>
<td>Abnormality (%)</td>
</tr>
<tr>
<td>Prematurity</td>
<td>PDA</td>
<td>Pueri child with CHD (2-4% risk)</td>
</tr>
<tr>
<td>CHARGE association</td>
<td>TEF, AVSD, ASD, VSD</td>
<td>Tetralogy of Fallot (35%)</td>
</tr>
<tr>
<td>DiGeorge</td>
<td>Aortic arch anomalies</td>
<td>Diabetes Mellitus (2-3%)</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>ASD, VSD, ATOF</td>
<td>PKU (25-50%)</td>
</tr>
<tr>
<td>Ehlers-Danlos</td>
<td>Mitral prolapse, dilated aortic root</td>
<td>SLE (20-40%)</td>
</tr>
<tr>
<td>Kartagener’s</td>
<td>Dextrocardia</td>
<td>Alcoholic (25-30%)</td>
</tr>
<tr>
<td>Marfan</td>
<td>Mitral prolapse, aortic dissection or insufficiency, dilated aortic root</td>
<td></td>
</tr>
<tr>
<td>Noonan</td>
<td>Pulmonary stenosis, ASD</td>
<td>Medications: Phenytoin</td>
</tr>
<tr>
<td>Osteogenesis Imperfecta</td>
<td>Aortic incompetence</td>
<td>Medications: Valproate</td>
</tr>
<tr>
<td>Turner</td>
<td>Coarctation, bicuspid aortic valve</td>
<td>Medications: Retinoid acid</td>
</tr>
</tbody>
</table>

VSD = Ventricular septal defect; ASD = atrial septal defect; PDA = patent ductus arteriosus; TEF = tetralogy of Fallot; TGA = transposition of great arteries;
PS = pulmonary stenosis; AS = aortic stenosis; HLHS = hypoplastic left heart syndrome; AVSD = atrioventricular septal defect

Investigations
- Echo, ECG, CXR

Cyanotic vs. Acyanotic Congenital Heart Disease
- Cyanosis: Blue mucus membranes, nail beds, and skin secondary to an absolute concentration of deoxygenated hemoglobin of at least 3 g/dL.
- Cyanotic heart disease: (i.e., R > L shunt) blood bypasses the lungs > no oxygenation occurs > high levels of deoxygenated hemoglobin enter the systemic circulation > cyanosis
- Acyanotic heart disease: (i.e., L > R shunt, obstruction occurring beyond lungs) blood passes through pulmonic circulation > oxygenation takes place > low levels of deoxygenated blood in systemic circulation > no cyanosis

Figure 2. Common Congenital Heart Diseases
Acyanotic Congenital Heart Disease

1. LEFT TO RIGHT SHUNT LESIONS
   - extra blood is displaced through a communication from the left to the right side of the heart → increased pulmonary blood flow → increased pulmonary pressures
   - shunt volume dependent upon three factors: size of defect, pressure gradient between chambers or vessels, peripheral outflow resistance
   - untreated shunts can result in pulmonary vascular disease, right ventricular hypertension and hypertrophy (RVH), and eventually R → L shunts

   Atrial Septal Defect (ASD)
   - three types: ostium primum (common in Down syndrome), ostium secundum (most common type, 50-70%), sinus venosus (defect located at entry of superior vena cava into right atrium)
   - epidemiology: 0.6-8% of congenital heart lesions
   - natural history: 80-100% spontaneous closure rate if ASD diameter <8 mm
   - if remains patent, congestive heart failure (CHF) and pulmonary hypertension can develop in adult life
   - history: often asymptomatic in childhood
   - physical exam: grade 2-3/6 pulmonic outflow murmur (SEM), a mid-diastolic rumble at the left lower sternal border, and a widely split and fixed S2
   - investigations
     - ECG: right axis deviation (RAD), mild RVH, right bundle branch block (RBBB)
     - CXR: increased pulmonary vasculature
   - treatment: elective surgical or catheter closure between 2-5 years of age

   Ventricular Septal Defect (VSD)
   - most common congenital heart defect (30-50% of CHD)
     - Small VSD (majority)
       - history: asymptomatic, normal growth and development
       - physical exam: early systolic to holosystolic murmur, best heard at left lower sternal border (LLSB)
       - investigations: ECG and CXR are normal
       - treatment: most close spontaneously
     - Moderate-to-large VSD
       - natural history: secondary pulmonary hypertension, CHF by 2 months of age
       - history: delayed growth and development, decreased exercise tolerance, recurrent URTIs or "asthma" episodes, CHF
       - physical exam: holosystolic murmur at LLSB with thrill, mid-diastolic rumble at apex, size of VSD is inversely related to intensity of murmur
       - investigations:
         - ECG: left ventricular hypertrophy (LVH), left atrial hypertrophy (LAH), RVH
         - CXR: increased pulmonary vasculature, cardiomegaly, CHF
       - treatment: treatment of CHF and surgical closure by 1 year of age

   Patent Ductus Arteriosus (PDA)
   - patent vessel between descending aorta and left pulmonary artery
   - epidemiology
     - functional closure within first 15 hours of life, anatomical closure within first days of life
     - 5-10% of all congenital heart defects
     - delayed closure of ductus is common in premature infants (1/3 of infants <1750 grams);
       this is different from PDA in term infants
     - natural history: spontaneous closure common in premature infants, less common in term infants
     - history: may be asymptomatic or have apneic or bradycardic spells, poor feeding, accessory muscle use
     - physical exam: tachycardia, bounding pulses, hyperactive precordium, wide pulse pressure, continuous “machinery” murmur, best heard at left infraclavicular area
     - investigations
       - ECG: may show LAH, LVH, BVH
       - CXR: normal to mildly enlarged heart, increased pulmonary vasculature, prominent pulmonary artery
       - diagnosis by echocardiography
     - treatment
       - indomethacin (Indocid™) – PGEI antagonist (PGEI maintains ductus arteriosus patency) in premature infants if necessary
       - catheter or surgical closure if PDA is contributing to respiratory compromise, poor growth or persists beyond 3rd month of life
Endocardial Cushion Defect (Atrioventricular [AV] Canal)
- spectrum from endocardial cushion VSD and ostium primum ASD to complete AV canal with common AV valve
- commonly associated with Down syndrome
- treatment
  - natural history depends on size of defect and valvular involvement, and should be repaired by age 6 months to prevent development of pulmonary hypertension
  - complete AV canal requires early complete surgical repair, preferably before 3 months of age

2. OBSTRUCTIVE LESIONS
- present with pallor, decreased urine output, cool extremities and poor pulses, shock or sudden collapse

Coarctation of the Aorta
- narrowing of aorta almost always at the level of the ductus arteriosus
- commonly associated with bicuspid aortic valve (50%); Turner syndrome (35%)
- few have high BP in infancy (160-200 mmHg systolic) but this decreases as collaterals develop
- if severe, presents with shock in the neonatal period when the ductus closes
- history: often asymptomatic
- physical exam: upper extremity systolic pressures of 140-145 mmHg, decreased blood pressure and weak/absent pulses in lower extremities, radial-femoral delay, absent or systolic murmur with late peak at apex, left axilla, and left back
- investigations: ECG-RVH early in infancy, LVH later in childhood
- prognosis and treatment
  - if associated with other lesions (e.g. PDA, VSD) can cause CHF
  - complications: hypertension
  - management: give prostaglandins to keep ductus arteriosus patent for stabilization, balloon arterioplasty or surgical correction in symptomatic neonate

Aortic Stenosis
- valvular (75%), subvalvular (20%), supravalvular and idiopathic hypertrophic subaortic stenosis (IHSS) (5%) 
- history: often asymptomatic but may be associated with CHF, exertional chest pain, syncope or sudden death
- physical exam: SEM at upper right sternal border (URSB) with aortic ejection click at the apex
- treatment
  - surgical repair if infant with critical aortic stenosis or older child with symptoms or peak gradient >50 mmHg
  - exercise restriction required

Pulmonary Stenosis
- valvular (90%), subvalvular, or supravalvular
- usually part of other congenital heart lesions (e.g. Tetralogy of Fallot) or in association with other syndromes (e.g. congenital rubella, Noonan syndrome)
- critical pulmonic stenosis: inadequate pulmonary blood flow, dependent on ductus for oxygenation, progressive hypoxia and cyanosis
- history: spectrum from asymptomatic to CHF
- physical exam: wide split S2 on expiration, SEM at ULSB, pulmonary ejection click
- investigations
  - ECG: RVH
  - CXR: dilated post-stenotic pulmonary artery
- treatment: surgical repair if critically ill or severe PS, or if presence of symptoms in older infants/children

Cyanotic Congenital Heart Disease
- systemic venous return re-enters systemic circulation directly
- most prominent feature is cyanosis (O2 sat <75%)
- differentiate between cardiac and other causes of cyanosis with hyperoxic test
  - obtain preductal, right radial ABG in room air; repeat ABG after the child inspires 100% oxygen
  - if PaO2 improves to greater than 150 mmHg, cyanosis less likely cardiac in origin
- survival depends on mixing via shunts (e.g. ASD, VSD, PDA)
- should not use O2 for these lesions
1. RIGHT TO LEFT SHUNT LESIONS

Tetralogy of Fallot
- 10% of all CHD, most common cyanotic heart defect diagnosed beyond infancy
- embryologically, a single defect with hypoplasia of the conus causing:
  - VSD
  - right ventricle (RV) outflow tract obstruction (RVOTO)
  - overriding aorta
  - RVH
- degree of RVOTO directly determines the direction and degree of shunt and therefore the extent of clinical cyanosis and degree of RVH
- infants may initially have a L → R shunt and therefore are not cyanotic but the RVOTO is progressive, resulting in increasing R → L shunting with hypoxemia and cyanosis
- history: hypoxic “tet” spells
  - primary pathophysiology is hypoxia, leading to increased pulmonary vascular resistance (PVR) and decreased systemic resistance, occurring in exertional states (e.g., crying, exercise)
  - paroxysm of rapid and deep breathing, irritability and crying
  - hyperpnea, increasing cyanosis often leading to deep sleep and decreased intensity of murmur (decreased flow across RVOTO)
  - peak incidence at 2-4 months of age
- if severe may lead to seizures, loss of consciousness, death (rare)
- management: O₂, knee-chest position, fluid bolus, morphine sulfate, propranolol
- physical exam: single loud S2 due to severe pulmonary stenosis (i.e. RVOTO)
- investigations
  - ECG: RAD, RVH
  - CXR: boot shaped heart (small PA, RVH), decreased pulmonary vasculature, right aortic arch (in 20%)
- treatment: surgical repair within first two years of life, or earlier if marked cyanosis, “tet” spells, or severe RV outflow tract obstruction

Ebstein’s Anomaly
- congenital defect of the tricuspid valve in which the septal and posterior leaflets are malformed and displaced into the RV leading to variable degrees of RV dysfunction, TS, TR or functional pulmonary atresia if RV unable to open pulmonic valves
- RA massively enlarged, interatrial communication (PFO) often allows R → L shunting
- TR and accessory conduction pathways (WPW) are often present – often associated with arrhythmia
- cause: unknown, associated with maternal lithium and benzodiazepine use in 1st trimester
- treatment
  - in newborns, consider closure of tricuspid valve + aortopulmonary shunt, or transplantation
  - in older children, tricuspid valve repair or valve replacement + ASD closure

2. OTHER CYANOTIC CONGENITAL HEART DISEASES

Transposition of the Great Arteries (TGA)
- 3-5% of all congenital cardiac lesions, most common cyanotic CHD in neonate
- parallel pulmonary and systemic circulations
  - systemic: body → RA → RV → aorta → body
  - pulmonary: lungs → LA → LV → pulmonary artery → lungs
- physical exam
  - no murmur if no VSD
  - newborn presents with progressive cyanosis unresponsive to oxygen therapy as the ductus arteriosus closes and mixing between the two circulations diminishes; severe hypoxemia, acidosis, and death can occur rapidly
  - if VSD present, cyanosis is not prominent and infant presents with CHF after a few weeks of life
- investigations
  - ECG: RAD, RVH
  - CXR: egg-shaped heart with narrow mediastinum (“egg on a string”)
- treatment
  - prostaglandin El (Prostin VR™) infusion to keep ductus open until septostomy or surgery (arterial switch procedure)
  - infants without VSD must be repaired within 2 weeks to avoid weak LV muscle

Hyoplastic Left Heart Syndrome
- 1-3% of all congenital cardiac lesions
- a spectrum of hypoplasia of left ventricle, atretic mitral and/or aortic valves, small ascending aorta, coarctation of the aorta with resultant systemic hypoperfusion
- most common cause of death from congenital heart disease in first month of life
- systemic circulation is dependent on ductus patency; upon closure of the ductus, infant presents with circulatory shock and metabolic acidosis
- treatment
  - intubate and correct metabolic acidosis
  - IV infusion of PGE1 to keep ductus open
  - surgical correction (overall survival 50% to late childhood) or heart transplant

Total Anomalous Pulmonary Venous Connection
- only 1-2% of CHD
- characterized by all of the pulmonary veins draining into the right-sided circulation (supracardiac - SVC or innominate vein, infracardiac - hepatic portal vein or IVC, intracardiac - coronary sinus or RA)
- no direct oxygenated pulmonary venous return to left atrium
- often associated with obstruction at connection sites
- an ASD must be present to allow blood to shunt into the LA and systemic circulation
- treatment: surgical repair if severe cyanosis or CHF related to pulmonary venous obstruction

Truncus Arteriosus
- a single great vessel arising from the heart which gives rise to the aorta, PA, and coronary arteries
- the truncal valve overlies a large VSD
- treatment: surgical repair within first 6 months of life to prevent development of pulmonary vascular disease

Congestive Heart Failure (CHF)
- see Cardiology

Etiology
- congenital heart disease (CHD)
- arteriovenous malformations (AVMs)
- cardiomyopathy
- arrhythmias
- acute hypertension
- anemia
- cor pulmonale
- myocarditis

Symptoms
- infant: feeding difficulties, easy fatiguability, exertional dyspnea, diaphoresis when sleeping or eating, respiratory distress, lethargy, cyanosis, FTT
- child: decreased exercise tolerance, fatigue, decreased appetite, failure to thrive, respiratory distress, frequent URTIs or "asthma" episodes
- orthopnea, paroxysmal nocturnal dyspnea, pedal/dependant edema are all uncommon in children

Physical Findings
- four key features: tachycardia, tachypnea, cardiomegaly, hepatomegaly
- failure to thrive (FTT)
- respiratory distress, gallop rhythm, wheezing, crackles, cyanosis, clubbing (with CHD)
- alterations in peripheral pulses, four limb blood pressures (in some CHDs)
- dysmorphic features associated with congenital syndromes
- CRV - cardiomegaly, pulmonary venous congestion

Management
- correction of underlying cause
- general: sitting up, O₂, sodium and water restriction, increased caloric intake
- pharmacologic: diuretics, digoxin, afterload reducers

Infected Endocarditis
- see Infectious Diseases
- 70% Streptococcus, 20% Staphylococcus (S. aureus, S. epidermidis)
- serial positive cultures are needed for definitive diagnosis, but rely on clinical suspicion and other investigations if initially negative (i.e. use Echo to look for vegetations)
- 10-15% of cases culture negative, this is a risk factor for poor prognosis
- Osler’s nodes, Janeway’s lesions, splinter hemorrhages are late findings in children
- antibiotic prophylaxis is necessary for all patients with:
  - cyanotic congenital heart disease (including Tetralogy of Fallot, TGA, Ebstein’s anomaly, total anomalous pulmonary venous return)
  - rheumatic valve lesions (except if no valve dysfunction)
  - prothetic heart valves
  - palliative shunts and conduits
- previous endocarditis
- pacemaker leads
- SBE prophylaxis: amoxicillin 50 mg/kg, 30 to 60 minutes before procedure. If allergic to penicillin, then use clindamycin 20 mg/kg
- high risk patients for GI/GU procedures may receive 2 doses amp + gent IV (30 min before procedure and 6 hours later)

### Dysrhythmias

- see Cardiology
- can be transient or permanent, congenital (structurally normal or abnormal) or acquired (toxin, infection, infarction)

#### Sinus Arrhythmia
- phasic variations with respiration
- present in almost all normal children

#### Premature Atrial Contractions (PACs)
- may be normal variant or can be caused by electrolyte disturbances, hyperthyroidism, cardiac surgery, digitalis toxicity

#### Premature Ventricular Contractions (PVCs)
- common in adolescents
- benign if single, uniform, disappear with exercise, and no associated structural lesions
- if not benign, may degenerate into more severe dysrhythmias

#### Supraventricular Tachycardia (SVT)
- most frequent sustained dysrhythmia in children
- not life-threatening but can lead to symptoms
- caused by re-entry via accessory connection (atrioventricular (AV) node) most common site
- characterized by a rate of greater than 210 bpm
- treatment
  - stable (alert, normal BP)
    - vagal manoeuvres
    - adenosine
    - synchronized cardioversion
  - unstable (decreased LOC, decreased BP)
    - immediate synchronized cardioversion

#### Complete Heart Block
- congenital heart block can be caused by maternal Rh or La antibody (e.g. in mothers with lupus)
- often diagnosed in utero – may lead to development of fetal hydrops
- clinical symptoms related to level of block (the lower the block, the greater the symptoms of inadequate cardiac output)
- symptomatic patients need a pacemaker

### Development

#### Developmental Delay
- developmental delay is defined as performance significantly below average in a given area

#### Epidemiology
- 5-10% of children have neurodevelopmental delay
- may have isolated delays in specific areas (motor, speech/language), or global delays

#### Etiology
- genetic/chromosomal disorders (trisomy 21, Fragile X)
- intrapartum asphyxia
- CNS abnormalities (meningitis/encephalitis, TORCH infections, structural)
- metabolic disorders (inborn errors of metabolism, hypothyroidism)
- environmental (psychosocial neglect, lead exposure, antenatal drug or alcohol exposure)
**Approach**
- detailed history
  - intrauterine exposures, perinatal events
  - family history, consanguinity
  - detailed developmental milestones-rate of acquisition, regression of skills
  - associated problems (feeding, seizures, behaviour, sleep)
  - social history
- physical examination
  - dysmorphology, hepatosplenomegaly, neurocutaneous markers, growth parameters, detailed neurological examination
- ancillary testing
  - neurodevelopmental assessment, hearing test, psychosocial evaluation, occupational therapy and/or physiotherapy assessments, genetics consultation
- laboratory testing
  - target testing based on history and physical exam
  - chromosomes, FISH, neuroimaging, metabolic testing, neuroelectrophysiologic testing

**Intellectual Disability**

**Epidemiology**
- 1% of general population; M:F = 1.5:1
- higher rates of sensory deficits, motor impairment, behavioural/emotional disorders, seizures, psychiatric illness

**Etiology**
- genetic: Down syndrome, Fragile X, PKU, other chromosomal disorders, developmental brain abnormality, inborn errors of metabolism
- prenatal: rubella, fetal alcohol syndrome, prenatal exposure to heroin, cocaine, TORCH infections, HIV, maternal DM, toxemia, maternal malnutrition, birth trauma/hypoxia
- perinatal: prematurity, low birth weight, cerebral ischemia, intracranial hemorrhage, maternal deprivation
- childhood: intracranial infection, head trauma, FTT, lead poisoning
- psychosocial factors: mild MR associated with low socioeconomic status (SES), limited parental education, parental neglect, teen pregnancy, family instability

**Diagnosis**
- below average general intellectual functioning as defined by an IQ of approximately 70 or below (2 standard deviations below the mean) AND
- deficits in adaptive functioning in at least two of:
  - communication, self-care, home-living, social skills, self-direction, academic skills
  - work, leisure, health, safety
- onset before 18 years of age

**Table 16. Classification of Intellectual Disability**

<table>
<thead>
<tr>
<th>Severity</th>
<th>% Cases</th>
<th>IQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>85%</td>
<td>50-70</td>
</tr>
<tr>
<td>Moderate</td>
<td>10%</td>
<td>35-49</td>
</tr>
<tr>
<td>Severe</td>
<td>3-4%</td>
<td>20-34</td>
</tr>
<tr>
<td>Profound</td>
<td>1-2%</td>
<td>&lt;20</td>
</tr>
</tbody>
</table>

**Treatment**
- main objective: enhance adaptive functioning level
- therapy
  - emphasize community-based treatment vs. institutionalization and early intervention
  - individual/family therapy, behaviour modification (to decrease aggressive/disturbing behaviours), multidisciplinary rehabilitation, medications for associated conditions
- education: life skills, vocational training, communication skills, family education
- psychosocial support of parents and respite care
Language Delay

Differential Diagnosis
- hearing impairment
  - spectrum of impairment – slight to profound loss
  - language development may seem normal for up to 6 months (including cooing and babbling) but may regress due to lack of feedback
  - risk factors for sensorineural hearing loss (>1 risk factor warrants infant screening, if newborn screening not available in jurisdiction for all newborns):
    - genetic syndromes / family history
    - congenital (TORCH) infections
    - craniofacial abnormalities
    - <1,500 g birthweight
    - hyperbilirubinemia/kernicterus
    - asphyxia / low Apgar scores
    - bacterial meningitis, viral encephalitis
- to evaluate hearing loss in children:
  - <6 months old: auditory brainstem response (ABR); tympanometry (impedance testing), evoked potentials
  - >6-8 months old: behaviour audiometry
  - >3-4 years old: pure tone audiometry
- cognitive disability
  - global developmental delay, mental retardation
  - both receptive and expressive language components affected
  - child often has interest in communication
- pervasive developmental disorder (PDD), including autism
  - poor social interaction and language impairment, stereotypical behaviours
- selective mutism
  - a childhood anxiety disorder with onset age 5-6
  - only speaks in certain situations, usually at home
  - healthy children with no hearing impairment
  - often above-average intelligence
- Landau-Kleffner syndrome (acquired epileptic aphasia)
  - presents in late preschool to early school age years, may be similar to autism
  - child begins to develop language normally, then sudden regression of language
  - child has severe aphasia with EEG changes, often has overt seizure activity
- mechanical problems
  - cleft palate
  - cranial nerve palsy
  - social deprivation

Management
- ENT and dental referral if mechanical cause
- speech therapy in disorders of fluency, receptive or expressive language
- psychiatric consultation in selective mutism, PDD

Learning Disorders

Definition
- a specific and persistent failure to acquire academic skills despite conventional instruction, adequate intelligence, and sociocultural opportunity
- a significant discrepancy between a child’s intellectual ability and his or her academic performance

Epidemiology
- prevalence: 2-10%
- psychiatric comorbidity = 10-25% of individuals with dysthymia, conduct disorder (CD), major depressive disorder (MDD), oppositional defiant disorder (ODD), attention deficit hyperactivity disorder (ADHD)

Diagnosis
- categorized by
  - individual scores on achievement tests in reading, mathematics or written expression (WISC III, WRAT) significantly below (>2 SD) that expected for age, education, and IQ
  - interferes with academic achievement or ADLs that require reading, mathematics, or writing skills
- types: reading, mathematics, disorders of written expression
- rule out occult seizure disorder, sensory impairments

Complications
- low self-esteem, poor social skills
- 40% school drop-out rate
Fetal Alcohol Spectrum Disorder (FASD)

- this disorder refers to the full range of problems resulting from the use of alcohol during pregnancy, including Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE)

Fetal Alcohol Syndrome
- prevalence of FAS: 1 in 300
- not known how much alcohol is harmful during pregnancy
- criteria for Diagnosis of Fetal Alcohol Syndrome
  a) growth deficiency – low birth weight and/or length at birth that continues through childhood
  b) abnormal craniofacial features – small head, short palpebral fissures, long smooth philtrum, thin upper lip
  c) central nervous system dysfunction – microcephaly and/or neurobehavioural dysfunction (e.g. hyperactivity, fine motor problems, attention deficits, learning disabilities, cognitive disabilities)
  d) strong evidence of maternal drinking during pregnancy
- cardiac and renal defects, hypospadias may occur
- FASD is one of the most common causes of mental retardation in the world

Fetal Alcohol Spectrum Disorder
- prevalence of FASD: 1 in 200
- child born to a mother who was known to be drinking heavily during pregnancy
- child has some but not all of physical characteristics of FAS; often missed diagnosis as features are subtle
- most children with FASD have normal stature and do not have microcephaly, however, they may show milder forms of the facial features present in FAS
- if present, short stature and microcephaly will persist through adolescence, while facial features will become more subtle with age

Endocrinology

Diabetes Mellitus (DM)

- see Endocrinology

TYPE 1 DIABETES (Insulin-Dependent DM)

Epidemiology
- insulin dependent, most common type in childhood
- prevalence: 1 in 400-500 children under 18 years of age
- can present at any age, bimodal peaks 5-7 years and puberty
- classic presentation: polyuria, polydipsia, abdominal pain, weight loss, and fatigue
- 25% present with diabetic ketoacidosis (DKA)

Etiology
- genetic predisposition and environmental trigger
  - autoimmune destruction of beta-cells of the pancreas (antibodies directed towards glutamic acid decarboxylase have been identified)
  - a non-immune variation has been described
  - diseases of pancreas (i.e. cystic fibrosis) and long term corticosteroids

Management of Uncomplicated Diabetes
- meal plan, exercise, education, psychosocial support
- insulin injections 2-3 times per day, blood glucose monitoring
- young children more susceptible to CNS damage with hypoglycemia with fewer benefits from tight control, hence target glucose range higher at 6-12 mmol/L (110-220 mg/dL)
- increasingly tighter control in older children, 4-8 mmol/L (70-140 mg/dL)
- continuous subcutaneous insulin infusion (CSII) pump
  - contains a cartridge full of short-acting insulin (LisproTM) or a syringe connected to a catheter that is inserted into the subcutaneous tissue
  - continuously delivers predetermined basal rates to meet nonprandial insulin requirements
  - bolus infusion to cover mealtime or snack time insulin requirements
  - requires as much or more blood glucose monitoring when compared to injections ± ketone monitoring - patients must be highly motivated
  - allows for tighter glycemic control
  - risk of DKA with operator or mechanical failure (catheter occlusion, battery failure, depleted insulin)

Diagnostic Criteria for Diabetes Mellitus
Symptoms (polyuria, polydipsia, weight loss) + random glucose ≥ 11.1 mmol/L (200 mg/dL)
OR
Fasting glucose ≥ 7.0 mmol/L
(126 mg/dL)
OR
2hr glucose during OGTT ≥ 11.1 mmol/L
(200 mg/dL)
OGTT = oral glucose tolerance test

If a child presents with polyuria and polydipsia, dip urine for glucose and ketones.
Complications of Type 1 Diabetes

- hypoglycemia
  - cause: missed/delayed meals, excess insulin, increased exercise, illness
  - complications: seizures, coma
  - must have glucagon kit for quick injections
  - infants may not show classic catecholaminergic signs with hypoglycemia
- hyperglycemia
  - cause: infection, stress, diet-to-insulin mismatch, eating disorder
  - complications: risk of DKA, long-term end-organ damage
- DKA
  - cause: new-onset diabetes, missed insulin doses, infection
  - medical emergency: most common cause of death in children with diabetes
    (attributed to cerebral edema)
- long-term complications (retinopathy, nephropathy, neuropathy)
  - usually not seen in childhood (often begins 5 years after presentation or 3-5 years after puberty)
- metabolic syndrome
- other auto-immune conditions (e.g., celiac disease, hypothyroidism)

**Blood Glucose Targets by Age**

<table>
<thead>
<tr>
<th>Age range</th>
<th>Pre-meal glucose target</th>
<th>HbA1C target</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>5.6-10.0 (100-180)</td>
<td>7.5-8.5%</td>
</tr>
<tr>
<td>6-12</td>
<td>5.0-10.0 (90-180)</td>
<td>&lt;8%</td>
</tr>
<tr>
<td>&gt;12</td>
<td>5.0-7.2 (90-130)</td>
<td>&lt;7.5%</td>
</tr>
</tbody>
</table>

**Diabetes Insipidus (DI)**

- DI is the inability of the kidneys to concentrate urine
- central:
  - due to decreased ADH production from the brain (genetic, due to trauma, surgery, radiation, neoplasm, meningitis)
  - presents with polyuria, polydipsia, enuresis
- nephrogenic:
  - renal unresponsiveness to ADH (genetic, drug-induced)
  - X-linked recessive condition that affects males in early infancy
  - polyuria, FTT, hyperpyrexia, vomiting, hypernatremic dehydration

**Diagnosis**

- symptoms: polyuria, enuresis, nocturia, polydipsia, dehydration
- labs: dilute urine (SG <1.010), hypernatremia, elevated serum osmolality, low urine osmolality
- water deprivation test; central cause if >50% change in urine osmolality after ADH administration

**Management**

- central: DDAVP intranasally, SC, or PO
- nephrogenic: low-solute diet, thiazide diuretics

**Syndrome of Inappropriate Antidiuretic Hormone (SIADH)**

- etiology: intracranial, malignancy, pulmonary disease, psychiatric disease, drugs
- common in hospitalized patients (associated with post-op pain and nausea)
- symptoms: asymptomatic, oliguria, volume expansion, or hyponatremic symptoms
  (nausea, vomiting, H/A, seizure, coma)
- labs: hyponatremia, urine Osm > plasma Osm, urine Na >20mmol/L
- management: fluid restriction, 3% NaCl for symptomatic hyponatremia

**Hypercalcemia/Hypocalcemia/Rickets**

- see Endocrinology, E38
**Hypothyroidism**

- see Endocrinology.

**Congenital Hypothyroidism**
- incidence: 1 in 4000 births; F:M = 2:1
- usually caused by malformation of the thyroid gland (agenesis or ectopic) also maternal factors – iodine deficiency, prenatal exposure to antithyroid medications or radioiodine
- diagnosis through newborn screening of TSH or T4
- usually asymptomatic in neonatal period because maternal T4 crosses the placenta but may have the following symptoms:
  - prolonged jaundice
  - constipation
  - sluggish, hoarse cry, lethargy, poor feeding
  - macroglossia, coarse facial features, large fontanelles, umbilical hernia
- prognosis
  - excellent if treatment started within 1-2 months of birth
  - if treatment started after 3-6 months of age may result in permanent developmental delay and/or mental retardation (mild to profound)
- management: thyroxine replacement

**Acquired Hypothyroidism**
- most commonly Hashimoto’s thyroiditis (autoimmune destruction of the thyroid)
- signs and symptoms similar to hypothyroidism in adults, but also:
  - delayed bone age, decline in growth velocity, short stature, goiter
  - sexual pseudoprecocity: early sexual development with short stature and delayed bone age
  - does not cause permanent developmental delay
- treated with L-thyroxine 10 μg/kg/day

**Hyperthyroidism**

- see Endocrinology.

**Congenital Hyperthyroidism**
- results from transplacental passage of maternal thyroid stimulating antibodies (mother with Graves’ disease)
- clinical manifestations in the neonate may be masked by transplacental maternal antithyroid medication
- presentation: tachycardia with congestive heart failure, irritability, craniosynostosis, poor feeding, failure to thrive, heart murmur, goitre
- spontaneous resolution by 2-3 months of life as antibodies cleared
- management: propylthiouracil until antibodies cleared, symptomatic treatment

**Graves’ Disease**
- peak incidence in adolescence; F:M = 5:1
- may exhibit classic signs and symptoms of hyperthyroidism, but also personality changes, school difficulty, mood instability
- management similar to adults: anti-thyroid drugs (propylthiouracil, methimazole), radiiodine reserved for older teens, surgical thyroidectomy
- children with a solitary thyroid nodule require prompt evaluation as 30-40% have carcinoma; the remainder have an adenoma, abscess, cyst, or multinodular goiter

**Juvenile Graves’ Disease**
- gradual onset over 6-12 months of diffuse goiter, ophthalmopathy, dermopathy
- increased appetite, weight loss or maintenance, fatigue, myopathy, sweating, menstrual irregularities
- treatment is propylthiouracil and propranolol
- thyroidectomy is sometimes performed

**Ambiguous Genitalia**

**Etiology**
- male pseudohermaphrodite (XY)
- inborn error of testosterone biosynthesis or Leydig cell hypoplasia
- 5-alpha-reductase deficiency, androgen receptor deficiency or insensitivity
- luteinizing hormone (LH)/HCG unresponsiveness
- small phallus, hypospadias, undescended testicles

Thyroid neoplasms that develop in childhood have a higher rate of malignancy; be suspicious of rapid and painless enlargement of the thyroid gland.
The electrolytes; medical of emergency dehydration replace child order fluids hypoglycemia, lifelong and of CAH and can is at 2-4 of of fluids 11-Hydroxylase

Clinical Presentation
- depends on the degree and the specific deficiency
- infants may present with FTT, shock, salt-wasting (adrenal crisis due to lack of aldosterone), hyperpigmentation (genital, areola), clitoral hypertrophy, fused labia
- hypertension is rare (usually seen in the 11-hydroxylase variant)
- adult onset (11-hydroxylase variant) more insidious, may present as hirsutism
- female: ambiguous genitalia to complete virilization, amenorrhea
- male: precocious puberty, with early adrenarche, dehydration
- accelerated linear bone growth in early years, but premature epiphyseal closure due to high testosterone, resulting in decreased adult height
- possible Addisonian picture (adrenal insufficiency) if adrenal output of cortisol severely compromised

Congenital Adrenal Hyperplasia (CAH)
- occurs in 1/15000 live births and is the most common cause of ambiguous genitalia
- autosomal recessive condition causing partial or total enzyme defect
- 21-hydroxylase deficiency causes 95% of CAH cases; this causes decreased cortisol and aldosterone with shunting toward overproduction of androgens
- cortisol deficiency leads to elevated ACTH, which causes adrenal hyperplasia
- clinical presentation depends on the specific deficiency and the cause – may present with shock, hyperkalemia if not suspected
- high ACTH, increased 17-OH progesterone, increased testosterone, DHEAS, urinary 17-ketosteroids, advanced bone age

Late-Onset 21-Hydroxylase Deficiency
- allelic variant of classic 21-hydroxylase deficiency – mild enzymatic defect
- girls present with amenorrhea
- boys present with precocious puberty with early adrenarche, dehydration
- accelerated linear growth in early puberty but early fusion of epiphyses leading to decreased adult height
- diagnosis
  - increased plasma 17-OH-progesterone after ACTH stimulation test
  - treatment
    - dexamethasone, spironolactone (anti-androgen)
    - mineralocorticoid replacement is not needed

Salt-Wasting 21-Hydroxylase Deficiency CAH (2/3 of cases)
- infants present with shock, FTT, low Na, high K, low Cl, low glucose, high ACTH
- adrenal insufficiency
- hyperpigmentation of genitals and areola

Simple Virilizing 21-Hydroxylase Deficiency
- virilization in girls

11-Hydroxylase Deficiency
- sexual ambiguity in females
- may have insidious onset; may present with hirsutism, occasionally hypertension

17-Hydroxylase Deficiency
- sexual ambiguity in males
Investigations
- low Na, high K, low cortisol, high ACTH if both glucocorticoid and mineralocorticoid deficiency
- increased serum 17-OH-progesterone (substrate for 21-hydroxylase)
- increased testosterone, DHEAS, urinary 17-ketosteroids
- advanced bone age

Treatment
- glucocorticoid replacement to lower ACTH
- in salt-wasting type mineralocorticoids given as well
- spironolactone is used in late-onset 21-hydroxylase deficiency as anti-androgen
- surgery to correct ambiguous genitalia

Table 17. Clinical Features of CAH Based on Enzyme Defect

<table>
<thead>
<tr>
<th>Enzyme Defect</th>
<th>Sexual Ambiguity</th>
<th>Postnatal Virilization</th>
<th>Salt Wasting</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-hydroxylase</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>salt-wasting</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>simple virilizing</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>late onset</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>11-hydroxylase</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>17-hydroxylase</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Precocious Puberty
- secondary sexual development <5 years in girls, <9 years in boys
  - incidence: 1 in 10,000
  - more common in females; more worrisome in males (higher incidence of pathology)
- indications for medical intervention to delay progression of puberty are male sex, age <6, bone age advancing more quickly than height age, and psychological issues
- GnRH agonists such as leuprolide are most effective at delaying central precocious puberty
- medications used in peripheral precocious puberty include ketoconazole (to block steroid production), 5-a reductase blockers (finasteride), steroid receptor blockers (spironolactone), aromatase blockers (testolactone, anastrozole)

True (Central) Precocious Puberty
- hypergonadotropic hypergonadism, hormone levels as in normal puberty
- premature activation of the hypothalamic-pituitary-gonadal axis
- much more common in females than males – 9:1
- differential diagnosis
  - idiopathic or constitutional (most common, especially females)
  - CNS disturbances: tumours, hamartomas, post-meningitis, increased ICP, radiotherapy
  - neurofibromatosis (NF), primary severe hypothyroidism

Pseudo (Peripheral) Precocious Puberty
- hypogonadotropic precocious puberty
- differential diagnosis
  - adrenal disorders: CAH, adrenal neoplasm
  - testicular/ovarian tumour
  - gonadotropin secreting tumour: hepatoblastoma, intracranial teratoma, germinoma
  - exogenous steroid administration
  - McCune-Albright syndrome: endocrine dysfunction resulting in precocious puberty, café-au-lait spots, and fibrous dysplasia of skeletal system

Investigations
- history: symptoms of puberty, family history of puberty onset, medical illness
- physical exam: growth velocity, Tanner staging, neurological exam
- estradiol, testosterone, LH, FSH, TSH, GnRH test
- bone age (often advanced)
- consider CT or MRI of head, U/S of adrenals, pelvis

Treatment
- GnRH analogs, GnRH agonist (Lupron™) – negative feedback to downregulate GnRH receptors
- medroxyprogesterone – slows breast and genital development
- treat underlying cause

Heterosexual Precocious Puberty
- development of secondary sexual characteristics opposite to genotypic sex
  - e.g. virilizing tumour (ovarian, adrenal), CAH, exogenous androgen exposure

A child with proven central precocious puberty should receive an MRI of the brain.
Delayed Puberty

- see Gynecology.
- absence of pubertal development by age 13 in girls and age 14 in boys
- more common in males, more suggestive of pathology in females

Central Causes
- delay in activation of hypothalamic-pituitary-gonadal axis
- hypogonadotrophic hypogonadism
- differential diagnosis
  - constitutional (bone age delayed) – most common (>90%)

Peripheral Causes
- hypergonadotrophic hypogonadism (e.g. primary gonadal failure)
- differential diagnosis
  - genetic (e.g. Turner syndrome, Klinefelter syndrome)
  - gonadal damage – infection, radiation, trauma
  - gonadal dysgenesis
  - hormonal defect – androgen insensitivity, 5-alpha-reductase deficiency

Investigations
- history: weight loss, short stature, family history of puberty onset, medical illness
- physical exam: growth velocity (minimum 4 cm/year), Tanner staging, neurological exam, complete physical exam
- hormone levels: estradiol, testosterone, LH, FSH, TSH, GnRH, test bone age
- consider CT or MRI of head, ultrasound of adrenals, pelvis
- karyotype in girls <3rd percentile in height (rule out Turner syndrome)

Management
- identify and treat underlying cause
- hormonal replacement: cyclic estradiol and progesterone for females, testosterone for males

Short Stature

Table 18. Short Stature

<table>
<thead>
<tr>
<th>NORMAL GROWTH VELOCITY (non-pathological short stature)</th>
<th>DECREASED GROWTH VELOCITY (pathological short stature)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional Growth Delay</td>
<td>Primordial (height, weight, and HC are affected)</td>
</tr>
<tr>
<td>- Delayed puberty</td>
<td>- Chromosomal (e.g. Turner, Down syndrome, dysmorphic features)</td>
</tr>
<tr>
<td>- May have family history of delayed puberty</td>
<td>- Skeletal dysplasia (e.g. achondroplasia, diastrophic dysplasia)</td>
</tr>
<tr>
<td>- May require short-term therapy with androgens/estrogens</td>
<td>- Intrauterine growth restriction (IUGR) (teratogen, placental insufficiency, infection)</td>
</tr>
<tr>
<td>- Delayed bone age</td>
<td>Endocrine (height affected more than weight) – “short and fat”</td>
</tr>
<tr>
<td>- Often mid-parental height is normal</td>
<td>- GH deficiency (slow growth velocity, decreased bone age, delayed puberty)</td>
</tr>
<tr>
<td>Familial</td>
<td>- Hypothyroidism</td>
</tr>
<tr>
<td>- Normal bone age</td>
<td>- Hypercortisolism (Cushing syndrome) (exogenous and endogenous)</td>
</tr>
<tr>
<td>- Treatment not indicated</td>
<td>- Hypopituitarism</td>
</tr>
<tr>
<td>- Family Hx of short stature</td>
<td>Chronic disease (weight affected more than height) – “short and skinny”</td>
</tr>
<tr>
<td></td>
<td>- Cyanotic congestive heart disease</td>
</tr>
<tr>
<td></td>
<td>- Celiac disease, inflammatory bowel disease, cystic fibrosis</td>
</tr>
<tr>
<td></td>
<td>- Chronic infections</td>
</tr>
<tr>
<td></td>
<td>- Chronic renal failure (often height more affected)</td>
</tr>
<tr>
<td></td>
<td>Psychosocial neglect (psychosocial dwarfism)</td>
</tr>
<tr>
<td></td>
<td>- Usually decreased height and weight (decreased head circumference if severe)</td>
</tr>
</tbody>
</table>

- special growth charts available for Turner syndrome, achondroplasia, Down syndrome (DS); these children grow along percentiles specific to their condition and growth velocity is normal
- children are usually in a percentile between their parents’ height
- decreased growth velocity may be more worrisome than actual height

Assessment of Short Stature
- height <3rd percentile; height crosses 2 major percentile lines, low growth velocity (<25th percentile)
- history: perinatal history, growth pattern, medical history, parental height and age of pubertal growth spurt
- physical exam: growth velocity (over 6 month period), sexual development
- growth hormone (GH) deficiency accounts for a small minority of children with short stature
Investigations
- bone age (anteroposterior x-ray of left hand and wrist)
- karyotype in girls to rule out Turner syndrome or if dysmorphic features present
- other tests as indicated by history and physical exam

Management
- depends on severity of problem as perceived by parents/child
- no treatment for non-pathological short stature
- GH therapy if requirements met (see Growth Hormone Deficiency)

Growth Hormone (GH) Deficiency
- GH important for chondrocyte proliferation and IGF-1 release
- GH has little effect on fetal growth (maternal IGF-1, uterine factors more important)
- IGF-1 acts at long bones, liver, negative feedback

Etiology
- congenital GH deficiency
  - idiopathic
  - embryologic CNS malformation: associated midface anomalies, neurologic defects, micropenis in males and hypoglycemia
  - perinatal asphyxia
  - rare mutations
- acquired GH deficiency
  - tumours (e.g. craniopharyngioma), trauma, cranial infection, irradiation, post-surgical

Clinical Presentation
- infantile features and fat distribution (short and chubby), delayed puberty, hypoglycemia, high-pitched voice

Investigations
- Testing for GH Deficiency (Stimulation Testing) only performed when:
  - height <3rd percentile
  - decreased growth velocity
  - midline craniofacial anomalies
  - episodes of hypoglycemia
  - delayed bone age, puberty
- physiologic increase in GH with: arginine, clonidine, insulin, dopamine, or propranolol
- positive test if failure to raise GH >8-10 ng/mL post-stimulation

Treatment
- GH Therapy if the following criteria are met:
  - GH shown to be deficient by 2 different stimulation tests
    - patient is short, insufficient growth velocity, <3rd percentile
    - bone age x-rays show unfused epiphyses
    - Turner syndrome, Noonan syndrome, chronic renal failure

Tall Stature
- constitutional tall stature is advanced height and bone age during childhood but not necessarily associated with tall adult height (obesity can contribute to this by causing bone age to advance more rapidly)

Etiology
- constitutional/familial: most common, advanced bone age/physical development in childhood but normal once adulthood reached
- endocrine: hypophysial (pituitary) gigantism, precocious puberty, thyrotoxicosis, Wiedemann-Bücklers syndrome
- genetic: Marfan, Turner, Williams syndromes, Noonan syndrome, homocystinuria

Investigations
- history and physical examination: differentiate familial from other causes
- calculate mid-parental height (predicted adult height)
- look for associated abnormalities (e.g. hyperextensible joints, long fingers in Marfan syndrome)

Treatment
- depends on etiology
- treatment only required in pituitary gigantism
- estrogen used in females to cause epiphyseal fusion (rarely indicated)
**Vomiting**

- investigations (based on history and physical exam)
  - bloody emesis: investigate for causes of upper gastrointestinal (GI) bleed
  - bilious emesis: rule out obstruction (upper GI series, U/S)
  - evaluate for gastroesophageal reflux (24-hour esophageal pH probe)
  - CBC, electrolytes, BUN, creatinine, ESR, venous blood gases, amylase, lipase
  - urine, blood, stool C&S
  - abdominal x-ray, U/S, contrast radiology, endoscopy
  - consider head imaging
- management
  - rehydration (see Pediatric Nephrology section)
  - treat underlying cause

**Vomiting in the Newborn Period**

**Tracheoesophageal Fistula (TEF)**
- incidence: 1:3,000-1:4,500
- clinical presentation (vary with type of fistula)
  - may have history of maternal polyhydramnios
  - may present after several months, if no associated esophageal atresia, with vomiting, coughing, and gagging
  - cyanosis with feeds, respiratory distress, recurrent pneumonia
  - frothy bubbles of mucus in mouth and nose that return after suctioning
  - associated anomalies in 50%; VACTERL association (see Pediatric Genetics, Dysmorphisms, and Metabolism, P44)
- x-ray: anatomic abnormalities, NG tube curled in pouch
- management
  - investigate for other congenital anomalies
  - early repair by surgical ligation to prevent lung damage and maintain nutrition and growth
- complications
  - pneumonia, sepsis, reactive airways disease
  - following repair: esophageal stenosis and strictures at repair site, gastroesophageal reflux and poor swallowing (i.e. dysphagia, regurgitation)

**Duodenal Atresia**
- incidence: 1:10 000, 50% are born prematurely
- clinical features
  - bile-stained vomiting if atresia distal to bile duct
  - no abdominal distention
  - dehydration
  - associated with Down syndrome, prematurity
  - often have history of maternal polyhydramnios
- abdominal x-ray: air-fluid levels on upright film; “double bubble” sign (dilated stomach and duodenum)
- differential diagnosis: annular pancreas, aberrant mesenteric vessels, pyloric stenosis
- treatment
  - decompression with NG tube
  - correction of metabolic abnormalities
  - surgical correction

**Pyloric Stenosis**
- incidence: 1:500, M:F = 4:1, onset common in first-born males, positive FHx
- clinical features
  - non-bilious projectile vomiting that occurs after feeding
  - usually starts at 2-4 weeks of age
  - infant hungry and alert, will re-feed
  - constipation, FTT, wasting
  - dehydration, may lead to prolonged jaundice
  - gastric peristalsis goes from left upper quadrant (LUQ) to epigastrum
  - “olive sign”: olive-shaped mass at margin of right rectus abdominus muscle
  - hypochloremic metabolic alkalosis
- diagnosis: clinical, abdominal U/S and x-ray
- treatment: surgical (pyloromyotomy)
Malrotation of the Intestine
- incidence: 1:500
- 80% experience symptoms in first two months of life
- 3 presentations
  - recurrent vomiting (bilious intermittently)
  - FTT with vomiting
  - sudden onset abdominal pain and then shock (if vomiting with bilious material, malrotation with volvulus until proven otherwise)
- clinical features
  - distended abdomen
  - vomiting due to volvulus and bands across duodenum
- diagnosis: abdominal U/S and upper GI series
- treatment: NG tube decompression and surgery
- complications: volvulus is a surgical emergency as it can result in bowel perforation, peritonitis, and bowel necrosis

Vomiting After the Newborn Period

Infectious and Inflammatory
- GI causes: gastroenteritis, peritonitis, appendicitis, hepatitis, ulcers, pancreatitis, cholecystitis
- non-GI causes: urinary tract infection (UTI), pyelonephritis, nephrolithiasis, otitis media, labyrinthitis, meningitis, pneumonia

Anatomic
- GI tract obstruction
  - intussusception, volvulus
  - foreign body (e.g., bezoar)

Gastroesophageal Reflux
- extremely common in infancy (up to 50%): thriving baby requires no investigation
- vomiting typically soon after feeding, non-bilious, rarely contains blood, small volume (<1 oz)
- investigations required if FTT, recurrent cough, pneumonia or bronchospasm, GI blood loss, symptoms persist after 18 months
  - 24-hour pH probe, UGI series to rule out anatomical cause, upper endoscopy and esophageal biopsy for suspected esophagitis
- management
  - conservative: thickened feeds, frequent and smaller feeds, elevate bed to 45°
  - medical:
    - short-term parenteral feeding to enhance weight gain
    - ranitidine, omeprazole: to decrease gastric acidity, decrease esophageal irritation
    - domperidone: to improve gastric emptying and GI motility
  - surgical: indicated for failure of medical therapy (Nissen fundoplication)
  - complications: esophagitis, strictures, Barrett’s esophagus, FTT, aspiration

Central Nervous System
- increased intracranial pressure (ICP) (e.g., hydrocephalus, neoplasm)
- drugs/toxins
- migraine, cyclic vomiting

Other
- metabolic/endocrine: DKA, inborn errors of metabolism, liver failure
- poisons/drugs: lead, digoxin, erythromycin, theophylline
- psychogenic: rumination syndrome, anorexia/bulimia
- food allergy
- overfeeding
- pregnancy

Acute Diarrhea

Table 19. Causes of Acute Diarrhea

<table>
<thead>
<tr>
<th>Infectious</th>
<th>Bacterial</th>
<th>Parasitic</th>
<th>Non-Infectious</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral</td>
<td>Salmonella</td>
<td>Giardia lamblia</td>
<td>Antibiotic-induced</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Campylobacter</td>
<td>Entamoeba histolytica</td>
<td>Non-specific: associated with systemic infection</td>
</tr>
<tr>
<td>Norwalk</td>
<td>Shigella</td>
<td></td>
<td>Hirschsprung’s disease</td>
</tr>
<tr>
<td>Enteric Adenovirus</td>
<td>Pathogenic E. coli</td>
<td></td>
<td>Toxin ingestion</td>
</tr>
<tr>
<td></td>
<td>E. coli</td>
<td></td>
<td>Primary disaccharide deficiency</td>
</tr>
<tr>
<td></td>
<td>C. difficile</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Diarrhea is defined as an increase in frequency and/or decreased consistency of stools compared to normal.
Normal stool volume:
Infants: 5-10 g/kg
Children: 200 g/day
VIRAL INFECTION
- most common cause of gastroenteritis in Canada and worldwide
- rotaviruses are the most common agent, often seen in winter months in temperate climates
- astroviruses are the second most important etiological agent, common in both developing and developed nations
- Norwalk virus is the third most common agent, it typically affects older children and adults
- clinical features
  - associated with URTIs
  - resolves in 3-7 days
  - slight fever, malaise, vomiting, vague abdominal pain

BACTERIAL INFECTION
- clinical features: severe abdominal pain, high fever, bloody diarrhea
- risk factors: travel, poorly cooked meat, poorly refrigerated foods

Investigations
- history and physical examination critical to determine degree of dehydration (see Pediatric Nephrology, Table 41)
  - rectal exam for fecal consistency and for microscopy (leukocytes suggestive of invading pathogen)
  - stool for culture and sensitivity (C&S), ova and parasites (O&P), electron microscopy for viruses
  - if severe: routine blood work, blood and urine cultures

Treatment
- prevention and treatment of dehydration is most important (see Dehydration, P73)
- oral rehydration therapy with frequent small volumes of pediatric rehydration solutions, IV may be required, see Fluid & Electrolyte Therapy section, P73
- early refeeding advisable, start with small amounts of easily digested carbohydrates, postpone dairy and fibrous vegetables
- antibiotic therapy when indicated, antidiarrheal medications not indicated
- notify Public Health authorities if appropriate

Chronicle Diarrhea

Investigations
- perform serial heights, weights, growth percentiles
- if child is growing well and thriving, minimal workup is required
- investigations depending on suspected diagnosis
  - stool: consistency, pH, reducing substances, microscopy, occult blood, O&P, C&S, C. difficile toxin, 3-day fecal fat
  - urinalysis
  - CBC, differential, ESR, smear, electrolytes, total protein, albumin
  - absorptive and nutritional status: albumin, carotene, Ca, PO₄, Mg, Fe, ferritin, folate, fat-soluble vitamins, PTT, INR
  - sweat chloride, thyroid function tests, urine vanillyl mandelic acid (VMA) and homovanillic acid (HVA), HIV test, lead levels
  - CXR, upper GI series and follow-through
  - specialized tests: endoscopy, small bowel biopsy

Table 20. Causes of Chronic Diarrhea

<table>
<thead>
<tr>
<th>G-3 months</th>
<th>3 months-3 years</th>
<th>3 years-10 years</th>
<th>Uncommon causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI infection</td>
<td>Toddler's diarrhea</td>
<td>GI infection</td>
<td>Constipation with overflow diarrhea</td>
</tr>
<tr>
<td>Disaccharidase deficiency</td>
<td>GI infection</td>
<td>Celiac disease</td>
<td>Drug induced</td>
</tr>
<tr>
<td>Cow's milk intolerance</td>
<td>Celiac disease</td>
<td>IBD</td>
<td>UTI</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td></td>
<td></td>
<td>Short bowel syndrome</td>
</tr>
</tbody>
</table>

Chronic Diarrhea Without Failure to Thrive

Infectious
- bacterial: Campylobacter, Salmonella
- antibiotic-induces: C. difficile colitis
- parasitic: Giardia lamblia
- post-infectious: secondary lactase deficiency
Toddler’s Diarrhea
- **epidemiology**
  - most common cause of chronic diarrhea during infancy
  - onset between 6-36 months of age, ceases spontaneously between 2-4 years
- **clinical presentation**
  - diagnosis of exclusion in thriving child (no weight loss/FTT, no fluid or electrolyte abnormalities)
  - diet history: too much juice overwhelms small bowel resulting in disaccharide malabsorption
  - stool may contain undigested food particles, 4-6 bowel movements (BM's) per day
- **management**
  - reassurance, self-limiting
  - four F’s (adequate Fibre, normal Fluid intake, 35-40% Fat, discourage excess Fruit juice)

Lactase Deficiency (Lactose Intolerance)
- **clinical features**
  - chronic, watery diarrhea
  - abdominal pain, bloating associated with dairy intake
- **primary lactose intolerance:** crampy abdominal pain with loose stool (older children, usually of East Asian and African descent)
- **secondary lactose intolerance:** older infant, persistent diarrhea (post viral/bacterial infection, celiac disease, or IBD)
- **diagnosis**
  - trial of lactose-free diet
  - watery stool, acid pH, positive reducing sugars
  - positive breath hydrogen test if >6 years
- **management**
  - lactose-free diet, soy formula
  - lactase-containing tablets, capsules, drops (e.g. Lacteeze™, Lactaid™)

Irritable Bowel Syndrome
- **diagnosis of exclusion in older child/adolescent; may be similar to recurrent abdominal pain**
- **management**
  - encourage high fibre diet
  - reassurance
  - medications (cAMP inhibitors) for refractory cases

**Chronic Diarrhea With Failure to Thrive**

1. **INTESTINAL CAUSES**

   **Celiac Disease**
   - 1:250 - 1:100 incidence
   - also known as “gluten-sensitive enteropathy”, caused by a reaction to gliadin (a gluten protein)
   - T-cell-mediated inflammation → damage to enterocytes
   - defect in mucosa: immune-mediated inflammation and destruction of absorptive villi
   - **clinical features**
     - presents at any age, usually 6-24 months with the introduction of gluten in the diet
     - FTT with poor appetite, irritability, apathy
     - anorexia, nausea, vomiting, edema, anemia, abdominal pain
     - wasted muscles, distended abdomen, flat buttocks, clubbing of fingers
     - rickets
     - non-GI manifestations: dermatitis herpetiformis, dental enamel hypoplasia, osteopenia/osteoporosis, short stature, delayed puberty
     - associated with other auto-immune disorders
   - **diagnosis**
     - anti-transglutaminase (tTG), antigliadin, antientomysial antibodies (anti-EMA), low D-xylose absorption
     - fat malabsorption studies
     - small bowel biopsy (gold standard): total villous atrophy with resolution after trial of gluten-free diet
   - **treatment**
     - gluten-free diet for life
   - complications if untreated
     - small bowel lymphoma
     - malnutrition, FTT

   **Celiac disease diet must avoid gluten present in “BROW” foods**
   - Barley
   - Rye
   - Oats
   - Wheat

   **Celiac disease is associated with an increased prevalence of IgA deficiency. Since tTG is an IgA-detecting test, you must order an accompanying IgA level!**
Milk Protein Allergy
- immune-mediated mucosal injury
- up to 50% of children intolerant to cow’s milk may be intolerant to soy protein as well
- history of atopy
- 2 scenarios
  - enterocolitis: vomiting, diarrhea, anemia, hematochezia
  - enteropathy: chronic diarrhea, hypalbuminemia
- treatment: casein hydrolysate formula (dairy-free e.g. Nutramigen™, Pregestimil™)

Inflammatory Bowel Disease (IBD) (see Gastroenterology)
- incidence: 15-30; 100,000, increasing in North America, mostly older children and teenagers

Other
- specific enzyme deficiencies
- liver disease, biliary atresia
- alpha-beta-lipoproteinemia
- short gut toxic or immunologic reaction
- blind loop syndrome
- giardiasis

2. PANCREATIC INSUFFICIENCY

Cystic Fibrosis (CF) (see Pediatric Respiratory section, P91)
- incidence: 1:20,000, autosomal recessive
- pancreatic insufficiency, cyclic neutropenia, and anemia
- skeletal abnormalities (metaphyseal dysostosis leading to short stature)
- recurrent pyogenic infections
- distinguished from CF by normal sweat chloride test, characteristic metaphyseal lesions, fatty pancreas on CT

3. OTHER
- diets rich in sorbitol, fructose (poorly absorbed carbohydrates)
- metabolic/endocrine
  - thyrotoxicosis, Addison’s disease, galactosemia
- immune defects
  - IgA deficiency, hypogammaglobulinemia, severe combined immunodeficiency (SCID), AIDS
- neoplastic
  - pheochromocytoma, lymphoma of small bowel, carcinoid tumours, secretory tumours
- food allergy
- laxative abuse

Constipation

Functional Constipation
- 99% of cases of constipation
- lack of fibre in diet or change in diet, poor fluid intake
- infants: often when introducing cow’s milk after breast milk because increased fat and solute amounts, lower water content
- toddlers/older children: can occur during toilet training, or due to pain on defecation, stool withholding
- complications
  - pain retention cycle: anal fissures and pain → withhold passing stool → chronic dilatation and overflow incontinence
- treatment
  - adequate fluid intake (if <6 months, 150 mL/kg/day)
  - adequate dietary fibre, mineral oil, gentle laxatives occasionally (chronic use not recommended)
  - appropriate toilet training technique

Hirschsprung’s Disease (congenital aganglionic megacolon)
- failure of normal innervation of the distal colon by the ganglion cells of the myenteric plexus
- colon remains contracted and impairs fecal movement
- incidence: M:F = 3:1; 1 in 5,000 live births
- clinical features
  - typically only rectosigmoid involvement but may extend to entire colon
  - no meconium within first 24 hours
  - palpable stool on abdominal exam with empty rectum on digital rectal exam
  - intermittent diarrhea, BM only with rectal stimulation
  - constipation, abdominal distention, vomiting, failure to thrive
- complications
  - enteroceles: may be fatal, peak incidence 2-3 months of age
  - toxic megacolon and perforation
- diagnosis
  - abdominal x-ray – cannot see gas in rectum
  - barium enema: proximal dilatation due to functional obstruction, empty rectum
  - manometric studies: shows failure of anal sphincter relaxation, may have false positives
  - rectal biopsy: definitive diagnosis (absent ganglion cells)
- treatment
  - nonsurgical if short segment: increase fibre and fluid intake, mineral oil
  - surgical: colectomy and re-anastomosis

Other Organic Disorders Causing Constipation
- endocrine: hypothyroidism, diabetes mellitus (DM), hypercalcemia
- neurologic: spina bifida
- anatomic: bowel obstruction, anus (imperforate, atresia, stenosis)
- drugs: lead, chemotherapy, opioids

**Acute Abdominal Pain**

**Table 21. Differential Diagnosis for Acute Abdominal Pain**

<table>
<thead>
<tr>
<th>Gastrointestinal</th>
<th>Other Systems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroenteritis</td>
<td>UTI</td>
</tr>
<tr>
<td>Incarcerated hernia, volvulus, intussusception</td>
<td>Henoch-Schönlein Purpura (HSP)</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>Sickle cell crisis</td>
</tr>
<tr>
<td>Malrotation</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Meckel's diverticulitis</td>
<td>DKA</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>Nephrolithiasis</td>
</tr>
</tbody>
</table>

**Assessment**
- description of pain (location, radiation, duration, constant vs. colicky, relativity to meals)
- associated symptoms: nausea, vomiting, diarrhea, fever
- physical examination: peritoneal signs, bowel sounds, rectal exam
- labs: CBC, differential, urinalysis to rule out urinary tract infection (UTI)

**Appendicitis**
- see General Surgery
- most common cause of acute abdomen after 5 years of age
- clinical features
  - low grade fever, anorexia
  - nausea, vomiting (after onset of pain)
  - abdominal pain, peritoneal signs
  - generalized peritonitis is a common presentation in infants/young children
- treatment: surgical
- complications: perforation, abscess

**Intussusception**
- 90% idiopathic, children with CF or GJ tube at significantly increased risk
- 50% between 3-12 months, 75% before 2 years of age
- telescoping of segment of bowel into distal segment → ischemia and necrosis
- usual site: ileocecal junction; jejunum in children with GJ tubes
- lead point of telescoping segment may be swollen Peyer’s patches, Meckel’s diverticulum, polyp, malignancy, Henoch-Schönlein Purpura
- clinical features
  - “classic triad”
    - abdominal pain
    - “palpable sausage-shaped mass: upper to mid-abdomen
    - “red currant jelly” stools (only in 10-15% of patients)
  - sudden onset of recurrent, paroxysmal, severe periumbilical pain with pain-free intervals
  - later vomiting and rectal bleeding
  - shock and dehydration
- diagnosis and treatment
  - U/S
    - air enema diagnostic, can be therapeutic (reduce intussusception in 75% of cases)
    - reduction under hydrostatic pressure
    - surgery rarely needed

---

**Notes**

- Study: Systematic review of studies assessing the effect of medical and dietary treatment of functional constipation.
- Patients: 37 included publications, a total of 1912 children with constipation.
- Intervention: PEG vs. placebo, vs. lactulose, and vs. other laxatives; Lactulose vs. other laxatives; Senic; Mineral oil; Fiber, etc.
- Outcome: defecation frequency.
- Results: no clinically significant difference between laxatives, and between PEG vs. placebo, although most studies failed to compare laxatives to placebo. There was greater treatment success with PEG as compared to all other laxatives.
Chronic Abdominal Pain

- 10-15% of children
- definition "rule of 3s" = 3 episodes of pain severe enough to affect activities, occurring in a child > 3 years of age over a period of 3 months
- distinguish organic from non-organic

Organic (<10%)

- gastrointestinal
  - constipation (cause vs. effect), infectious
  - IBD, esophagitis, peptic ulcer disease, lactase intolerance
  - anatomic anomalies, masses
  - pancreatic, hepatobiliary
- genitourinary causes
  - recurrent urinary tract infections, nephrolithiasis, chronic PID, mittelschmerz
  - neoplastic

Functional/Recurrent Abdominal Pain (RAP) (90%)

- school age, peak 8-10 years
- prevalence: 10% of school children, F>M
- characteristics
  - vague, crampy periumbilical or epigastric pain, vivid imagery to describe pain, clustering of episodes
  - seldom awakens child from sleep
  - aggravated by exercise, alleviated by rest
  - psychological factors related to onset and/or maintenance of pain, school avoidance
  - psychiatric comorbidity: anxiety, somatoform, mood, learning disorders, sexual abuse, eating disorders, elimination disorders
  - diagnosis by exclusion of organic disorders
  - investigations as indicated
    - CBC, ESR, urinalysis, stools for O&P, C&S, occult blood
  - treatment
    - continue to attend school
    - manage any emotional or family problems, counselling
    - trial of high fibre diet, trial of lactose-free diet
    - reassurance
  - prognosis
    - pain resolves in 30-50% of kids within 2-6 weeks of diagnosis
    - 30-50% of kids with RAP have functional pain as adults (e.g. irritable bowel syndrome)

Abdominal Mass

<table>
<thead>
<tr>
<th>Table 22. Differential Diagnosis for Abdominal Mass</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal</td>
<td>Hydronephrosis</td>
<td>Nephroblastoma (Wilms)</td>
</tr>
<tr>
<td></td>
<td>Polycystic kidney disease (PCKD)</td>
<td>Renal cell carcinoma (RCC)</td>
</tr>
<tr>
<td></td>
<td>Hamartoma</td>
<td></td>
</tr>
<tr>
<td>Adrenal</td>
<td>Ovarian cysts</td>
<td>Neuroblastoma</td>
</tr>
<tr>
<td>Ovarian</td>
<td></td>
<td>Ovarian tumours</td>
</tr>
<tr>
<td>Other</td>
<td>Splenomegaly</td>
<td>Lymphoma</td>
</tr>
<tr>
<td></td>
<td>Pyloric stenosis</td>
<td>Rhabdomyosarcoma</td>
</tr>
<tr>
<td></td>
<td>Abdominal hernia</td>
<td>Tetroperitoneal</td>
</tr>
<tr>
<td></td>
<td>Teratoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fecal impaction</td>
<td></td>
</tr>
</tbody>
</table>

- 50% of abdominal masses in the newborn are renal in origin

Upper Gastrointestinal Bleeding

- see Gastroenterology
Lower Gastrointestinal Bleeding

- see Gastroenterology.

**ETIOLOGY**

**Acute**
- infectious
- bacterial, parasitic, antibiotic-induced (C. difficile)
- necrotizing enterocolitis in preterm infants
- anatomic
  - malrotation/volvulus, intussusception
  - Meckel's diverticulitis
  - anal fissures, hemorrhoids
- vascular/hematologic
  - Henoch-Schönlein Purpura (HSP)
  - hemolytic uremic syndrome (HUS)
  - coagulopathy

**Chronic**
- anal fissures (most common)
- colitis
- inflammatory bowel disease (IBD)
- allergic (milk protein)
- structural
  - polyps (most are hamartomas)
  - neoplasms (rare)
  - coagulopathy

**Assessment**
- hemodynamic status, evidence of FTT, fever
- anal and rectal exam
  - tags, fissures, anal fistulas, polyps
  - foreign body
  - blood
  - stool appearance
- NG aspirate
  - lower GI bleed may present as melena (if it involves the small bowel) or hematochezia
- stool cultures (C. difficile)
- urinalysis and microscopy
- CBC, smear, differential, platelets, ESR, electrolytes, urea, creatinine, INR, PTT, albumin, iron studies, amoeba titers
- radiologic investigations
  - abdominal x-ray (AXR) to rule out obstruction

**Treatment**
- acute stabilization: ABCs, volume and blood replacement, bowel rest (NPO, NG tube)
- once stable, endoscopy and surgery as indicated

Genetics, Dysmorphisms and Metabolism

- minor anomaly = an unusual anatomic feature that is of no serious medical or cosmetic consequence to the patients
- major anomaly
  - 1°
    - malformation – results from an intrinsically abnormal developmental process (e.g. polydactyly)
  - 2°
    - disruption – results from the extrinsic breakdown of, or an interference with, an originally normal developmental process (e.g. amniotic band disruption sequence)
    - deformation – results from mechanical forces (e.g. potter deformation sequence)

**Mendelian Inheritance**
- disorders caused by mutation of one or both copies of a gene, inherited in one of several patterns
- autosomal – encoded by genes on one of 22 pairs of autosomes
  - autosomal dominant (AD) = disorder is expressed in a heterozygote (inheritance is 'vertical', both males and females are affected and can transmit the trait); e.g. neurofibromatosis type I
  - autosomal recessive (AR) = disorder is manifest only in homozygotes (inheritance is 'horizontal', disease not found in multiple generations, parents of an affected child are usually normal); e.g. cystic fibrosis

**Definitions**
- Association = non-random concurrence of independent malformations whose etiology is unknown (e.g. VACTERL association)
- Sequence = pattern of multiple anomalies derived from a single known or presumed prior anomaly or mechanical factor (e.g. oligohydramnios sequence)
- Syndrome = recognized pattern of developmentally independent malformations having one known etiology (e.g. Down syndrome)
- X-linked – encoded by a gene on the X chromosome
- males have a single X chromosome and are affected, females have two X chromosomes, and recessive X-linked disorders are rarely expressed in females; i.e. Duchenne Muscular Dystrophy (DMD)

### Approach to the Dysmorphic Child

- 2-3% of infants are born with a serious congenital defect, 1% of newborns have a monogenic disease, 0.5% have a chromosomal disorder and 1-3% have a multifactorial illness
- genetic disorders are the most common cause of infant death in developed countries
- diagnosis of syndromes is based on pattern of dysmorphic features and organ involvement

#### History
- prenatal/obstetrical history (see Obstetrics)
- complete 3 generation family pedigree: consanguinity, stillbirths, neonatal deaths, specific illnesses, intellectual disability, multiple miscarriages, ethnicity

#### Physical Examination
- growth parameters and pattern: head circumference (HC), height (HT), and weight (WT)
- skull: contour and symmetry
- hair: texture and pattern
- neck: look for redundant nuchal skin/webbed neck
- facial gestalt: compare with siblings and parents
- ears: structure, size, placement and rotation
- eyes and adnexa: distance apart, orientation, eyelids and eyelashes, any folds or creases, coloboma, fundus
- nose: nasal bridge, nostrils
- philtrum: length and shape
- mouth: lips, palate, tongue and teeth
- chin: size and position
- thorax: shape, size, and nipple spacing
- hands and feet: creases, structure (e.g. overlapping fingers/toes), and nails
- limbs: proportions and amputations
- spine: scoliosis, kyphosis
- genitalia: ambiguous
- skin: hair tufts, sacral dimples/sinus

#### Investigations
- ask for serial photographs if child is older, family pictures
- x-rays if bony abnormalities or if suspect a congenital infection
- cytogenetic/chromosome studies ± skin fibroblasts
- biochemistry: specific enzyme assays
- genetic probes now available e.g. Fragile X, microdeletion 22; in the future, microarray techniques
- prenatal counselling and recurrence risk assessment
- skin fibroblasts if mosaicism suspected.

### Genetic Syndromes

<table>
<thead>
<tr>
<th>Table 23. Common Genetic Syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Down syndrome</td>
</tr>
<tr>
<td>Incidence</td>
</tr>
<tr>
<td>Most common abnormality of autosomal chromosomes</td>
</tr>
<tr>
<td>Cranial/brain</td>
</tr>
<tr>
<td>Eyes</td>
</tr>
<tr>
<td>Ears</td>
</tr>
<tr>
<td>Facial features</td>
</tr>
</tbody>
</table>
### Table 23. Common Genetic Syndromes (continued)

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Trisomy 21</th>
<th>Trisomy 18</th>
<th>Trisomy 13</th>
</tr>
</thead>
</table>
| **Skeletal/MSK** | • Short stature  
• Excess nuchal skin  
• Joint hyperflexibility (80%) including dysplastic hips, vertebral anomalies, atlantoaxial instability | • Short stature  
• Arthrogryposis multiplex congenita | • Severe growth retardation  
• Polydactyly, clenched hand |
| **Cardiac defect** | • 40%, particularly AVSD | • 60% (VSD, PDA, ASD) | • 80% (VSD, PDA, ASD) |
| **GI** | • Duodenal/esophageal/anal atresia, TE fistula, Hirschsprung disease, chronic constipation | • Hirschsprung's disease | • Polycystic kidneys, cryptorchidism |
| **GU** | • Cryptorchidism, rarely fertile | • Polycystic kidneys | • Polycystic kidneys |
| **CNS** | • Hypotonia at birth  
• Low IQ, developmental delay, hearing problems | • Hypotonia  
• Microcephaly | • Hypo- or hypertension  
• Seizures, deafness |
| **Other features** | • Simian (transverse palmar) crease, clinodactyly and absent middle phalange of the 5th finger  
• 1% lifetime risk of leukemia | • Small for gestational age (SGA)  
• Rocker-bottom feet | • Single umbilical artery  
• Midline anomalies: scalp, pituitary, palate, heart, umbilicus, anus |

**Prognosis/Management**  
- **Trisomy 21:**  
  - Prognosis: long-term  
  - Management:  
    - Recommended chromosomal analysis  
    - Echo, thyroid test, atlanto-occipital x-ray at 2 and 12 years (controversial), hearing test, ophthalmology assessment  
    - Early intervention programs help children reach full potential  
- **Trisomy 18:**  
  - 44% die in 1st month  
  - 10% survive past 1 year (profound intellectual disability in survivors)  
- **Trisomy 13:**  
  - 33% die in 1st month, 59% by 2nd month, 90% by 1 year from birth  
  - Profound intellectual disability in survivors

### Table 24. Most Common Sex Chromosome Disorders

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Turner Syndrome</th>
<th>Noonan Syndrome</th>
<th>Klinefelter Syndrome</th>
<th>Fragile X Syndrome</th>
</tr>
</thead>
</table>
| **Genotype** | 45X (most common)  
Mosaic: 45XO with p deletion, 45XO/47XXX | 46XX, 46XY | 47 XXY (most common)  
48XXX, 48XXXY | X-linked |
| **Incidence** | 1:1000 live female births  
Risk not increased with advanced maternal age | 1:2000 live female births  
Risk not increased with advanced maternal age | 1:1000 live male births  
Increased risk with advanced maternal age | 1:3000 males  
1:6000 females |
| **Phenotype** | Short stature, short webbed neck, low posterior hair line, webbed neck | Certain phenotypic features similar to females with Turner syndrome  
- Short stature, webbed neck  
- Broad chest, widely spaced nipples  
- Lymphedema of hands and/or feet, cystic hygroma in newborn with polyhydramnios, lung hypoplasia  
- Congenital heart disease, pulmonary stenosis  
- Pectus excavatum | Male may suffer from developmental delay, long limbs, genital hypoplasia  
- Growth retardation  
- Mental retardation | Most common X-linked gene:  
- Dosage compensation gene  
- Overgrowth:  
  - Prominent jaw, forehead, and nasal bridge  
  - Long, thin face with large protuberant ears, macroorchidism  
  - Hypertelorism, high arched palate |
| **IQ & Behaviour** | Mildly deficient to normal intelligence | Moderate intellectual disability in 25% of patients | Mild intellectual disability  
- Behavioural or psychiatric disorders - anxiety, shyness, aggressive behavior, antisocial acts | Mild to moderate intellectual disability, 20% of affected males have normal IQ  
- ADHD and/or autism |
| **Genital & Reproductive Function** | Streak ovaries with deficient follicles, infertility, primary amenorrhea, impaired development of secondary sexual characteristics | Delayed puberty | Infertility due to hypogonadism/hypogonadism | Mild to moderate intellectual disability, 20% of affected males have normal IQ  
- ADHD and/or autism |
| **Diagnosis/Prognosis/Management** | Normal life expectancy if no complications | Increased risk of X-linked diseases  
Management:  
- Echo, ECG to screen for cardiac malformation  
- GH therapy for short stature  
- Estrogen replacement at time of puberty for development of secondary sexual characteristics (same as males) | Affected males may require testosterone replacement therapy at puberty  
- Echo, ECG | Cyogenetic studies: region on Xq which fails to condense during mitosis, fragile X marker  
- Molecular testing: overamplification of the trinucleotide repeat, length of segment is proportional to severity of clinical phenotype (genetic anticipation) |
### Muscular Dystrophy (MD)

- a group of inherited diseases characterized by progressive skeletal and cardiac muscle degeneration

#### Duchenne Muscular Dystrophy (DMD)
- 1/4,000 males, 1/3 spontaneous mutations, 2/3 X-linked recessive
- missing structural protein dystrophin → muscle fibre fragility → fibre breakdown → necrosis and regeneration
- clinical features
  - proximal muscle weakness by age 3; Gower’s sign (i.e. child uses hands to “climb up” the legs to move from a sitting to a standing position); waddling gait; toe walking common
  - hypertrophy of calf muscles and wasting of thigh muscles
  - decreased reflexes
  - dystrophin is expressed in the brain, and boys with DMD may have delayed motor and cognitive development; this is not progressive
  - cardiomyopathy
  - moderate intellectual compromise
- diagnosis
  - family history (pedigree analysis)
  - increased CK (50-100x normal) and lactate dehydrogenase
  - muscle biopsy, electromyography (EMG)
- complications
  - patient usually wheelchair-bound by 12 years of age
  - early flexion contractures, scoliosis, develop osteopenia of immobility, increased risk of fracture
  - death due to pneumonia/respiratory failure or CHF in 2nd-3rd decade
- treatment
  - supportive (i.e. physiotherapy, wheelchairs, braces), prevent obesity
  - surgical (for scoliosis)
  - use of steroids (e.g. prednisone or deflazacort)
  - gene therapy trials underway

#### Becker’s Muscular Dystrophy
- X-linked recessive, due to a mutation in dystrophin gene with some protein production
- symptoms similar to Duchenne but onset is later in childhood and progression is slower
- death due to respiratory failure in 4th decade

### Associations

- Associations are a non-random occurrence of multiple malformations with unknown etiology, while syndromes are a pattern of anomalies that have a known etiology
- two common associations are VACTERL and CHARGE

**VACTERL** should be suspected when a child is found to have tracheo-esophageal fistula:

- **V** Vertebral dysgenesis (70%)
- **A** Anal atresia (imperforate anus) ± fistula (80%)
- **T** Cardiac abnormalities – VSD (53%)
- **E** Tracheo-Esophageal fistula ± esophageal atresia (70%)
- **R** Renal anomalies (53%)
- **L** Limb anomalies – radial dysplasia, pre-axial polydactyly, syndactyly (65%)
- may also present with a single umbilical artery or TTT
- prognosis: may have normal health and mental development with aggressive treatment of abnormalities

### Table 25. Other Genetic Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>DiGeorge Syndrome</th>
<th>Prader-Willi Syndrome</th>
<th>Angelman Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Genotype</strong></td>
<td>Microdeletions of 22q11</td>
<td>Lack of paternally imprinted genes on chromosome 15q11</td>
<td>Lack of paternally imprinted genes on chromosome 15q11</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>Second most common genetic diagnosis (next to Down syndrome)</td>
<td>1:5000</td>
<td>Severe intellectual disability, seizures, tremulousness, hypotonia</td>
</tr>
<tr>
<td><strong>Clinical Features</strong></td>
<td>“CATCH 22”</td>
<td>“H30”: hypotonia and weakness, hypoparathyroidism, speech delay</td>
<td>“H30”: hypotonia and weakness, hypoparathyroidism, speech delay</td>
</tr>
<tr>
<td></td>
<td>Genetic CHD (may account for up to 5% of all cases of CHD)</td>
<td>Development delay (variable)</td>
<td>Development delay (variable)</td>
</tr>
<tr>
<td></td>
<td>Anomalies: craniofacial anomalies typically micrognathia and low set ears</td>
<td>Hypopigmentation, DM II</td>
<td>Hypopigmentation, DM II</td>
</tr>
<tr>
<td></td>
<td>Thymic hypoplasia “immunodeficiency”/recurrent infections</td>
<td>Short stature, almond-shaped eyes, small hands and feet with tapering of fingers</td>
<td>Short stature, almond-shaped eyes, small hands and feet with tapering of fingers</td>
</tr>
<tr>
<td></td>
<td>Cognitive impairment</td>
<td>Development delay (variable)</td>
<td>Development delay (variable)</td>
</tr>
<tr>
<td></td>
<td>Hypoparathyroidism, hypocalcemia</td>
<td>Hypopigmentation, DM II</td>
<td>Hypopigmentation, DM II</td>
</tr>
<tr>
<td></td>
<td>22q11 microdeletions</td>
<td>Cognitive impairment</td>
<td>Cognitive impairment</td>
</tr>
<tr>
<td><strong>Causes of Increased CK</strong></td>
<td>Prolonged exercises (5-10x increase)</td>
<td>Trauma</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td></td>
<td>Diagnosis</td>
<td>Increased CK (50-100x normal) and lactate dehydrogenase</td>
<td>Muscle biopsy, electromyography (EMG)</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>Cardiac defects</td>
<td>Cardiac defects</td>
</tr>
<tr>
<td></td>
<td>Outcome</td>
<td>Respiratory failure or CHF</td>
<td>Respiratory failure or CHF</td>
</tr>
<tr>
<td><strong>Malignant Ectodermal Dysplasia (MELAS)</strong></td>
<td>Extreme skeletal staining</td>
<td>High risk of sudden death</td>
<td>High risk of sudden death</td>
</tr>
<tr>
<td><strong>Cranial Dysplasia</strong></td>
<td>Cognitive impairment</td>
<td>Development delay (variable)</td>
<td>Development delay (variable)</td>
</tr>
<tr>
<td><strong>Craniosynostosis</strong></td>
<td>Intellectual disability</td>
<td>Development delay (variable)</td>
<td>Development delay (variable)</td>
</tr>
<tr>
<td><strong>Neurofibromatosis</strong></td>
<td>Intellectual disability</td>
<td>Development delay (variable)</td>
<td>Development delay (variable)</td>
</tr>
<tr>
<td><strong>Down Syndrome</strong></td>
<td>Intellectual disability</td>
<td>Development delay (variable)</td>
<td>Development delay (variable)</td>
</tr>
</tbody>
</table>

*Note: This table is a simplified representation of the information available.*
• CHARGE
  C Coloboma
  H congenital Heart disease
  A choanal Atresia
  R mental Retardation
  G GU anomalies
  E Ear anomalies
  etiology thought to be due to abnormal development rather than a genetic mechanism

**Metabolic Disease**

• an inherited disorder of intermediary metabolism; often autosomal recessive
• infants and older children may present with failure to thrive (FTT) or developmental delay
• currently in Canada and the United States, newborns may be tested for CAH, congenital hypothyroidism, galactosemia, sickle cell disease (in certain ethnic groups), PKU, maple syrup urine disease, homocystinuria, and biotinidase deficiency
• types of disorders
  • proteins: PKU, tyrosinemia, organic acid disorders, urea cycle defects
  • carbohydrates: galactosemia, glycogen storage diseases
  • fats: fatty acid oxidation defects
  • organelle disorders: congenital disorders of glycosylation, mucopolysaccharidosis

**Clinical Manifestations**

• vomiting and acidosis after feeding initiation (amino acid or carbohydrate metabolic disorder)
• hepatosplenomegaly (metabolites accumulate in the liver)
• neurologic syndrome: acute and chronic encephalopathy, intellectual disability, megalencephaly (mucopolysaccharide disorders)
• severe acidosis (aminoaciduria), hyperammonemia (urea cycle and organic acid disorders)
• growth retardation, seizures, coma, hypoglycemia
• autonomic manifestations (e.g. pallor, sweating, tremor)

**Physical Exam**

• odour: burnt sugar, sweaty feet, musty, ammonia-like
• skin: hypo/hyperpigmentation, rash, xanthomas
• hair: alopecia, baldness, abnormal architecture, fair colouring
• eyes: cornea (clouding, crystals), lens (cataracts, dislocation), retina (macular cherry red spot, pigment retinopathy, optic atrophy)

**Initial Investigations**

• electrolytes, ABGs (calculate anion gap, rule out acidosis)
• CBC with differential and smear
• blood glucose (hypoglycemia seen with organic acidemia, fatty acid oxidation defects and glycogen storage diseases)
• lactate, ammonium (hyperammonemia with urea cycle defects), plasma Ca and Mg
• routine urinalysis: ketonuria must be investigated
• others: urine, urine nitroprusside, amino acid screen, CSF glycine, free fatty acids
  (3-beta-hydroxybutyrate ratio >4 in fatty acid oxidation defect)
• storage diseases: urine mucopolysaccharide and oligosaccharide screen

**Phenylketonuria (PKU)**

• incidence: 1 in 10,000
• screened in all newborns
• etiology: deficiency of phenylalanine hydroxylase prevents conversion of phenylalanine to tyrosine leading to build up of toxic metabolites
• mothers who have PKU may have infants with congenital abnormalities
• presentation
  • baby is normal at birth then develops a musty odour, eczema, hypertonia, tremors, and mental retardation
  • hypopigmentation due to low tyrosine (fair hair, blue eyes)
• treatment
  • PKU screening at birth
  • dietary restriction of phenylalanine starting within the first 10 days of life
  • duration of dietary restriction controversial – lifelong or until end of puberty, should be resumed during pregnancy to maintain normal phenylalanine levels

**Galactosemia**

• incidence: 1 in 60,000, autosomal recessive disease
• most commonly due to deficiency of galactose-1-phosphate uridylytransferase leading to an inability to process lactose/galactose
• increased risk of sepsis
• if the diagnosis is not made at birth, liver and brain damage may become irreversible
features neonate who ingests lactose/galactose exhibits signs of liver and renal failure, jaundice, PT/T and cataracts
• treatment
  • elimination of galactose from the diet (i.e. dairy, breast milk)
  • most infants are fed a soy-based diet

**Hematology**

### Physiologic Anemia

- high hemoglobin (>170 g/L) and reticulocyte count at birth as a result of relatively hypoxic environment in utero
- after birth, levels start to fall due to shorter fetal RBC lifespan, decreased RBC production (during first 6-8 weeks of life virtually no erythropoiesis due to new O2 rich environment) and increasing blood volume secondary to growth
- lowest levels about 100 g/L at 8-12 weeks age (earlier and more exaggerated in premature infants); levels rise spontaneously with activation of erythropoiesis
- no treatment usually required

**Iron Deficiency Anemia**

- most common cause of childhood anemia
- full term infants exhaust iron reserves by 6 months age
- preterm infants have lower reserves – exhaust by 2-3 months of age
- common diagnosis between 6 months-3 years and 11-17 years: periods of rapid growth and increased iron requirements; adolescents also have poor diet and menstrual losses
- can cause irreversible effects on development if untreated (behavioural and intellectual deficiencies) in infancy
- presentation: usually asymptomatic until marked anemia, pallor, fatigue, pica (eating non-food materials), tachycardia, systolic murmur
- complications: angular cheilitis, glossitis, koilonychia

**Etiology**

- dietary risk factors
  • "milk baby" – baby (9-24 months old) receiving large volumes (>20 oz per day) of cow’s milk usually by bottle leading to poor intake of iron-rich foods
  • formula without iron
  • delayed introduction of iron fortified infant cereal
  • blood loss
    • iatrogenic: repeated blood sampling (especially in hospitalized neonates)
    • true cow’s milk allergy: occult bleeding and protein-losing enteropathy secondary to G1 inflammation

**Investigations**

- CBC: low MCV and MCH, reticulocyte count normal or high (absolute number low), normal WBC
- Mentzer index (MCV/RBC) can help distinguish between two most common causes of microcytic anemia: iron deficiency anemia from thalassemia. If ratio <13 suggestive of thal, >13 suggestive iron deficiency
- blood smear: hypochromic, microcytic RBCs, pencil shaped cells, poikilocytosis
- iron studies: low ferritin, low iron, high TIBC
- initial therapy: trial of iron

**Prevention**

- breast-fed full-term infants: after 6 months, give iron-fortified cereals and iron-rich foods
- non-breast-fed infants: give iron-fortified formula from birth
- premature infants: give iron supplements from 1 month to 1 year of age

**Management**

- encourage diverse, balanced diet, limit homogenized milk to 16-20 oz/day
- oral iron therapy – 6 mg/kg/day elemental iron, divided BID to TID, for 3 months to replete iron stores
  • increased reticulocyte count in 2-3 days (peaks day 5-7)
  • increased hemoglobin in 4-30 days
  • repletion of iron stores in 1-3 months
  • re-check hemoglobin levels after 1 month of treatment
- poor response to oral iron therapy: non-compliance, ongoing blood loss, incorrect diagnosis, insufficient duration of therapy, high gastric pH (antacid use)
Anemia of Chronic Disease

- most often normocytic, normochromic (microcytic, hypochromic may occur with chronic infection/malignancy)
- multi-factorial in origin
- chronic inflammatory states including juvenile idiopathic arthritis (JIA), chronic infections, chronic renal failure, and malignancies
- iron stores are variable and ferritin levels are unreliable (acute phase reactant) therefore bone marrow assessment may be necessary for diagnosis
- anemia of chronic renal failure predominantly caused by decreased EPO production
  - treatment with erythropoietin

Hemoglobinopathies

SICKLE CELL DISEASE
- see Hematology
- identification of specific genotypes important due to differences in frequency, type and severity of clinical complications (most severe: SS, less severe: SC, 5-beta thalassemia, rare: SD). Also important for genetic counselling.

Pathophysiology
- caused by a genetic defect in beta-globin genes
  - HbS: single amino acid replacement (glutamic acid → valine)
- red blood cells sickle under conditions of stress (low pO₂, dehydration, fever, acidosis)
- acute intravascular sickling results in infarction of tissue (capillary occlusion and thrombosis – spleen, lungs, bones, brain, digits)
- hemolysis causes chronic, well-compensated normochromic normocytic anemia (Hb 60-90 g/L)
- increased incidence in people of African and Mediterranean heritage
- greatest cause of mortality is infection

Presentation
- newborns from high-risk families undergo screening; may be part of provincial newborn screening program
- clinical disease presents after 5-6 months of age after fall in fetal Hb
- anemia, fever, jaundice, splenomegaly, crisis (dactylitis is often the first presentation)
- sickle cell trait: asymptomatic (may have microscopic hematuria)

Types of Crises
- vaso-occlusive crisis
  - due to obstruction of blood vessels by rigid, sickled cells → tissue hypoxia → cell death; presents as fever and pain in any organ; most commonly in long bones of arms and legs, chest, abdomen, CNS (stroke), dactylitis (in young children), priapism
- acute chest crisis: fever, chest pain, progressive respiratory distress, increased WBC count, pulmonary infiltrates
- aplastic crisis – depression of erythropoiesis (decreased reticulocyte count to <1%, decreased Hb), generally associated with infection (especially parvovirus B19)
- acute splenic sequestration – sudden massive pooling of red cells in spleen, splenomegaly, tender spleen, acute fall in hemoglobin, shock, increased reticulocyte count

Functional Asplenia
- splenic dysfunction usually by 5 years of age secondary to autoinfarction
- susceptible to infection by encapsulated organisms (especially S. pneumoniae)
- requires prophylactic antibiotics, pneumococcal/meningococcal/H. influenzae type b vaccination, and immediate evaluation of any fever

Other Manifestations
- increased incidence of osteomyelitis (especially due to Salmonella)
- long term complications: growth delay, bony abnormalities – e.g. avascular necrosis (AVN) of femoral head, gallstones, retinopathy, restrictive lung disease (screen with PFTs), cardiomyopathy (screen with echo)

Management
- acute crises
  - admit for supportive and symptomatic treatment
  - fluids (1.5x maintenance; 1x maintenance only if in chest crisis), analgesia (morphine, multi-modal), antibiotics (e.g. 3rd gen. cephalosporins), incentive spirometry to decrease risk of chest crisis
  - straight transfusions for symptomatic/significant anemia (e.g. aplastic crisis), evolving chest crisis
  - RBC exchange transfusion for impending stroke, severe chest crisis, persistent priapism
  - O₂ if respiratory distress or chest crisis (with incentive spirometry)
  - cultures and CBC if febrile, reticulocyte counts, CXR or LP if indicated
• chronic
  • early aggressive treatment of infections, prophylactic antibiotics (daily oral penicillin)
  • pneumococcal, meningococcal, hepatitis B, Hib, and influenza vaccines
  • folate supplementation if folate deficient
  • hydroxyurea if frequent crises (raises HbF level)
  • transcranial doppler ultrasound to assess risk of stroke
  • chronic transfusion program if history of stroke or abnormal transcranial doppler
  • genetic counselling and education
  • annual ophthalmologic exam (after 10 years old)
  • referral to hematology

**HEREDITARY SPHEROCYTOSIS**
• red cell membrane protein abnormality, causes a spherening of RBCs which are removed by the spleen
• genetics
  • autosomal dominant (positive family history in 75%)
  • high spontaneous mutation rate (no family history in 25%)
• wide range of clinical severity from well-compensated, mild hemolytic anemia to severe hemolytic anemia with growth failure, splenomegaly, gallstones, neonatal jaundice and chronic transfusion requirements in infancy
• diagnosis: spherocytes (circular RBCs) on blood smear, osmotic fragility test
• management
  • transfusion, splenectomy as indicated
  • genetic counselling

**GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY**
• X-linked recessive; the most common enzyme deficiency worldwide
• higher prevalence in Mediterraneans, African Americans, Asians
• enzyme-deficient RBC unable to defend against oxidative stress (infection, drugs) → form Heinz bodies (Hb precipitates within RBCs) → phagocytosed by splenic macrophages creating “bite cells” (RBCs that appear to have bites taken out of them, also known as “cookie cells”)
• presents with acute hemolytic anemia (hemoglobinuria, decreased haptoglobin, increased LDH, and elevated indirect bilirubin) with jaundice, pallor and dark urine (rarely causes chronic anemia)
• diagnosis: G6PD enzyme assay
• management: supportive, hydration, transfusion, phototherapy
• prevention: avoid known oxidants (e.g. fava beans, antimalarials (primquine), sulfonamides)

**Bleeding Disorders**
• see Hematology

**Coagulation Defects**
• characterized by bleeding into joints (hemarthroses) and muscles
• large spreading ecchymoses and hematomas

**Platelet Abnormalities**
• characterized by petechiae, purpura, bruises, mucocutaneous bleeding (i.e. epistaxis, gingival bleeding), menorrhagia, prolonged bleeding from superficial cuts

**Table 26. Classification of Bleeding Disorders**

<table>
<thead>
<tr>
<th>Site of Pathophysiology</th>
<th>Mechanism</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Vessels</td>
<td>Vascilitis</td>
<td>Henoch–Schönlein purpura</td>
</tr>
<tr>
<td>Platelets</td>
<td>Decreased production</td>
<td>Drugs, marrow infiltration, leukemia/lymphoma</td>
</tr>
<tr>
<td></td>
<td>Increased destruction</td>
<td>Immune thrombocytopenic purpura, infection, drugs</td>
</tr>
<tr>
<td></td>
<td>Increased consumption</td>
<td>DIC, giant hemangioma, hypoplasia</td>
</tr>
<tr>
<td></td>
<td>Dysfunction</td>
<td>von Willebrand disease, drugs (ASA), uremia</td>
</tr>
<tr>
<td>Coagulation Pathway</td>
<td>Vitamin K deficiency</td>
<td>Hemorrhagic disease of the newborn</td>
</tr>
<tr>
<td></td>
<td>Factor VIII deficiency</td>
<td>Hemophilia A</td>
</tr>
<tr>
<td></td>
<td>Factor IX deficiency</td>
<td>Hemophilia B</td>
</tr>
<tr>
<td></td>
<td>Abnormal vWF</td>
<td>von Willebrand disease</td>
</tr>
</tbody>
</table>

**Immune Thrombocytopenic Purpura (ITP)**
• most common cause of thrombocytopenia in childhood
• peak age: 2-6 years, M–F
• incidence 5 in 100,000 children per year
• caused by antibodies that bind to platelet membranes → splenic uptake (Fe-receptor mediated) → destruction of platelets

• presentation and course
  - 50% present 1-3 weeks after viral illness (URTI, chicken pox)
  - sudden onset of petechiae, purpura, epistaxis in an otherwise well child
  - no lymphadenopathy, no hepatosplenomegaly
  - labs: thrombocytopenia with normal RBC, WBC
  - if atypical presentation (≤1 cell line abnormal, hepatosplenomegaly), do bone marrow to rule out leukemia
  - differential diagnosis: leukemia, drug-induced thrombocytopenia, HIV, infection (viral), SLE
  - highest risk of bleeding in first 1-2 weeks

• management
  - self-limited in children; spontaneous recovery in >80% of cases
  - usually choose to treat because spontaneous recovery takes a few months, and risk of bleeding (especially intracranial hemorrhage with platelets <20)
  - IVIG or oral prednisone (mainstays of treatment), IV anti-D (if blood group Rh positive)
  - splenectomy (only for life-threatening bleeding)
  - avoid ASA/NSAIDs
  - no contact sports
  - reassurance: very low risk of serious hemorrhage (3%), and CNS hemorrhage rare (<0.5%)
Table 28. Antibiotic Treatment of Pediatric Bacterial Infections (continued)

<table>
<thead>
<tr>
<th>Infection</th>
<th>Pathogens</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia (Community Acquired, Bacterial)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal</td>
<td>GBS, Gram-negative bacilli (E. coli), C. trachomatis, S. aureus, Listeria</td>
<td>• Amoxicillin + gentamicin, add erythromycin if Chlamydia suspected</td>
</tr>
<tr>
<td>1-3 mos</td>
<td>S. pneumoniae, C. trachomatis, B. pertussis, S. aureus, H. influenzae</td>
<td>• Cefuroxime ± macrolide (erythromycin) or Ampicillin ± macrolide</td>
</tr>
<tr>
<td>3 mos-5 yrs</td>
<td>S. pneumoniae, S. aureus, H. influenzae, Mycoplasma pneumoniae</td>
<td>• Amoxicillin or amoxicillin + clavulane or cefuroxime</td>
</tr>
<tr>
<td>&gt;5 yrs</td>
<td>As above</td>
<td>• Macrolide (1st line) or cefuroxime or amoxicillin/amoxicillin or clavulin</td>
</tr>
</tbody>
</table>

Fever

Figure 3. Approach to the Febrile Child

Acute Otitis Media (AOM)

Epidemiology
- peak incidence 3 mo-3 yrs

Etiology
- bacterial (70%) – S. pneumoniae (25-40%), non-typable H. influenzae (10-30%), M. catarrhalis (5-15%), Group A Streptococcus (3%), S. aureus
- viral (20%) – commonly RSV, influenza, parainfluenza, adenovirus

Definitions
- certain diagnosis: 1) recent, usually abrupt, onset of signs and symptoms of middle ear inflammation and effusion 2) presence of middle ear effusion (MEE) 3) middle ear inflammation (MEI)
- uncertain diagnosis: does not meet all three criteria
- severe illness: moderate to severe otalgia or fever >39°C
- non-severe illness: mild otalgia and fever <39°C
Meningitis

- peak age: 6-12 months; 90% occurs in <5 years old

Risk Factors
- immunocompromised (e.g. HIV, asplenia, prematurity)
- neuroanatomical defects (e.g. dermal sinus, neurosurgery)
- parameningeal infection (e.g. sinusitis, mastoiditis, orbital cellulitis)
- environmental (e.g. day-care centres, household contact)

Etiology
- 0-3 months: Group B Strept., E. coli, L. monocytogenes, other Gram-negatives, viral (HSV, enteroviruses)
- 3 months-3 years: S. pneumoniae, N. meningitidis, H. influenzae, TB, viral (enteroviruses, herpes virus 6, HSV)
- 3-18 years: S. pneumoniae, N. meningitidis, H. influenzae, viral (enteroviruses, adenoviruses, herpes viruses)

Pathophysiology
- URTI → compromise in integrity of mucosa → blood stream invasion from respiratory tract → hematogenous seeding of meninges → meningeal and CNS inflammation

Clinical Presentation
- toxic
- ± URTI prodrome
- fever, lethargy, irritability, photophobia, nausea/vomiting, headache, stiff/sore neck
- younger infants: may not demonstrate localizing signs, may have non-specific symptoms (poor feeding, irritability, lethargy), bulging fontanelle, increasing head circumference
- signs of meningitis
  - Brudzinski's sign: reflex flexion of hips and knees upon active flexion of the neck
  - Kernig's sign: reflex contraction and pain in hamstrings upon extension of leg that is flexed at the hip
  - opisthotonos: spasm in which head and heels are bent backward and body bowed forward
  - neck rigidity

<table>
<thead>
<tr>
<th>Table 29. Treatment of AOM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>&lt;6 mos</td>
</tr>
<tr>
<td>6 mos to 2 yrs</td>
</tr>
<tr>
<td>≥2 yrs</td>
</tr>
</tbody>
</table>

The Concept and Practice of a Wait-and-See Approach to Acute Otitis Media

Curent Opinion in Pediatrics, 2008, 28:21-8

Purpose: To summarize recent AOM trials comparing antibiotics versus a "wait and see" prescription.

Study Characteristics: Guidelines formulated based on evidence from three recent clinical trials.

Recommendations:
- Treat immediately with antibiotics when:
  - Age < 6 months
  - Ill appearance (shock, unresponsive)
  - Recent AOM
  - Suspect of another concurrent bacterial illness (e.g. pneumonia)
  - Recent treatment with antibiotics (within last 7 days)
- Perforated TM (including tympanostomy tubes)
- Immunosuppressed
- Clinical abnormalities
- Poor access to medical care

Observation option only appropriate if follow-up can be ensured if persistent symptoms. Consider a safety-net antibiotic prescription.
• signs of increased ICP: headache, diplopia, ptosis, CN VI palsy, bradycardia with hypertension, apnea, papilledema is uncommon
• seizure in 20-30% of patients with bacterial meningitis
• petechial rash (meningococcemia): associated with poor prognosis

**Diagnosis**
- lumbar puncture (LP) for cerebrospinal fluid (CSF)
  - raised opening pressure (norms: recumbent and relaxed, less flexed position <160 mm H₂O, flexed lateral decubitus position = 100-280 mm H₂O)
  - cloudy in bacterial infection
- CSF examination: WBC, protein, glucose, Gram stain, C&S, latex agglutination tests (if partially treated bacterial meningitis), Zielh-Neelsen stain (if TB suspected)
- viral versus bacterial meningitis (see Table 30)
- bloodwork: CBC, blood cultures (positive in 90% cases), blood glucose, electrolytes (to monitor for SIADH)

**Table 30. CSF Findings of Meningitis**

<table>
<thead>
<tr>
<th>Component</th>
<th>Normal Child</th>
<th>Normal Newborn</th>
<th>Bacterial Meningitis</th>
<th>Viral Meningitis</th>
<th>Herpes Meningitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (x10³)</td>
<td>0-8</td>
<td>0-30</td>
<td>&gt;1000</td>
<td>100-500</td>
<td>10-1000</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>0-10</td>
<td>1-3</td>
<td>&gt;50</td>
<td>&lt;40</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>30-60</td>
<td>35-121</td>
<td>&lt;30</td>
<td>&gt;30</td>
<td>&gt;30</td>
</tr>
<tr>
<td>Protein (mg/dL)</td>
<td>20-30</td>
<td>19-149</td>
<td>&gt;100</td>
<td>50-100</td>
<td>&gt;75</td>
</tr>
<tr>
<td>RBC</td>
<td>0-2</td>
<td>0-2</td>
<td>0-10</td>
<td>0-2</td>
<td>0-10</td>
</tr>
</tbody>
</table>


**Complications**
- mortality: neonate 15-20%, children <1-8%; pneumococcus > meningococcus > Hib
- morbidity: up to 50% may have neurobehavioural morbidity, severe neurodevelopmental sequelae in 10-20%
- acute
  - SIADH → hyponatremia → brain edema → seizures
  - subdural effusion/empyema
  - brain abscess, disseminated infection (osteomyelitis, septic arthritis, abscess)
  - shock/DIC
- chronic
  - hearing loss
  - intellectual disability, learning disorders
  - neurological deficit, seizure disorder
  - hydrocephalus

**Treatment**
- isolation with appropriate infection control procedures until 24 hr after culture-sensitive antibiotic therapy
- bacterial: empiric antibiotics, see Table 28
- viral: supportive, acyclovir for HSV meningitis
  - most cases of viral meningitis can be sent home (except HIV)
  - if neonatal, use high dose ampicillin as part of regimen until GBS and Listeria ruled out
  - monitor: glucose, acid-base and volume status
  - anticonvulsants may be needed to treat seizures
- prophylaxis
  - *H. influenzae* type b vaccine – routine
  - meningococcal vaccine – if asplenia, complement deficiency, for outbreaks, routine in some provinces
  - pneumococcal vaccine – if immunocompromised, asplenia, routine in some provinces
  - BCG vaccine – if born in TB-endemic area
  - antibiotic prophylaxis for contacts and index case
    - *H. influenzae* – rifampin
    - *N. meningitidis* – rifampin, ceftriaxone or ciprofloxacin
  - report to public health: acute meningitis (bacterial, viral, other)

**HIV Infection**
- see Infectious Diseases, ID28

**Epidemiology**
- risk of vertical transmission 20-30% born to untreated HIV infected women (risk decreases from 25% to <1% with appropriate antiretroviral treatment during pregnancy)
- transmission
  - infants and children: transplacental (most common), maternal blood, breast milk
  - adolescents: sexual intercourse, needles (IV drug use and tattoos), blood products
Risk Factors
- HIV positive mother
- IV illicit drug use (IVDU)
- mother is with HIV positive partner
- unprotected sex
- receipt of blood products (rare)
- sexual abuse

Incubation
- time from contracting infection to developing symptoms is usually <2 years, but can be several years

Clinical Features of AIDS in Infants and Children
- signs and symptoms occur often within the first year, most within two years of age
  - encephalopathy
  - recurrent/persistent thrush
  - chronic interstitial pneumonitis (relatively common); Pneumocystis jiroveci pneumonia (PJP) infection (formerly PCP)
  - hepatomegaly
  - FTT, opportunistic infections, lymphadenopathy

HIV Testing
- should be offered to all women as early as possible in pregnancy (requires consent)
- 1st step: screening for HIV Ab with ELISA
- if positive do 2nd step: confirmatory test for Ab using Western blot or immunofluorescence (sensitivity and specificity of 99%)
  - maternal HIV antibodies can persist up to 18 months (can result in a false positive HIV test), typically test every 6 months from 0-18 months if asymptomatic
  - if breastfeeding, repeat test 3 months after stopping breastfeeding
- other tests: viral nucleic acid by PCR, viral culture, viral antigen
- if sexually active, must re-test 6 months after 1st test (if negative)

Management
- adequate nutrition (breast feeding contraindicated in developed countries)
- prompt treatment of infections
- prophylaxis
  - TMP/SMX for PJP
  - azithromycin for mycobacterium avium complex (MAC)
  - nystatin, ketoconazole, acyclovir if indicated
- ± IVIG
- immunizations
  - all routine immunizations (including MMR and varicella if well)
  - avoid OPV, BCG and yellow fever
  - pneumococcal, influenza, and varicella vaccines
- suppression of HIV
  - HAART (highly active anti-retroviral therapy)
- HIV positive pregnant women should be offered antiretroviral therapy along with resources for formula feeding to decrease perinatal transmission.
  - elective C-section if not on therapy, or if significant viral load

Pharyngitis and Tonsillitis

Etiology
- viral (adenoviruses, enteroviruses, EBV virus) – 80%
- bacterial (Group A Streptococcus) – 20%
- others: fungal (Candida), Kawasaki’s, retropharyngeal/peritonsillar abscess, epiglottitis, bacterial tracheitis
- cannot be reliably distinguished on clinical features alone

Clinical Features
- refer to Table 31
- exudative tonsillitis: GAS, adenovirus, EBV, diphtheria
- soft palate petechiae: GAS, EBV

<table>
<thead>
<tr>
<th>Table 31. Clinical Features of Pharyngitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viral</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Onset</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Clinical Features</td>
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<tr>
<td></td>
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</tbody>
</table>
**Streptococcal (GAS) Pharyngitis**

**Clinical Features**
- Group A *Streptococcus* (GAS) infection
- most commonly school aged, uncommon in children <3 yrs
- Mcisaac Criteria: no cough, tender anterior cervical lymphadenopathy, erythematous tonsils with exudate, fever >38°C, age 3-14
  - score 0-1: no culture, no antibiotic; 2-3: culture, treat if positive; 4: antibiotics

**Management**
- >2 years old, culture before treatment or do rapid Strep antigen test
  - rapid strep test only 70-90% sensitive (pick up 20% of carriers of GAS), culture if negative (throat swab for culture is gold standard, sensitivity 90-95%)
- symptomatic
  - if 1 symptom, no culture or antibiotics
  - if >1 symptom, culture → antibiotics
    - penicillin V or amoxicillin 40 mg/kg/day PO divided bid x 10 days
    - erythromycin 40 mg/kg/day PO divided tid x 10 days if allergic to penicillin
    - acetaminophen for discomfort
- can prevent rheumatic fever if treated within 9-10 days
- antibiotics do not alter the risk of post-streptococcal glomerulonephritis
- tonsillectomy for proven, recurrent streptococcal tonsillitis
- complications
  - if untreated, can lead to
    - suppurative complications: otitis media, sinusitis, cervical adenitis, pneumonia, mastoiditis
    - direct extension: retropharyngeal/peritonsillar abscess
    - scarlet fever, rheumatic fever
    - hematogenous spread: bone/joint infection, meningitis, SBE
    - acute glomerulonephritis (irrespective of antibiotic treatment)
    - invasive GAS disease: illness associated with isolation of GAS from normally sterile sites (blood, CSF; or pleural fluid)
- treatment of invasive GAS disease
  - admit
  - IV clindamycin 40 mg/kg divided into 3-4 doses + IV penicillin 250,000-400,000 U/kg/day divided into 6 doses
  - other illnesses caused by strep: impetigo, cellulitis, bacteremia, vaginitis, toxic shock syndrome
- streptococcal toxic shock: illness associated with isolation of GAS from normally sterile sites (blood, CSF, or pleural fluid) + hypotension, renal impairment, coagulopathy, liver impairment, RDS, rash, soft tissue necrosis (necrotizing fasciitis, myositis, or gangrene)

**SCARLET FEVER**
- erythrogenic strain of Group A *Streptococcus*
- acute onset of fever, sore throat, strawberry tongue
- 24-48 hours after pharyngitis, rash begins in the groin, axillae, neck, antecubital fossa
- within 24 hours, “sandpaper” rash becomes generalized with perioral sparing, non-pruritic, non-painful
- rash fades after 3-4 days, may be followed by peeling
- treatment: penicillin, amoxicillin or erythromycin (if penicillin allergic) x 10 days

**RHEUMATIC FEVER**
- Jones Criteria (revised)
  - requires 2 major OR 1 major and 2 minor PLUS evidence of preceding strep infection (history of scarlet fever, group A streptococcal pharyngitis culture, rapid Ag detection test only useful if positive, anti-streptolysin O titers [ASOT])
  - major criteria: “SPACE”
    - Subcutaneous nodules, pea-sized, firm, non-tender nodules typically on extensor surfaces
    - Pancarditis involving pericardium, myocardium, endocardium
    - Arthritis (migratory): very tender, red, warm, swollen joints, affects mostly large joints
    - Chorea (Sydenham’s): may be characterized by clumsiness, difficulty with handwriting
    - Erythema marginatum: begins as pink macules on trunk with central blanching; non-pruritic
  - minor criteria
    - previous history of rheumatic fever or rheumatic heart disease
    - polyarthralgia
    - fever
    - elevated ESR or C-reactive protein or leukocytosis
    - prolonged PR interval
Toronto Treatment Clinical Complications Clinical Diagnosis

• EBV ± heterophil spread
• supportive steroids
• acyclovir false CBC
• acute: myocarditis, conduction system (sinus tachycardia, atrial fibrillation), valvulitis (acute MR), pericarditis
• chronic: rheumatic valve heart disease – mitral and/or aortic insufficiency/stenosis, increased risk of infectious endocarditis ± thromboembolic phenomenon
• onset of symptoms usually after 10-20 year latency from acute carditis of rheumatic fever

Infectious Mononucleosis

- the “great imitator”: systemic viral infection that affects many organ systems
- Epstein-Barr virus (EBV): a member of herpesviridae
- incubation: 1-2 months
- spread through saliva (“kissing disease”), sexual activity

Clinical Features
- prodrome: 2-3 days of malaise, anorexia
- infants and young children: often asymptomatic or mild disease
- older children and young adults: may develop typical infectious mononucleosis syndrome
  - fever, tonsillar exudate, generalized lymphadenopathy, pharyngitis
  - ± hepatosplenomegaly
  - ± rash (rash more frequent with patients treated with amoxicillin/ampicillin)
  - any “-itis” (including arthritis, hepatitis, nephritis, myocarditis)
  - chronic fatigue
- resolves over 2-3 weeks although fatigue may persist for several months
- administration of amoxicillin results in rash in >90% of cases

Complications
- aseptic meningitis, encephalitis, Guillain-Barré, splenic rupture, agranulocytosis, myocarditis (rare)

Diagnosis
- heterophil antibody test (Monospot™ test) 85% sensitive in adults and older children, only 50% sensitive <4 yrs of age
- false positive results with HIV, SLE, lymphoma, rubella, parvovirus
- EBV titres
- CBC + differential: atypical lymphocytes, lymphocytosis, Downey cells, ± anemia, ± thrombocytopenia

Treatment
- throat culture to rule out streptococcal pharyngitis
- supportive care (bed rest, fluids, saline gargles for sore throat, acetaminophen)
- if airway obstructed secondary to node and/or tonsillar enlargement, admit to hospital, steroids
- patients with splenic enlargement often not apparent clinically so all patients should avoid contact sports for 6-8 weeks
- acyclovir not useful

Pertussis

- Bordetella pertussis, whooping cough, “100-day cough”
- incubation: 6-20 days; infectivity: 1 week before paroxysms to 3 weeks after
- increase in number of reported cases since early 1990’s
- spread: highly contagious; via air droplets released during intense coughing
- greatest incidence among children <1 year and adolescents

Clinical Presentation
- prodromal catarrhal stage
  - 1-2 weeks, most contagious
  - coryza, mild cough
• paroxysmal stage
  • 2-4 weeks
    • paroxysms of cough, sometimes followed by inspiratory whoop (whoop may be absent in children <6 months or adults)
    • infants may present with apnea
    • ± vomiting with coughing spells
    • onset of attacks precipitated by yawning, sneezing, eating, physical exertion
    • can have severe symptoms for 6 weeks, cough for 6 months
    • pressure effect - subconjunctival hemorrhage, rectal prolapse, hernias, epistaxis
  • convalescent stage
    • 1-2 weeks, noninfectious
    • occasional paroxysms of cough, but decreased frequency and severity, lasts up to 6 months

Diagnosis
• clinical: URTI symptoms followed by paroxysms of cough in an afebrile child
• lymphocytosis
• PCR of nasopharyngeal swab or aspirate

Complications
• otitis media
• respiratory complications
  • sinusitis, secondary pneumonia, atelectasis, pneumonomeidastinum, pneumothorax, interstitial or subcutaneous emphysema secondary to ruptured alveoli
• neurological complications
  • seizures, encephalopathy (1:100,000), intracranial hemorrhage

Treatment
• supportive care
  • hospitalize if paroxysms of cough are associated with coryza and/or apnea, (give O₂)
  • erythromycin 40 mg/kg/day x 10 days started within 3 weeks after onset of cough
  • isolate until 5 days of treatment
  • treatment will decrease infectivity but not change course of illness
  • shortens period of communicability
• antibiotic prophylaxis: erythromycin for all household contacts
• prevention: acellular pertussis vaccine (Pentacel™) in infants and children, and pertussis booster (Adacel™) in adolescents and adults

Varicella (Chickenpox)
• varicella-zoster virus (VZV)
• incubation: 10-21 days, infectivity: 1-2 days pre-rash until vesicles have crusted over
• transmission rate: 80% in household contacts, via respiratory secretions (airborne) and vesicular fluid
• primary infection with virus usually results in life-long immunity: >95% of young adults with varicella are immune
• maternal infection in first or early second trimester (<2% risk) can cause congenital varicella syndrome (low birth weight, CNS abnormalities, digit/limb abnormalities, cutaneous scarring, eye defects)
• maternal infection 5 days before to 2 days after delivery can lead to severe varicella of neonate

Clinical Presentation
• 1-3 day prodrome: fever and respiratory symptoms
• characteristic polymorphic rash
  • very pruritic
  • crops of red macules which quickly become vesicles surrounded by erythema
  • “dewdrop on erythematous base”
  • vesicles burst and lesions crust over
  • on trunk, face, scalp, conjunctivae, vagina, oral mucosa, palms and soles
  • new crops usually stop forming after 5-7 days

Complications
• secondary bacterial infection (most common)
  • infection with staph, GAS
  • presents as impetigo, abscesses, cellulitis, necrotizing fasciitis, sepsis
  • cerebellar ataxia, pneumonia, hepatitis, encephalitis
  • immuno-compromised patients: varicella may be life-threatening
• neonates born to mothers who develop varicella from 5 days before to 2 days after delivery are considered high risk
  • must administer varicella-zoster immune globulin (VZIG) and follow for signs of infection/sepsis, consider starting acyclovir
• virus latent in sensory ganglia and reappears as herpes zoster in 68/100,000 individuals
  • incidence is increased in immuno-compromised patients
Treatment
• supportive (hydration, acetaminophen, antipruritics, AVOID salicylates)
• proper hygiene, discourage scratching
• acyclovir for severe disease, immunocompromised patients, neonates
• avoid contact with others until lesions are dry and crusted and no new ones are appearing

Prophylaxis and Prevention
• immunization (see Routine Immunization, P5)
• VZIG for post-exposure in high risk susceptible patient (within 96 hours of exposure)

Roseola
• human herpes virus 6
• incubation: 5-15 days; infectivity and spread: unknown
• typically affects children <3 years

Clinical Presentation
• high fever (>39.5°C) lasting 3-5 days, cough, respiratory symptoms, nasal congestion
• pharynx, tonsils and tympanic membranes are erythematous
• cervical, posterior cervical lymphadenopathy, bulging anterior fontanelle (if CNS involvement)
• fever ceases before rash appears
  - pink non-pruritic macules and maculopapules
  - macules coalesce and disappear in 1-2 days

Treatment
• supportive (acetaminophen)

Complications
• febrile seizures
• encephalitis

Measles
• morbillivirus
• incubation: 10-14 days; infectivity: 4 days pre-rash, spread by airborne route

Clinical Presentation
• prodrome: “3 C’s” – cough, coryza, conjunctivitis, fever, eyelid edema
• Koplik spots (1-2 days before and after rash): small white papules on red base on buccal mucosa
• maculopapular rash spreads over face and hairline spreading in a descending fashion over the body over 3 days

Diagnosis
• clinical examination and positive serology for measles IgM

Treatment
• supportive and symptomatic (appropriate treatment of secondary bacterial infection)
• prophylactic immunoglobulin to prevent disease if administered within 6 days of exposure
• vitamin A supplementation in selected children

Complications
• secondary bacterial infection (laryngotracheobronchitis, otitis media, sinusitis), bronchopneumonia, croup
• encephalitis (1:1,000): ataxia, vomiting, seizures, coma
• subacute sclerosing panencephalitis (1:100,000): slow measles virus infection of brain manifesting years later, characterized by progressive cerebral deterioration with myoclonic jerks, fatal within 6-12 months

Mumps
• paramyxovirus
• incubation: 12-25 days; infectivity: 7 days pre-parotitis to 7 days post-parotitis, spread by droplets
• diagnosis: urine or saliva for viral serology

Clinical Presentation
• fever, headache, parotitis (bilateral; pushes earlobes up and out), myalgia, malaise
• 30-40% of cases are subclinical with minimal symptoms
Treatment
• supportive

Complications
• meningencephalomyelitis: over 10% of patient with parotitis
• orchitis, epididymitis, infertility
• pancreatitis: may see elevated serum amylase without symptoms
• other: ocular complications, thyroiditis, hearing impairment, myocarditis, arthritis, thrombocytopenia, cerebellar ataxia, glomerulonephritis

Rubella
• rubivirus
• incubation: 14-21 days
• infectivity: 7 days pre-rash to 5 days post-rash, spread by droplets
• diagnosis: serology for rubella IgM; may not be detected 4-5 days after rash onset

Clinical Presentation
• prodrome of nonspecific respiratory symptoms and suboccipital adenopathy
• rash
  • maculopapular, initially on face, then spreading to entire body
  • pruritic, disappearing by fourth day
• congenital rubella syndrome (CRS)
  • mother infected in first 4 months of pregnancy (highest risk)
  • infection in utero, failure of rubella vaccine is <5% and rarely results in CRS
  • cataracts/congenital glaucoma, congenital heart disease, hearing impairment (common), purpura ("blueberry muffin baby"), hepatosplenomegaly, jaundice, microcephaly, developmental delay, radiolucent bone disease
• prevention: routine childhood immunization, assure immunity of women of childbearing age with vaccination

Treatment
• symptomatic

Prognosis
• excellent prognosis in patients with acquired disease
• irreversible defects in congenitally infected patients

Complications
• arthritis/arthralgia: polyarticular (fingers, wrists, knees), lasts days to weeks
• encephalitis

Reye Syndrome
• acute hepatic encephalopathy and noninflammatory fatty infiltration of liver and kidney
• mitochondrial injury of unknown etiology results in reduction of hepatic mitochondrial enzymes, diagnosis by liver biopsy
• associated with aspirin ingestion by children with varicella or influenza infection
• 40% mortality

Clinical Presentation
• vomiting
• hyperventilation, tachycardia, decerebrate posturing
• respiratory failure
• agitated delirium, coma, death

Treatment
• should be tailored based on severity of presentation
• IV glucose (to counteract effects of glycogen depletion)
• fluid restriction, mannitol (if cerebral edema)
• prevention: avoid aspirin with viral illness

Erythema Infectiosum
• parvovirus B19, “fifth disease”
• incubation: 4-14 days; infectivity: prior to onset of rash
Clinical Presentation
- initial 7-10 days: flu-like illness with fever
- day 10-17: rash appears (immune response)
  - raised maculopapular lesions on cheeks ("slapped cheek" appearance), forehead, chin, circumoral sparing
  - warm, nontender, may be pruritic, may also appear on extensor surfaces, trunk, neck, buttocks
- days to weeks: rash fades, may reappear with local irritation (heat, sunlight)

Treatment
- supportive
- blood transfusions for some with aplastic crisis

Complications
- arthritis (10%, pain and stiffness in peripheral joints), vasculitis
- infection during pregnancy may lead to fetal hydrops, fetal loss
- aplastic crisis: reticulocytopenia occurs for 1 week during illness, unnoticed in normal individuals, but severe anemia in patients with chronic hemolytic anemia

Urinary Tract Infection (UTI)

Definition
- urine specimen with >10⁶ colonies/ml of a single organism

Epidemiology and Etiology
- 3-5% of girls, 1% of boys
  - <1 yr: more common in boys
  - >1 yr F:M = 10:1
- E. coli (80-90%), Klebsiella, Proteus (especially boys), S. saprophyticus, Enterococcus, and Pseudomonas
- risk factors: female, vesicoureteral reflux (VUR), diabetes, immunocompromised, urinary stasis (neurogenic bladder), voiding dysfunction, wiping from back to front

Symptoms and Diagnosis
- cystitis: dysuria, urgency, frequency, suprapubic pain, incontinence, malodorous urine
- pyelonephritis: abdominal or flank pain, fever, malaise, nausea, vomiting (may present as non-specific illness in newborn)
- sterile specimen required: suprapubic aspiration, transurethral catheter, clean catch
- dipstick for nitrates, leukocytes, and blood; urine C&S (definitive diagnosis)
- if systemically ill: CBC, electrolytes, Cr, BUN, blood cultures

Radiologic Evaluation
- U/S to assess for renal growth, hydronephrosis, or structural anomalies and voiding cystourethrography (VCUG) to assess for VUR for all children <2 yrs presenting with febrile UTI
- dimercapto-succinic acid (DMSA) if VCUG abnormal or history of pyelonephritis to assess for renal scarring
- nuclear studies to follow VUR or assess function

Treatment
- encourage fluid intake (promotes urinary flow)
- uncomplicated UTI: oral cephalexin, or cefixime x 7d
- complicated UTI (acutely ill, <2-3 months, vomiting, immunocompromised): admit for hydration, IV ampicillin and aminoglycoside
- prophylaxis: TMP-SMX for all kids with reflux, awaiting investigations and/or >3 UTIs/yr, Trimethoprim alone if <2 mo
- follow-up
  - if no clinical response within 48 hr re-culture urine

Complications
- long term morbidity: focal renal scarring may lead to hypertension and end-stage renal disease

Propylaxis After First Febrile Urinary Tract Infection in Children: A Multicenter Randomized Controlled, Noninferiority Trial
Pediatrics 2010; 122:1064-1071
Study: Randomized, controlled, open-label, 2 arms, noninferiority trial
Patients: 336 patients aged 2 mo to <3 years who had a first episode of febrile UTI
Intervention: No prophylaxis with prophylaxis
Outcome: Recurrence rate of febrile UTI and rate of renal scarring
Results: No significant difference in recurrence rate or in the rate of renal scarring between the prophylaxis and no-prophylaxis group.
Neonatology

Normal Baby at Term

- RR: 40-60 breaths/min
- HR: 120-160 beats/min when awake
- sBP: 50-80 mmHg; dBP: 30-40 mmHg
- weight: 2,500-4,500 g
- glucose: >2.6 mmol/L (45 mg/dL)

Gestational Age (GA) and Size

Definitions

- classification by gestational age (GA)
  - pre-term: <37 weeks
  - term: 37-42 weeks
  - post-term: >42 weeks
- classification by birth weight
  - small for gestational age (SGA): 2 SD < mean weight for GA or <3rd percentile
  - appropriate for gestational age (AGA): within 2 SD of mean weight for GA
  - large for gestational age (LGA): 2 SD > mean weight for GA or >97th percentile
- GA can be determined after birth using Dubowitz/Ballard scores:
  - assessment at delivery of physical maturity (e.g. planter creases, lanugo, ear maturation) and neuromuscular-maturity (e.g. posture, arm recoil) translates into a score from -10 to +50
  - higher score means greater maturity (increased GA)
  - -10 = 20 weeks; +50 = 44 weeks
  - ideal = 35-40 which corresponds to GA 38-40 weeks
  - only accurate ± 2 weeks

Table 32. Abnormalities of Gestational Age and Size

<table>
<thead>
<tr>
<th>Features</th>
<th>Causes</th>
<th>Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-term Infants &lt;37 weeks</td>
<td>Most common cause unknown</td>
<td>Respiratory distress syndrome, anemia of prematurity, chronic lung disease, bronchopulmonary dysplasia</td>
</tr>
<tr>
<td></td>
<td>Maternal disease e.g. pre-eclampsia</td>
<td>Feeding difficulties, respiratory distress syndrome (RDS)</td>
</tr>
<tr>
<td></td>
<td>Drug/EDH, smoking</td>
<td>Hypocalcemia, hypoglycemia, hypothyroidity</td>
</tr>
<tr>
<td></td>
<td>Chromosomal</td>
<td>Anemia, jaundice</td>
</tr>
<tr>
<td></td>
<td>Multiple pregnancy</td>
<td>Retinopathy of prematurity</td>
</tr>
<tr>
<td></td>
<td>Placental insufficiency</td>
<td>Intracranial/intraventricular hemorrhage</td>
</tr>
<tr>
<td>Post-term Infants &gt;42 weeks</td>
<td>Wizened-looking, leathery skin</td>
<td>Patent ductus arteriosus (PDA)</td>
</tr>
<tr>
<td></td>
<td>Meconium staining</td>
<td></td>
</tr>
<tr>
<td>SGA Infants &lt;3rd percentile</td>
<td>Asymmetric (head-sparing), late onset, growth arrest</td>
<td>Hypoxia, meconium aspiration</td>
</tr>
<tr>
<td></td>
<td>Intrinsic causes: placental insufficiency, poor nutrition, hypertension, multiple pregnancies, drugs, EDH, smoking</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>Symmetric early onset, lower growth</td>
<td>Perinatal hypoxia</td>
</tr>
<tr>
<td></td>
<td>Intrinsic causes: potential infections (TORCH), congenital abnormalities, syndromal, idiopathic</td>
<td>Hypovolemic (polycythemic), jaundice</td>
</tr>
<tr>
<td>LGA Infants &gt;97th percentile</td>
<td>Maternal diabetes</td>
<td>Hypomotility</td>
</tr>
<tr>
<td></td>
<td>Racial or familial factors</td>
<td>Patent ductus arteriosus (PDA)</td>
</tr>
<tr>
<td></td>
<td>Certain syndromes</td>
<td></td>
</tr>
</tbody>
</table>

Routine Neonatal Care

Performed in delivery suite
1. erythromycin ointment – applied to both eyes for ophthalmia neonatorum (gonorrhea, chlamydia) prophylaxis
2. vitamin K IM – to avoid hemorrhagic disease of newborn
3. screening tests
   - varies across Canada and United States (see NNSGRC websites)
   - new tandem mass spectrometry (MS/MS) can detect 25 inborn errors of metabolism (IEM) in a single process from heel pric
   - 100% sensitivity and 83-99% specificity depending on IEM
- in Ontario, newborn screening tests for
  - endocrine disorders (congenital adrenal hyperplasia, congenital hypothyroidism)
  - cystic fibrosis
  - hemoglobinopathies (HbSS, HbSc, sBthal)
  - inborn errors of metabolism (22 in total)
    - 3 categories: fatty acid oxidation defects, aminoacidopathies, organic acid defects
    - others: biotinidase deficiency and galactosemia
4. if mother Rh negative: send cord blood for blood group, and direct antiglobulin test
5. if indicated: G6PD deficiency testing
6. if mother hepatitis B surface antigen positive: HBlg and start hepatitis B vaccine series

**Approach to the Depressed Newborn**

- a depressed newborn lacks one or more of the following characteristics for a normal newborn
  - pulse >100 bpm
  - cries when stimulated
  - actively moves all extremities
  - has a good strong cry
- between 5-10% of newborn babies require assistance with breathing after delivery

**Table 33. Etiology of Respiratory Depression in the Newborn**

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory problems</td>
<td>Respiratory Distress Syndrome/Hyaline Membrane Disease</td>
</tr>
<tr>
<td></td>
<td>CNS depression</td>
</tr>
<tr>
<td></td>
<td>Meconium aspiration</td>
</tr>
<tr>
<td></td>
<td>Pneumonia</td>
</tr>
<tr>
<td></td>
<td>Pneumothorax</td>
</tr>
<tr>
<td>Anemia (severe)</td>
<td>Erythroblastosis fetalis</td>
</tr>
<tr>
<td></td>
<td>Secondary hydrops fetalis</td>
</tr>
<tr>
<td>Maternal causes</td>
<td>Drugs/anesthesia</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>Pregnancy-induced hypertension</td>
</tr>
<tr>
<td>Congenital malformations/Birth injury</td>
<td>Nuchal cord</td>
</tr>
<tr>
<td>Shock/Cyanosis/Congenital heart disease</td>
<td>Hyperthermia</td>
</tr>
<tr>
<td></td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>Infection</td>
</tr>
</tbody>
</table>

**Diagnosis**

- vital signs
- take a good maternal history
  - include prenatal care, illnesses, use of drugs, labour, previous high risk pregnancies, infections during pregnancy, current infections, duration of ruptured membranes, blood type and Rh status, amniotic fluid status, gestational age, meconium, Apgar scores
- clinical findings (observe for signs of respiratory distress: cyanosis, tachypnea, retractions, and grunting)
- laboratory results (CBC, ABG, pH, blood type)
- transillumination or chest x-ray (if suspecting pneumothorax or diaphragmatic hernia)

**Management**

- ABC's
- suction if meconium present and infant is depressed
- apply tactile stimulation (do not 'spank')
- provide air/oxygen and assisted ventilation if apneic or HR <100 bpm
- monitor oxygen saturation and heart rate (if HR <60 bpm, start chest compressions )
- treat the underlying cause
- counsel and provide explanation and support to family
Neonatal Resuscitation

- assess Apgars at 1 and 5 minutes
- if <7 at 5 minutes then reassess q5 min, until >7
- do not wait to assign Apgar score before initiating resuscitation

Table 34. Apgar Score

<table>
<thead>
<tr>
<th>Sign</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>Absent</td>
<td>&lt;100/min</td>
<td>&gt;100/min</td>
</tr>
<tr>
<td>Respiratory Eff</td>
<td>Absent</td>
<td>Slow, irregular</td>
<td>Good, crying</td>
</tr>
<tr>
<td>Irritability</td>
<td>No response</td>
<td>Grimace</td>
<td>Cough/cry</td>
</tr>
<tr>
<td>Tone</td>
<td>Limp</td>
<td>Some fixation of extremities</td>
<td>Active motion</td>
</tr>
<tr>
<td>Colour</td>
<td>Blue/pale</td>
<td>Body pink, extremities blue (acrocyanosis)</td>
<td>Completely pink</td>
</tr>
</tbody>
</table>

Initial Resuscitation

- anticipation – know maternal history, history of pregnancy, labour, and delivery, prepare equipment
- steps to take for all infants (“before ABC’s”)
  - provide warmth: warm (radiant heater, warm towels), dry the newborn (remove wet towels)
  - position and clear airway: “sniffing” position
  - stimulate infant if needed: rub back gently or flick soles of feet EXCEPT if meconium present (in which case suction FIRST)
  - assess breathing, heart rate and colour

- Airway
  - if meconium is present and
    - baby is vigorous (strong respiratory effort, good muscle tone, HR >100): suction mouth and nose after delivery of head
    - baby is not vigorous: free flow O₂, intubate and suction trachea
  - if no meconium is present, remove secretions by wiping mouth and nose with towel or gentle suction of mouth then nose

- Breathing
  - if HR <100 or apneic, apply positive pressure ventilation (PPV)
  - PPV at rate of 40-60/min, 100% O₂ with enough pressure to see visible chest expansion

- Circulation
  - if HR <60 after 30 sec of effective ventilation, start chest compressions (“60 or less, compress”)
  - chest compressions at lower 1/3 of the sternum at 1/3 of the AP depth at a rate of 120 events/min (3 compressions: 1 ventilation = 90 compressions/min: 30 breaths/min)

Table 35. Drugs Used in Neonatal Resuscitation

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Schedule</th>
<th>Indications</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>epinephrine (adrenalin)</td>
<td>0.1-0.3 mg/kg/dose of 1:10,000 solution IV q0.1-0.3 min intratracheal q5-60 min</td>
<td>HR &lt;60 and not rising</td>
<td>Side effects: tachycardia, hypertension, cardiac arrhythmias</td>
</tr>
<tr>
<td>naloxone (Narcan**)</td>
<td>0.1 mg/kg of 0.04 mg/mL solution IV q0.25 mg/kg/dose</td>
<td>Newborn with respiratory depression and maternal narcotic use 4 hours before delivery</td>
<td>Do not use for chronic opiate exposure – may cause withdrawal symptoms including hypertension, irritability, poor feeding</td>
</tr>
<tr>
<td>fluid bolus</td>
<td>10 mL/kg/dose over 5-10 min</td>
<td>Evidence of hypovolemia</td>
<td>Action of narcotic results in use of naloxone</td>
</tr>
</tbody>
</table>

Sepsis in the Neonate

Table 36. Sepsis Considerations in the Neonate

Early Onset (0-5 days)

- Vertical transmission, 95% present within 24 hr
- Risk factors:
  - Maternal infection: UTI, GBS positive, previous child with GBS sepsis or meningitis
  - Maternal fever/monthly discharge/chorioamnionitis
  - Prolonged rupture of membranes (>18 hrs)
  - Preterm labour
  - Pathogens: GBS, E. coli, Listeria

Late Onset (5-28 days)

- Acquired after birth
- Most common in preterm infants in NICU (due to coagulase negative staph)
- Also in healthy, full-term
- Same pathogens plus:
  - Streptococcus, Methicillin-resistant, Staphylococcus
Signs of Sepsis
- no reliable absolute indicator of occult bacteremia in infants <3 months, most consistent result has been WBC <5
- temperature instability (hypo/hyperthermia)
- respiratory distress, cyanosis, apnea
- tachycardia/bradycardia
- lethargy, irritability
- poor feeding, vomiting, abdominal distention, diarrhea
- hypotonia, seizures, confusion, lethargy, coma
- jaundice, hepatomegaly, petechiae, purpura

Cyanosis

Approach to Neonatal Cyanosis
- 2 major types
- peripheral cyanosis
  - can be normal transiently but may indicate sepsis, temperature instability
- central cyanosis
  - 2 major categories
    - deoxygenated hemoglobin
      - respiratory
        - upper (choanal atresia, macroglossia, airway hypoplasia, laryngeal web/cyst, foreign body)
        - lower (pneumonia, meconium aspiration syndrome (MAS), pneumothorax, diaphragmatic hernia, AV fistula, pulmonary hypoplasia)
      - cardiovascular (congenital heart disease, PPHN)
      - neurologic
        - CNS (asphyxia, hemorrhage, seizure, narcotics/sedatives)
        - neuromuscular (myasthenia gravis, botulism)
      - hematologic (polycythemia)
    - sepsis
  - abnormal hemoglobin (methemoglobinemia, carboxyhemoglobinemia)
- note: while carboxyhemoglobinemia (secondary to carbon monoxide poisoning) results in impaired binding of oxygen to hemoglobin, it does not discolor the blood and may therefore not register on pulse-oximetry and cyanosis may not be evident clinically. In addition, with methemoglobinemia pulse oximetry typically reads higher than the true level of oxyhemoglobin. This is due to the fact that methemoglobin alters the absorption of red light at the two wavelengths that pulse oximetry uses to predict oxygen saturation.

Management
- ABGs
- elevated CO₂ suggests respiratory cause
- hypoxic test (to rule out CHD): get baseline pO₂ in room air, then pO₂ on 100% O₂ x 10-15 min
- pO₂ <150 mmHg; suggests congenital heart disease (see Pediatric Cardiology, 118)
- pO₂ >150 mmHg; suggests respiratory (airway, chest, lungs), brain or blood problems
- CXR - look for respiratory abnormalities (respiratory tract malformations, evidence of shunting, pulmonary infiltrates) and cardiac abnormalities (cardiomegaly, abnormalities of the great vessels).

Persistent Pulmonary Hypertension of the Newborn (PPHN)

Clinical Presentation
- incidence 1.9/1000 live births
- present within 12 hours of birth with severe hypoxemia/cyanosis but relatively mild respiratory distress

Pathophysiology
- due to persistence of fetal circulation as a result of persistent elevation of pulmonary vascular resistance
- R to L shunt through PDA, foramen ovale, intrapulmonary channels → decreased pulmonary blood flow and hypoxemia → further pulmonary vasoconstriction

Risk Factors
- asphyxia, MAS, RDS, sepsis, structural abnormalities (e.g. diaphragmatic hernia, pulmonary hypoplasia) (secondary PPHN)
- primary PPHN occurs in absence of risk factors
Investigations
- measure pre- and post-ductal oxygen levels
- echocardiogram reveals increased pulmonary artery pressure and a R → L shunt, also
  used to rule out other cardiac defects

Treatment
- maintain good oxygenation (\(\text{SaO}_2 > 95\%\)) in at risk infants
- \(\text{O}_2\) given early and tapered slowly, minimize stress and hypoxia, alkalization, inotropes
  (to make systemic pressure greater than pulmonary pressure)
- mechanical ventilation, high frequency oscillation (HFO)
- nitric oxide
- extracorporeal membrane oxygenation (ECMO) used in some centres

Apnea
- periodic breathing is a normal respiratory pattern seen in newborns during sleep in which
  periods of rapid respiration are alternated with apneic episodes lasting 5-10 seconds
- apnea: absence of respiratory gas flow for more than 15-20 seconds (or less if associated
  with bradycardia or cyanosis) – 3 types
  - central: no chest wall movement
  - obstructive: chest wall movement continues
  - mixed: combination of central and obstructive apnea

Differential Diagnosis
- in term infants, apnea always requires full work-up
- apnea <24 hrs – strongly associated with sepsis
- apnea >24 hrs
  - CNS
    - apnea of prematurity: combination of CNS prematurity and obstructive apnea,
      resolves by 36 weeks GA, diagnosis of exclusion
    - seizures
    - intracranial hemorrhage (ICH)
    - hypoxic injury
    - infectious: sepsis, meningitis, necrotizing enterocolitis (NEC)
    - GI: gastroesophageal reflux disease (GERD), aspiration with feeding
    - metabolic: hypoglycemia, hyponatremia, hypocalcemia
    - cardiovascular: low and high blood pressure, anemia, hypovolemia, PDA, heart failure
  - drugs: morphine

Management
- \(\text{O}_2\), continuous positive airway pressure (CPAP), mechanical ventilation
- tactile stimulation
- correct underlying cause
- medications – methylxanthines (caffeine) stimulate the CNS and diaphragm and are used
  for apnea of prematurity (not in term infants)

Respiratory Distress in the Newborn

Clinical Presentation
- tachypnea: RR >60/min; tachycardia: HR >160/min
- grunting, intercostal indrawing, nasal flaring
- dusky, central cyanosis
- decreased air entry, crackles on auscultation

Differential Diagnosis of Respiratory Distress
- pulmonary
  - respiratory distress syndrome (RDS)
  - transient tachypnea of the newborn (TTN)
  - meconium aspiration syndrome (MAS)
  - pleural effusions, pneumothorax
  - congenital lung malformations
- infectious
  - sepsis
  - pneumonia (GBS + others)
- cardiac
  - congenital heart disease (cyanotic, acyanotic)
  - persistent pulmonary hypertension of the newborn (PPHN)
- hematologic
  - blood loss
  - polycythemia
Treatment

- **anatomic**
  - tracheoesophageal fistula
  - congenital diaphragmatic hernia
  - upper airway obstruction (see Otolaryngology)
    - choanal atresia
    - Pierre-Robin sequence (retrognathia and/or micrognathia plus cleft palate, and glossoptosis)
    - laryngeal (malacia)
    - tracheal (malacia, vascular ring)
    - mucous plug
    - cleft palate
- **metabolic**
  - hypoglycemia
  - inborn errors of metabolism (amino acidemia, organic acidemia, urea cycle disturbance, galactosemia, 1st lactic acidosis)
- **neurologic**
  - CNS damage (trauma, hemorrhage)
  - drug withdrawal syndromes

**Investigations**

- CXR, ABG or capillary blood gas, CBC, blood glucose
- blood cultures
- ECHO, ECG if indicated

### Respiratory Distress Syndrome (RDS)

- also known as “hyaline membrane disease”

**Pathophysiology**

- surfactant deficiency → poor lung compliance due to high alveolar surface tension and atelectasis → decreased surface area for gas exchange → hypoxia + acidosis → respiratory distress
- surfactant decreases alveolar surface tension, improves lung compliance and maintains functional residual capacity
- there is usually sufficient surfactant production by 36 weeks

**Risk Factors**

- prematurity
- low birth weight
- rare at term
- maternal diabetes: insulin inhibits the cortisol surge necessary for surfactant synthesis
- C-section without labour
- asphyxia, acidosis, sepsis, meconium aspiration
- males > females
- hypothermia
- second born twin

**Clinical Presentation**

- signs of respiratory distress (tachypnea, tachycardia, grunting, intercostal indrawing, nasal flaring, cyanosis, lung crackles)
- onset within first few hours of life, worsens over next 24-72 hours
- infants may develop respiratory failure and require ventilation
- CXR: decreased aeration and lung volumes, reticulonodular pattern throughout lung fields with air bronchograms, atelectasis; may resemble pneumonia, if severe can see white-out

**Prevention**

- steroid therapy (e.g. Celestone®) for mothers (12 mg q24h x 2 doses) who are at risk of preterm birth
- monitor lecithin-sphingomyelin (L/S) ratio with amniocentesis, L/S > 2:1 indicates lung maturity
- prophylactic surfactant often given to high risk infants (<28 weeks) at birth

**Treatment**

- supportive
  - O₂ assisted ventilation (CPAP, or intubation and mechanical ventilation)
  - administer fluids cautiously to avoid pulmonary edema
- endotracheal surfactant administration

**Prognosis**

- in severe prematurity and/or prolonged ventilation, increased risk of bronchopulmonary dysplasia (BPD)/chronic lung disease

**Complications**

- bronchopulmonary dysplasia
- pulmonary air leaks (pneumothorax)
**Transient Tachypnea of the Newborn (TTN)**

- also known as "wet lung syndrome" and respiratory distress syndrome type II

**Pathophysiology**
- delayed resorption of fetal lung fluid → accumulation of fluid in peribronchial lymphatics and vascular spaces → tachypnea

**Risk Factors**
- full term or near-term infant
- no labour/short labour (hypothetical lack of catecholamine release)
- C-section (lungs are not compressed during passage through pelvic floor)
- diabetic mother/gestational weight >4500 g
- maternal asthma
- male sex

**Clinical Presentation**
- tachypnea within the first few hours of life, mild retractions, grunting, nasal flaring, without signs of severe respiratory distress
- usually resolves in 24-72 hours
- CXR: fluid in fissures, increased vascularity, slight cardiomegaly

**Treatment**
- supportive: O₂, careful fluid administration, may use CPAP

**Prognosis**
- full recovery expected within 2-5 days
- in the past it was generally believed that TTN was a self-limiting condition which, once resolved, had no long-term sequelae. Current research suggests that children with TTN may be at increased risk of developing wheezing syndromes (such as asthma) in childhood

**Meconium Aspiration Syndrome (MAS)**

- 10-15% of all infants are meconium stained at birth, ~5% of meconium stained infants get MAS
- usually associated with fetal distress in utero, or post-term infant

**Clinical Presentation**
- respiratory distress within hours of birth
- small airway obstruction, chemical pneumonitis → tachypnea, barrel chest with audible crackles
- CXR: hyperinflation, streaky atelectasis, patchy and coarse infiltrates
- 10-20% have pneumothorax

**Complications**
- hypoxemia, hypercapnea, acidosis, PPHN, pneumothorax, pneumomediastinum, pneumonia, sepsis, respiratory failure, death

**Treatment**
- supportive care, assisted ventilation (important to maintain adequate oxygenation)
- ventilated infants often require sedation
- may benefit from surfactant replacement (surfactant function is inhibited by presence of meconium)
- inhaled nitric oxide, extracorporeal membrane oxygenation at some centres

**Prevention**
- in utero: careful monitoring
- after delivery of the head: suction oro/nasopharynx
- at birth: intubate and suction below cords if infant is depressed
- note: presence of meconium staining alone is NOT an indication for tracheal suctioning
  - If the infant is vigorous, intubation and suctioning of lower airway is unnecessary

**Pneumonia**

- see *Pediatric Respiriology*, p89
- consider in infants with prolonged or premature rupture of membranes (PROM), maternal fever, or if mother GBS positive
- suspect if infant exhibits temperature instability, WBC low or left-shifted
- symptoms may be non-specific
- CXR: hazy lung + distinct infiltrates (may be difficult to differentiate from RDS)
Diaphragmatic Hernia

- if resuscitation required at birth, DO NOT mask – bag because air will enter stomach and further compress lungs; infant requires endotracheal intubation

Clinical Presentation
- respiratory distress, cyanosis
- scaphoid abdomen and barrel-shaped chest
- affected side dull to percussion and breath sounds absent, may hear bowel sounds instead
- heart sounds shifted to contralateral side
- asymmetric chest movements, trachea deviated away from affected side
- resultant pulmonary hypoplasia on affected and contralateral side
- may present outside of neonatal period
- often associated with other anomalies (cardiovascular, CNS lesions)
- CXR: portion of GI tract in thorax (usually left side), displaced mediastinum

Treatment
- surgery

Chronic Lung Disease (CLD)

- also known as BPD (bronchopulmonary dysplasia)
- most frequently associated with very preterm birth
- may develop after prolonged intubation/ventilation with high pressures and high O₂ concentration (often after ventilation for RDS)
- defined as O₂ requirement at 28 days/36 wks GA and abnormal CXR findings (lung opacification, then cysts with sites of over distention and atelectasis, appears spongy)
- chronic respiratory failure may lead to pulmonary hypertension, poor growth, and right-sided heart failure

Treatment
- no good treatments
- gradual wean from ventilator, optimize nutrition
- dexamethasone may help decrease inflammation and encourage weaning, however use of dexamethasone is associated with increased risk of adverse neurodevelopmental outcome so indications for use are limited

Prognosis
- patients with BPD continue to have significant impairment and deterioration in lung function late into adolescence
- studies show an inverse relationship between FEV₁ at school age and duration of supplemental oxygen
- some lung abnormalities may persist into adulthood including: airway obstruction, airway hyperreactivity, and emphysema
- associated with increased risk of adverse neurodevelopmental outcome

Hypoglycemia

- glucose <2.6 mmol/L (40 mg/dL)

Etiology
- decreased carbohydrate stores (premature, IUGR)
- infant of a diabetic mother (IDM): maternal hyperglycemia → fetal hyperglycemia and hyperinsulinism → hypoglycemia in the newborn infant because of high insulin levels
- sepsis
- endocrine: hyperinsulinism due to islet cell hyperplasia (e.g. Beckwith-Wiedemann syndrome), panhypopituitarism
- inborn errors of metabolism: fatty acid oxidation defects, galactosemia

Clinical Findings
- signs often non-specific and subtle: lethargy, poor feeding, irritability, tremors, apnea, cyanosis, seizures

Management
- identify and monitor infants at risk, (pre-feed blood glucose checks)
- begin oral feeds within first few hours of birth
- if hypoglycemic, provide glucose IV (D10, D12.5)
- if persistent hypoglycemia (past day 3), hypoglycemia unresponsive to IV glucose, and/or no predisposing cause for hypoglycemia, send the following “critical bloodwork” during an episode of hypoglycemia:
  - insulin
  - cortisol
  - growth hormone (GH)
  - beta-hydroxybutyrate
  - lactate
Jaundice

- jaundice visible at serum bilirubin levels of 85-120 μmol/L (5-6 mg/dL)
- look at sclera, mucous membranes, palmar creases, tip of nose, frenulum
- jaundice more severe/prolonged (due to increased retention of bilirubin in the circulation) with:
  - prematurity
  - acidosis
  - hypoalbuminemia
  - dehydration
- note: scleral icterus (yellow discolouration of the white of the eyes) is caused by bilirubin in the scleral conjunctiva (not the sclera itself)

![Figure 4. Approach to Neonatal Hyperbilirubinemia](image)

**PHYSIOLOGIC JAUNDICE**

**Epidemiology**
- term infants: onset 2-3 days of life, resolution by 7 days of life
- premature infants: higher peak and longer duration

**Pathophysiology**
- increased hematocrit and decreased RBC lifespan
- immature glucuronyl transferase enzyme system (slow conjugation of bilirubin)
- increased enterohepatic circulation

**Table 37. Risk Factors**

<table>
<thead>
<tr>
<th>Maternal Factors</th>
<th>Perinatal Factors</th>
<th>Neonatal Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnic group (e.g. Asian, native American)</td>
<td>Birth trauma (cerebral, haematoma, ecchymoses)</td>
<td>Infection</td>
</tr>
<tr>
<td>• Complications during pregnancy (e.g. of diabetic mother, if or ABO incompatibility)</td>
<td>Prematurity</td>
<td>Genetic factors</td>
</tr>
<tr>
<td>• Breast feeding</td>
<td></td>
<td>Polycythemia</td>
</tr>
</tbody>
</table>

**Table 38. Causes of Neonatal Jaundice by Age**

<table>
<thead>
<tr>
<th>&lt;24 hours</th>
<th>24-72 hours</th>
<th>72-96 hours</th>
<th>Prolonged (&gt;1 week)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALWAYS PATHOLOGIC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hemolytic</td>
<td>• Physiologic, polycythemia</td>
<td>• Physiologic ± breastfeeding jaundice</td>
<td>• Breast milk jaundice</td>
</tr>
<tr>
<td>• Rh or ABO incompatibility</td>
<td>• Dehydration (breastfeeding jaundice)</td>
<td></td>
<td>• Protracted physiologic jaundice in preterm</td>
</tr>
<tr>
<td>• Sepsis</td>
<td>• Hemolysis</td>
<td>• Hypothyroidism</td>
<td>• Neonatal hepatitis</td>
</tr>
<tr>
<td>• GBS</td>
<td>• G6PD deficiency</td>
<td></td>
<td>• Conjunctivitis dysfunction</td>
</tr>
<tr>
<td>• Congenital infection (TORCH)</td>
<td>• Pyruvate kinase deficiency</td>
<td></td>
<td>e.g. Gilbert syndrome, Crigler-Najjar syndrome</td>
</tr>
<tr>
<td></td>
<td>• Splenomegaly</td>
<td></td>
<td>Inborn errors of metabolism</td>
</tr>
<tr>
<td></td>
<td>• Jaundice, hemorrhage, hematomat</td>
<td></td>
<td>e.g. Galactosemia</td>
</tr>
<tr>
<td></td>
<td>• Sepsis/congenital infection</td>
<td></td>
<td>Bilary tract obstruction</td>
</tr>
</tbody>
</table>

**Breast Feeding Jaundice**
- common
- due to lack of milk production and subsequent dehydration, leading to exaggerated physiologic jaundice
Breast Milk Jaundice
- rare (1 in 200 breast-fed infants)
- inhibitor of glucuronyl transferase found in breast milk
- onset 7 days of life, peak at 2nd to 3rd week of life

PATHOLOGIC JAUNDICE
- must be investigated if:
  - jaundice at <24 hours of age
  - serum unconjugated bilirubin rises rapidly or is excessive for patient's age and weight (>85 μmol/L per day or >220 μmol/L before 4 days of age)
  - conjugated bilirubin >35 μmol/L (2.0 mg/dL)
  - persistent jaundice lasting beyond 1-2 weeks of age
- investigations
  - unconjugated hyperbilirubinemia:
    - hemolytic work-up: CBC, blood group (mother and infant), peripheral blood smear, Coombs test, bilirubin (conjugated, unconjugated)
    - if baby is unwell or has fever, septic work-up: CBC + differential, blood and urine cultures ± LP, CXR
    - other: TSH, G6PD screen (in males)
  - conjugated hyperbilirubinemia: consider liver enzymes (AST, ALT), coagulation studies (PT, PTT), serum albumin, ammonia, TSH, TORCH screen, septic work-up, galactosemia screen (erythrocyte galactose-1-phosphate uridylytransferase levels), metabolic screen, abdominal U/S, HIDA scan, sweat chloride

TREATMENT OF UNCONJUGATED HYPERBILIRUBINEMIA
- to prevent kernicterus (see below)
- breast feeding does not need to be discontinued, ensure adequate feeds and hydration
- get lactation consultant support, mother to pump after feeds
- treat underlying causes (e.g. sepsis)
- phototherapy
  - insoluble unconjugated bilirubin is converted to excretable form via photoisomerization
  - serum bilirubin should be monitored during and immediately after therapy (risk of rebound because photoisomerization reversible when phototherapy discontinued)
  - contraindicated in conjugated hyperbilirubinemia: results in “bronzed” baby
  - side effects: hypernatremic dehydration, eye damage, skin rash, diarrhea
  - use published guidelines for initiation of phototherapy
- exchange transfusion
  - prevents toxic effects of bilirubin by removal from body
  - indications: depending on level and rate of rise of bilirubin
  - side effects: infections, transfusional reactions
  - most commonly performed for hemolytic disease and G6PD

KERNICTERUS

Etiology
- unconjugated bilirubin concentrations exceed albumin binding capacity and bilirubin enters and is deposited in the brain resulting in permanent damage (often basal ganglia or brainstem)
- incidence increases as serum bilirubin levels increase above 340 μmol/L (19.5 mg/dL)
- can occur at lower levels in presence of sepsis, meningitis, hemolysis, hypoxia, hypothermia, hypoglycemia and prematurity

Clinical Presentation
- up to 15% of infants have no obvious neurologic symptoms
- acute form
  - first 1-2 days: lethargy, hypotonia, poor feeding, high-pitched cry, emesis, seizures
  - middle of first week: hypertonia, opisthotonic posturing, fever, bulging fontanelle, pulmonary hemorrhage
- chronic form (first year and beyond)
  - hypotonia, delayed motor skills, extrapyramidal abnormalities (choreothetoid cerebral palsy), gaze palsy, MR, sensorineural hearing loss

Prevention
- exchange transfusion

Complications
- sensorineural deafness, choreothetoid cerebral palsy (CP), gaze palsy, mental retardation

BILIARY ATRESIA
- atresia of the extrahepatic bile ducts
- cholestasis and increased conjugated bilirubin after the first week of life
- incidence: 1/10,000-15,000 live births

Clinical Presentation
- dark urine, pale stool, jaundice (persisting for >2 weeks), abdominal distention, hepatomegaly

Diagnosis
- HIDA scan
- liver biopsy
Treatment
• surgical drainage procedure
• hepatopancreatico-enterostomy (Kasai procedure most successful if before 8 weeks of age)
• usually ultimately requires liver transplantation
• Vitamins A, D, E, and K diet should be enriched with medium-chain triglycerides to ensure adequate fat ingestion

Bleeding Disorders in Neonates

Clinical Presentation
• oozing from the umbilical stump, excessive bleeding from peripheral venipuncture/heel stick sites/IV sites, large caput succedaneum, cephalohematoma (in absence of significant birth trauma), and prolonged bleeding following circumcision.

Approach to Bleeding Disorders in Neonates
• 4 major categories
  1. increased platelet destruction
     • maternal ITP, SLE
     • neonatal alloimmune thrombocytopenia (NAIT)
     • infection
     • DIC
     • drugs
     • extensive localized thrombosis
  2. decreased platelet production/function:
     • bone marrow replacement
     • pancytopenia
     • Fanconi anemia
     • trisomy 13 and 18
  3. metabolic:
     • congenital thyrotoxicosis
     • inborn error of metabolism
  4. coagulation factor deficiencies/presence of inhibitors (see Hematology)
     • haemophilia A
     • haemophilia B
     • hemorrhagic disease of the newborn

NEONATAL ALLOIMMUNE THROMBOCYTOPENIA (NAIT)

Pathophysiology
• platelet equivalent of Rh disease of the newborn
• occurs when mother is negative for human platelet antigen (HPA) and fetus is positive
• development of maternal IgG antibodies against HPA antigens on fetal platelets

Epidemiology
• 1/4000-5000 live births

Clinical Features
• clinical features: petechiae, purpura, thrombocytopenia in otherwise healthy neonate
• severe NAIT can lead to intracranial bleeding

Diagnosis
• maternal and paternal platelet typing and identification of platelet alloantibodies

Treatment
• IVIG to mother prenatally, starts in second trimester; treat neonate with IVIG and transfusion of infant with washed maternal platelets or donor HPA negative platelets

AUTOIMMUNE THROMBOCYTOPENIA

Pathophysiology
• caused by antiplatelet antibodies from maternal ITP or SLE
• passive transfer of antibodies across placenta

Clinical Presentation
• similar presentation to NAIT but bleeding usually less severe

Treatment
• steroids to mother x 10-14 days prior to delivery, or IVIG to mother before delivery or to infant after delivery
• caution: transfusion of infant with maternal or random donor platelets will result in destruction of platelets
HEMORRHAGIC DISEASE OF THE NEWBORN
- caused by vitamin K deficiency
- factors II, VII, IX, X are vitamin K-dependent, therefore both PT and PTT are abnormal

Etiology and Clinical Presentation
- neonates at risk of vitamin K deficiency because:
  - vitamin K poorly transferred across the placenta
  - insufficient bacterial colonization of colon at birth (synthesize vit K)
  - dietary intake of vitamin K inadequate in breastfed infants
- 2 types
  1. early vitamin K deficiency bleeding (VKDB)
     - caused by maternal ingestion of oral anticoagulants, anticonvulsants, or antituberculosis agents
     - presents with ICH within the first 24 hours of life
  2. classical VKDB
     - occurs in infants who did not receive vit K at birth and are breast feeding
     - presents between days 1 and 7

Prevention
- vitamin K IM administration at birth to all newborns

Necrotizing Enterocolitis (NEC)
- intestinal inflammation associated with focal or diffuse ulceration and necrosis
- primarily affecting terminal ileum and colon
- affects 1-5% of preterm newborns admitted to NICU

Pathophysiology
- postulated mechanism of bowel ischemia → mucosal damage, and enteral feeding
  providing a substrate for bacterial growth and mucosal invasion, leading to bowel necrosis or gangrene and perforation

Risk Factors
- prematurity (immature defenses)
- asphyxia, shock (poor bowel perfusion)
- hyperosmolar feeds
- enteral feeding with formula (breast milk can be protective)
- sepsis

Clinical Presentation
- distended abdomen
- increased amount of gastric aspirate/vomitus with bile staining
- frank or occult blood in stool
- feeding intolerance
- diminished bowel sounds
- signs of bowel perforation (sepsis, shock, peritonitis, DIC)

Investigations
- abdominal x-ray: intramural air (“train tracks”), free air, fixed loops, thickened bowel wall, portal venous gas
- Pneumonitis Intestinalis → gas in the bowel wall (seen on abdominal x-ray). In neonatal period, this is most commonly associated with necrotizing enterocolitis.
- CBC, ABG, blood culture
- high or low WBC, low platelets, hyponatremia, acidosis, hypoxia, hypercapnea

Treatment
- NPO (minimum 1 week), vigorous IV fluid resuscitation, NG decompression, supportive therapy
- TPN
- antibiotics (usually ampicillin, gentamicin ± metronidazole if risk of perforation x 7-10 days)
- serial abdominal x-rays detect early perforation
- peritoneal drain/surgery if perforation
- surgical resection of necrotic bowel and surgery for complications (e.g. perforation, strictures)

Intraventricular Hemorrhage (IVH)
- intracranial hemorrhage originating in the periventricular subependymal germinal matrix (GM)
- incidence and severity inversely proportional to GA

Risk Factors
- extreme prematurity, need for vigorous resuscitation at birth, pneumothorax, ventilated preterm infants, sudden increase in arterial blood pressure with volume expansion, hypotensive event, hypertension, RDS, fluctuating cerebral blood flow, coagulopathy
Clinical Presentation
- many infants with IVH are asymptomatic
- subtle signs: apnea, bradycardia, changes in tone or activity, altered level of consciousness
- catastrophic presentation: bulging fontanelle, drop in hematocrit, acidosis, seizures, hypotension

Classification
- Papile classification
  - grade I: GM hemorrhage
  - grade II: IVH without ventricular dilatation
  - grade III: IVH with ventricular dilatation
  - grade IV: GM hemorrhage or IVH with parenchymal extension
- parenchymal hemorrhage may also occur in the absence of intraventricular hemorrhage
- 50% of IVH occurs within 8 hours of birth; 90% occurs by day 3
- routine head ultrasound screening of all preterm infants <32 weeks gestation throughout NICU stay

Management of Acute Hemorrhage
- supportive care to maintain blood volume and acid-base status
- avoid fluctuations in blood pressure and cerebral blood flow
- follow-up with serial imaging

Prognosis
- outcome depends on Grade of IVH
- short-term outcomes for severe IVH: mortality, posthemorrhagic hydrocephalus (PHH), posthemorrhagic infarction
- possible long-term major neurological sequelae: cerebral palsy, cognitive deficits, motor deficits, visual and hearing impairment
- grades I and II hemorrhages have a relatively favourable prognosis
- greatest morbidity and mortality is seen with Grade 4 hemorrhage and PHH requiring ventriculoperitoneal shunt placement
- premature babies are also at risk of PVL (periventricular leukomalacia) – radiologically seen as cysts or ischemic areas in the periventricular white matter, also putting them at risk of adverse neurological outcome

Retinopathy of Prematurity (ROP)
- interruption in the growth of developing retinal vessels

Pathophysiology
- early vasoconstriction and obliteration of the capillary bed → repair response → neovascularisation
- retinal detachment occurs in a small percentage

Risk Factors
- association with period of high oxygen concentrations is now not so clear
- extreme prematurity is the most significant risk factor

Clinical Presentation
- ROP is classified by stage (I-V, with V being most severe)
- see Ophthalmology

Assessment
- ophthalmoscopic examination
  - infants with birthweight ≤1500 g or ≤30 weeks GA: starting at 4-6 weeks of chronologic age or at 32 weeks corrected age (whichever is later) with exams q2-3 weeks until retinal maturity with no disease or disease is regressing
  - infants with ROP or very immature vessels: exams q1-2 weeks

Management
- laser photocoagulation for severe prethreshold and threshold ROP
- follow-up eye examinations for myopia, strabismus, amblyopia, glaucoma, and late detachment

Prognosis
- stage I and II: 90% spontaneous regression
- stage III+: ~50% spontaneous regression; with treatment, incidence of poor visual outcome reduces by ~50%
Common Neonatal Skin Conditions

Table 39. Common Neonatal Skin Conditions

<table>
<thead>
<tr>
<th>Neonatal Skin Conditions</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasomotor Response (Cutis Marmorata, acrocyanosis)</td>
<td>Transient mottling when exposed to cold; usually normal, particularly in prems</td>
</tr>
<tr>
<td>Vernix Caseosa</td>
<td>Soft creamy white layer covering baby at birth</td>
</tr>
<tr>
<td>Slate-grey nevus of childhood (&quot;Mongolian spots&quot;)</td>
<td>Blush grey macules over lower back and buttocks (may look like bruises); common in dark skinned infants</td>
</tr>
<tr>
<td>Capillary Hemangioma</td>
<td>Raised red lesion which increases in size after birth and involutes; 50% resolved by 5 yrs, 90% by 9 yrs</td>
</tr>
<tr>
<td>Erythema Toxica</td>
<td>Erythematous vesiculo-pustular rash, lesions disappear and reappear in minutes to hours, resolves by 2 weeks</td>
</tr>
<tr>
<td>Milia</td>
<td>Lesions 1-2 mm firm white pearly papules on nose bridge, cheeks, and palate; self-resolving</td>
</tr>
<tr>
<td>Pustular melanosis</td>
<td>Brown macular base with dry vesicles, seen more commonly in African American infants</td>
</tr>
<tr>
<td>Angiomatous lesions (Salmon patch)</td>
<td>Transitory vascular capillary hemangiomas of the eyelids and neck (&quot;Angel Kiss&quot; and &quot;Stork Bite&quot;), usually disappears with age</td>
</tr>
<tr>
<td>Neonatal Acne</td>
<td>Self-resolving</td>
</tr>
</tbody>
</table>

Nephrology

Dehydration

Table 40. Assessment of Dehydration

<table>
<thead>
<tr>
<th>Point of Assessment</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume deficit</td>
<td>History, physical examination</td>
</tr>
<tr>
<td>Osmolar disturbance</td>
<td>Serum Na</td>
</tr>
<tr>
<td>Acid-base disturbance</td>
<td>Blood pH, pCO₂, bicarbonate</td>
</tr>
<tr>
<td>Potassium</td>
<td>Serum K</td>
</tr>
<tr>
<td>Renal function</td>
<td>BUN, creatinine, urine specific gravity/osmolality, urine sediment</td>
</tr>
</tbody>
</table>

Table 41. Assessment of Severity of Dehydration

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse (HR)</td>
<td>Normal, full</td>
<td>Rapid</td>
</tr>
<tr>
<td>Blood Pressure (BP)</td>
<td>Normal</td>
<td>Normal-low</td>
</tr>
<tr>
<td>Urine Output (U/O)</td>
<td>Decreased</td>
<td>Markedly decreased</td>
</tr>
<tr>
<td>Oral Mucosa</td>
<td>Slightly dry</td>
<td>Dry</td>
</tr>
<tr>
<td>Anterior Fontanelle</td>
<td>Normal</td>
<td>Sunkien</td>
</tr>
<tr>
<td>Eyes</td>
<td>Normal</td>
<td>Sunkien</td>
</tr>
<tr>
<td>Skin Turgor</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Capillary Refill</td>
<td>Normal (&lt;3 sec)</td>
<td>Normal to increased</td>
</tr>
</tbody>
</table>

% loss of Pre-Illness Body Weight

<table>
<thead>
<tr>
<th></th>
<th>&lt;2 years</th>
<th>&gt;2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>3%</td>
<td>6%</td>
<td>9%</td>
</tr>
</tbody>
</table>

Fluid and Electrolyte Therapy

Principles of Treatment

- provision of maintenance daily fluid and electrolyte requirements (see Table 42)
- PLUS replacement of deficit fluids and electrolytes (see Table 43)
- PLUS replacement of ongoing losses (consider urine output, bowel movements/diarrhea, fever)
Table 42. Maintenance Fluid and Electrolyte Requirements

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>100:50:20 Rule</th>
<th>4:2:1 Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10 kg</td>
<td>(24-hour maintenance fluids)</td>
<td>(hourly rate of maintenance fluids)</td>
</tr>
<tr>
<td>11-20 kg</td>
<td>100 cc/kg/day</td>
<td>4 cc/kg/hr</td>
</tr>
<tr>
<td>&gt;20 kg</td>
<td>50 cc/kg/day</td>
<td>2 cc/kg/hr</td>
</tr>
<tr>
<td>Electrolyte Requirements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na</td>
<td>3 mEq/kg/day</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>2 mEq/kg/day</td>
<td></td>
</tr>
<tr>
<td>Cl</td>
<td>3 mEq/kg/day</td>
<td></td>
</tr>
</tbody>
</table>

Table 43. Correction of Fluid and Electrolyte Deficits

<table>
<thead>
<tr>
<th>Dehydration</th>
<th>5%</th>
<th>10%</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isotonic (80%)</td>
<td>Na 4-5 mmol/kg</td>
<td>Na 8-10 mmol/kg</td>
<td>1/2 total replacement over 1st 8 hours, then 1/2 over 18 hours</td>
</tr>
<tr>
<td>Hypotonic (9%)</td>
<td>Na 5-6 mmol/kg</td>
<td>Na 10-12 mmol/kg</td>
<td>If Na &gt;105, correct as above</td>
</tr>
<tr>
<td>Hypertonic (1%)</td>
<td>Na 2-4 mmol/kg</td>
<td>Na 2-4 mmol/kg</td>
<td>Correct over 48-72 hours</td>
</tr>
</tbody>
</table>

Note: For all types dehydration, H2O for 5% dehydration = 50mL/kg; for 10% dehydration = 100 mL/kg
To calculate exact deficit: (Na deficit) = [(Na target - (Na actual) x body weight (kg) x total body water (L)]
To lower serum Na by a predictable amount, remember: 4 mL/kg of free H2O lowers serum Na by 1 mmol/L.

Common IV Fluids
- first month of life: D5W/0.2 NS + 20 mEq KCl/L (only add KCl if voiding well)
- children: D5W/0.9 NS + 20 mEq KCl/L or D5W/0.45 NS + 20 mEq KCl/L
- NS: as bolus to restore circulation in dehydrated children

Table 44. Common Manifestations of Renal Disease

<table>
<thead>
<tr>
<th>Nephrology</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate</td>
<td></td>
</tr>
<tr>
<td>Renal mass</td>
<td>Dysplasia, polycystic disease, hydronephrosis, tumour</td>
</tr>
<tr>
<td>Hematuria</td>
<td>Asphyxia, malformation, trauma, renal vein thrombosis</td>
</tr>
<tr>
<td>Anuria/eluguria</td>
<td>Agenesis, obstruction, asphyxia</td>
</tr>
<tr>
<td>Child and Adolescent</td>
<td>Differential Diagnosis</td>
</tr>
<tr>
<td>Colored/cardioue urine</td>
<td>Hemoglobinuria (hemolysis)</td>
</tr>
<tr>
<td>Gross hematuria</td>
<td>Myoglobinuria (rhabdomyolysis)</td>
</tr>
<tr>
<td></td>
<td>Hematuria (e.g. glomerulonephritis), pigmenturia</td>
</tr>
<tr>
<td>Edema</td>
<td>Glomerulonephritis, benign hematuria, trauma, cystitis, tumour, stones</td>
</tr>
<tr>
<td></td>
<td>Nephrotic syndrome, nephritis, acute/chronic renal failure (also consider cardiac or liver disease)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Acute glomerulonephritis, renal failure, dysplasia (also consider coarctation of aorta, drugs, endocrine causes)</td>
</tr>
<tr>
<td>Polyuria</td>
<td>DM, central and nephrogenic diabetes insipidus, hypercalcemia, polyuic renal failure</td>
</tr>
<tr>
<td>Oliguria</td>
<td>Dehydration, acute tubular necrosis (ATN), interstitial nephritis</td>
</tr>
<tr>
<td>Urgency</td>
<td>Urinary tract infection (UTI), vaginitis</td>
</tr>
</tbody>
</table>

Hematuria
- definition: five or more RBC/hpf, in three consecutive centrifuged urine samples
- 0.5-2% prevalence of asymptomatic microscopic hematuria in school-aged children
- history of prior acute infection (upper respiratory, skin or GI)
- family history: dialysis, transplant, SLE, familial hematuria
- physical exam: BP, edema, rash, arthritis

Etiology
- nephrologic
  - glomerular disease
    - recurrent gross hematuria: IgA nephropathy, benign familial hematuria, Alport syndrome
    - post-streptococcal GN, lupus nephritis, HSP, HUS, Goodpasture disease (rare in childhood)
  - tubulo-interstitial: ATN, interstitial nephritis, pyelonephritis, hypercalcuria
- infection: bacterial, TB, viral, UTI, pyelonephritis

Causes of Coloured Urine with Negative Dipstick
- URINE BLEAD
- Urates
- Rifampin
- Ibuprofen
- Nicotinamide
- Exogenous (food colouring)
- Beets
- Lead
• hematologic: coagulopathies, thrombocytopenia, sickle cell disease or trait, renal vein thrombosis
• anatomic abnormalities: congenital, trauma, polycystic kidneys, vascular abnormalities, tumours (Wilms)
• other: exercise, drugs

Approach to Hematuria

1. Gross Hematuria (visible blood in urine) – must confirm presence of RBCs
   - UTI
   - perineal irritation (pinworm, anal fissure)
   - coagulopathy
   - trauma
   - nephrolithiasis
   - proteinuria, hypercalciuria
   - tumour
   - glomerular
     - IgA nephropathy
     - glomerular basement membrane disorders
     - Alport syndrome
     - benign familial hematuria
     - postinfectious glomerulonephritis
     - Henoch-Schonlein purpura nephritis
     - SLE nephritis
   - urinalysis (U/A)
     - renal source
     - cola/tea-coloured urine
     - casts, proteinuria, dysmorphic RBCs
     - associated symptoms and signs (e.g. edema, azotemia, hypertension)
     - post-renal source
     - bright red urine, initial and terminal stream hematuria, clots
     - normal RBC morphology, <2+ proteinuria, no casts
     - very large renal bleeding can look like a lower urinary tract bleed

2. Symptomatic Microscopic Hematuria
   - UTI
   - acute glomerulonephritis
   - familial hematuria
   - Henoch-Schonlein purpura (HSP)
   - SLE
   - HTN
   - hypercalciuria
   - nephrolithiasis
   - tumour

3. Asymptomatic Microscopic Isolated Hematuria
   - benign familial hematuria in 2/3 of cases
   - dipstick sensitive, but high false positive rate:
     - 5% of school-aged children positive on a single urine dipstick
     - with repeat testing <0.5% will have persistent hematuria
   - repeat 2-3 samples over 2-3 weeks and monitor for clinical symptoms

4. Asymptomatic Microscopic Hematuria
   - definition: 5-10 RBC/HPF of centrifuged urine
   - dipsticks are very sensitive, but have a high false positive rate
     - 5% of school-aged children have a false positive on a single test but <1% on repeated testing
   - mild/early acute glomerulonephritis
   - benign familial hematuria in 2/3 of cases (no associated proteinuria)
   - tumour

Investigations

• CBC, urine dip and culture, creatinine, BUN, 24-hr urine collection for creatinine and protein, Ca, serum C3 and C4 level
• if suspected postinfectious glomerulonephritis: antistreptolysin O titer, ANA, throat swab
• if above do not yield a diagnosis, consider U/S ± Doppler to rule out structural anomalies
• treat underlying cause if applicable
  - supportive treatment (e.g. antihypertensives, fluid restriction, dietary modifications)
  - referral to pediatric nephrologist
  - may warrant renal biopsy depending on findings
Proteinuria

- a small amount of protein is found in the urine of healthy children <4 mg/m²/h or <100 mg/m²/d
- definition
  - qualitative: 1+ in dilute, 2+ in concentrated urine (specific gravity >1.015)
  - quantitative: >4 mg/m²/h on timed urine (>40 mg/m²/h is nephrotic range)
  - urine dipstick is the least accurate (false positives if urine pH <8 or SG >1.025)
  - protein/creatinine ratio on spot urine is more accurate (normal <0.5 if 6 mo-2 yrs; <0.2 if over 2 yrs)
  - 24-hour protein is the most accurate (normal <100 mg/m²/day)
  - microalbuminuria assesses risk of progressive glomeronephropathy in diabetes (normal <30 mg albumin/gram creatinine on first morning void)
- progressive proteinuria is the best predictor of renal disease
- transient proteinuria: due to fever (>38.3°C/101°F), dehydration, exercise, seizures, stress
- persistent proteinuria (>1+ on dipstick)
  - orthostatic (more common in adolescents – usually benign): elevated protein excretion when upright and normal when recumbent; rarely exceeds 1 g/m²/d
  - glomerular (e.g. nephrotic syndrome, glomerulonephritis)
  - tubulointerstitial (e.g. Fanconi syndrome, ATN)
  - structural abnormalities of urinary tract (e.g. hydronephrosis)

Hemolytic Uremic Syndrome (HUS)

Epidemiology
- most common cause of acute renal failure in children
- more common from 6 months to 4 years of age

Pathophysiology
- E. coli O157:H7 verotoxin ("hamburger disease") or shiga toxin
  - toxin binds, invades and destroys colonic epithelial cells, causing bloody diarrhea
  - toxin enters the systemic circulation, attaches and injures endothelial cells (especially in kidney) causing a release of endothelial products (e.g. von Willebrand factor, platelet aggregating factor)
  - form platelet/fibrin thrombi in multiple organ systems (e.g. renal, pancreas, brain) resulting in thrombocytopenia
  - RBCs are forced through occluded vessels resulting in fragmented RBC (schistocytes) and removed by the reticuloendothelial system (hemolytic anemia)
  - other, rare forms of HUS in childhood are due to bacteria (e.g. S. pneumoniae), viruses, familial inheritance, or drugs

Clinical Presentation
- triad: acute renal failure, thrombocytopenia, microangiopathic hemolytic anemia
- initial presentation of abdominal pain and diarrhea, followed by bloody diarrhea
• within 5-7 days the patient begins to show signs of anemia, thrombocytopenia and renal insufficiency
  • history: weakness, lethargy, oliguria
  • physical exam: pallor, jaundice (hemolysis), edema, petechiae, hypertension

Investigations
• CBC, platelets, blood smear, urinalysis, BUN, creatinine, stool culture and shigella toxin assay

Treatment
• supportive treatment; nutritional support; monitor electrolytes; dialysis if electrolyte abnormality cannot be corrected, fluid overload, or BUN >100 mg/dL; PRBC for symptomatic anemia
• steroids not helpful; antibiotics not indicated

Prognosis
• 5-10% mortality, 10-30% kidney damage

Nephritic Syndrome

• acute, subacute or chronic
  • hematuria with RBC casts, proteinuria (<50 mg/kg/day, not nephrotic-range), azotemia, hypertension
  • renal failure (oliguria)

POST-STREPTOCOCCAL GLOMERULONEPHRITIS

Risk Factors
• most common in children, aged 4 to 8 year old, M > F
• occurs 1-3 weeks following group A beta-hemolytic streptococcal infection of skin or throat

Pathophysiology
• antigen-antibody mediated complement activation
• diffuse, proliferative glomerulonephritis

Diagnosis
• elevated serum antibody titres against strep antigens (ASOT, anti DNAseB)

Prognosis
• 95% of children recover completely within 1-2 weeks
• 5-10% have persistent hematuria

Management
• symptomatic treatment: fluid restriction, antihypertensives, diuretics
• in severe cases: hemodialysis or peritoneal dialysis may be necessary
• eradication of infection (penicillin or erythromycin)

Table 45. Major Causes of Acute Glomerulonephritis

<table>
<thead>
<tr>
<th></th>
<th>Decreased C3</th>
<th>Normal C3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-infectious GMIN</td>
<td>IgA Nephropathy</td>
<td></td>
</tr>
<tr>
<td>Membranoproliferative</td>
<td>Idiopathic rapidly progressive GMIN</td>
<td></td>
</tr>
<tr>
<td>Type I (50-80%)</td>
<td>Anti-GBM disease</td>
<td></td>
</tr>
<tr>
<td>Type II (&gt;80%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>Polyarteritis nodosa</td>
<td></td>
</tr>
<tr>
<td>SBE</td>
<td>Wegener’s granulomatosis</td>
<td></td>
</tr>
<tr>
<td>Shunt nephritis</td>
<td>Goodpasture’s syndrome</td>
<td></td>
</tr>
<tr>
<td>Cryoglobulinemia</td>
<td>Henoch-Schönlein purpura (HSP)</td>
<td></td>
</tr>
</tbody>
</table>

Nephrotic Syndrome

Clinical Presentation
• severe proteinuria (>50 mg/kg/day or >40 mg/m²/hr)
• hypoalbuninemia (<20 g/L (<2.0 g/dL))
• edema (usually first sign, initially see facial swelling, especially periorbital, and pretibial edema)
• hyperlipidemia >5.17 mmol/L (200 mg/dL)
• secondary findings: hypocalcemia, hyperkalemia, hyponatremia, hypercoagulability (decreased PTT)
Etiology
Primary Nephrotic Syndrome
- minimal change disease (MCD) (76%)
  - peak occurrence between 2-6 years of age, more common in boys than girls (2:1)
  - often treated empirically with steroids without kidney biopsy, 90% steroid responsive
- membranous glomerulonephritis (8%)
- focal segmental glomerular sclerosis (FSGS) (7%)
- membranoproliferative glomerulonephritis (5%)

Secondary Nephrotic Syndrome
- vasculitis
- infections (e.g. hepatitis B & C, syphilis, HIV)
- medications (e.g. captopril, penicillamine, NSAIDs, anticonvulsants)
- malignancy
- hereditary (e.g. sickle cell disease, Alport syndrome)
- metabolic, inflammatory (e.g. lupus nephropathy, rheumatoid arthritis)

Complications
- risk of infections (e.g. spontaneous peritonitis, cellulitis, sepsis)
- hypercoagulability due to decreased intravascular volume and antithrombin III depletion
  (pulmonary embolism, renal vein thrombosis)
- side effects of drugs (diuretics, steroids, immunosuppressants)
- hypotension, shock, renal failure

Investigations
- to rule out secondary causes of NS: serum complement levels, BUN, Cr, serum chemistries,
  ANA, antistreptolysin O titre, in certain cases HIV, Hep B/C and syphilis titers
- consider kidney biopsy if
  - HTN (higher risk of FSGS), steroid resistant, frequent relapses (>2 relapses in 6 month period),
    low serum complement, severely decreased renal function
  - presentation before first year of life (high likelihood of congenital nephrotic syndrome)
  - presentation after 10 years of age to rule out more serious renal pathology than MCD

Management
- salt and water restriction, diuretic may be required
- optimal nutrition, including high-quality protein
- daily weights to assess therapeutic progress
- varicella antibody titre if not immune
- pneumococcal vaccine after remission (avoid live vaccines)
- initial treatment of MCD
  - oral prednisone (or equivalent) 60 mg/m²/day in divided doses (max. dose 80 mg/day) for up to 12 weeks
  - a negative tuberculin skin test should be performed before starting steroid medications
  - a measurable decrease in protein excretion may take at least 7 to 10 days following
    initiation of treatment, and proteinuria clears by third week of oral prednisone
  - up to 2/3 of patients experience relapses
  - if unresponsive to steroids, frequent relapses or steroid-resistant (proteinuria continues
    beyond 3 months)
  - consider renal biopsy or treat with cytotoxic agent (i.e. cyclophosphamide or
    chlorambucil), immunomodulating agents such as levamisole and cyclosporine A,
    and high-dose pulse corticosteroid with guidance of a pediatric nephrologist

Hypertension in Childhood

Etiology
- consider white coat hypertension for all ages

Table 46. Etiology of Childhood Hypertension by Age Group

<table>
<thead>
<tr>
<th>System</th>
<th>&lt;1 year</th>
<th>1-6 years</th>
<th>7-12 years</th>
<th>&gt;13 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Coarctation of the aorta</td>
<td>Neuroblastoma</td>
<td>Coarctation of aorta</td>
<td>Essential hypertension</td>
</tr>
<tr>
<td>Endocrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>Renal artery/vein thrombosis</td>
<td>Renal artery steatomatisis</td>
<td>Renal parenchymal disease</td>
<td>Renal parenchymal disease</td>
</tr>
<tr>
<td></td>
<td>Congenital renal disease</td>
<td>Renal parenchymal disease</td>
<td>Renal parenchymal disease</td>
<td>Renal parenchymal disease</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Bronchopulmonary dysplasia</td>
<td>Hypercalcemia</td>
<td></td>
<td>Essential hypertension</td>
</tr>
</tbody>
</table>
Table 47. 95th Percentile Blood Pressures (mmHg)

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50th Percentile for Height</td>
<td>75th Percentile for Height</td>
</tr>
<tr>
<td>1</td>
<td>104/58</td>
<td>105/59</td>
</tr>
<tr>
<td>6</td>
<td>111/73</td>
<td>112/73</td>
</tr>
<tr>
<td>12</td>
<td>123/60</td>
<td>124/61</td>
</tr>
<tr>
<td>17</td>
<td>129/64</td>
<td>130/65</td>
</tr>
</tbody>
</table>

Adapted from “Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents working group report from the National High Blood Pressure Education Program”.

Investigations
- labs
  - urine dipstick for blood and protein (suggests renal disease)
  - urine catecholamines and their metabolites (may suggest pheochromocytoma)
  - electrolytes, creatinine, catecholamines, renin, aldosterone
- imaging
  - echocardiography
  - abdominal U/S
  - doppler studies, angiography, or radionuclide imaging of renal arteries

Management
- treat underlying cause
- weight reduction, reduction in salt intake, exercise
- first line antihypertensives are thiazide diuretics, but none of the antihypertensives have been formally studied in children
- referral to specialist
- medications used in hypertensive emergencies: nifedipine, hydralazine, labetalol, sodium nitroprusside
- assessment and management of end organ damage (e.g. retinopathy, LVH)

Neurology

Seizure Disorders
- see Neurology

Differential Diagnosis of Seizures in Children
- benign febrile seizure (most common)
- hypoxic ischemic encephalopathy ("asphyxia")
- intracranial hemorrhage, trauma
- metabolic causes (e.g. hypoglycemia, hypocalcemia, hyponatremia)
- CNS infection
- idiopathic epilepsy and epileptic syndromes
- neurocutaneous syndromes
- CNS tumour
- arteriovenous malformation
- ingestions/drug withdrawal
- rule out conditions that mimic seizure:
  - breath holding
  - night terror
  - benign paroxysmal vertigo
  - narcolepsy
  - pseudoseizure
  - syncope
  - tic
  - hypoglycemia
  - TIA

Investigations
- CBC, electrolytes, calcium, magnesium, glucose
- toxicology screen if indicated
- EEG, CT, LP, if indicated
  - EEG may be indicated for first-time non-febrile seizure
  - EEG/CT not indicated for benign febrile seizures recurrence risk, determine seizure type, or epileptic syndrome

Heart problems such as long QT syndrome and hypertrophic cardiomyopathy are often misdiagnosed as epilepsy. Include cardiac causes of syncope in your differential diagnosis, particularly when the episodes occur during physical activity.
CHILDHOOD EPILEPTIC SYNDROMES

Infantile Spasms
- onset 4-8 months
- brief, repeated symmetric contractions of neck, trunk, extremities (flexion and extension) lasting 10-30 seconds
- occur in clusters; often associated with developmental delay
- 20% unknown etiology; may have good response to treatment
- 80% due to metabolic or developmental abnormalities, encephalopathies, or are associated with neurocutaneous syndromes; these have poor response to treatment
- can develop into West syndrome (infantile spasms, psychomotor developmental arrest, and hyperarrhythmia) or Lennox Gastaut
- typical EEG: hypersynchrony (high voltage slow waves, spikes and polyspikes, background disorganization)
- treatment: ACTH, vigabatrin, benzodiazepines

Lennox-Gastaut
- onset commonly 3-5 years of age
- characterized by triad of 1) multiple seizure types, 2) diffuse cognitive dysfunction and 3) slow generalized spike and slow wave EEG
- seen with underlying encephalopathy and brain malformations
- treatment: valproic acid, benzodiazepines and ketogenic diet; however, response often poor

Juvenile Myoclonic Epilepsy (Janz)
- adolescent onset (12-16 years of age); autosomal dominant with variable penetrance
- myoclonus particularly in morning; frequently presents as generalized tonic-clonic seizures
- typical EEG: 3-5 Hz irregular spike and wave, increased with photic stimulation
- requires lifelong treatment (valproic acid); prognosis excellent

Childhood Absence Epilepsy
- multiple absence seizures per day that may generalize in adolescence or resolve spontaneously
- peak age of onset 6-7, F>M, strong genetic predisposition
- each seizure is less than 30 seconds, no post-ictal state, may have multiple seizures per day
- typical EEG: 3/sec spike and wave
- treatment: valproic acid or ethosuximide

Benign Focal Epilepsy of Childhood with Rolandic/Centrotemporal Spikes
- onset peaks at 5-10 years of age, 16% of all non-febrile seizures
- focal motor seizures involving tongue, mouth, face, upper extremity usually occurring in sleep-wake transition states
- remains conscious but aphasic post-ictally
- remits spontaneously in adolescence; no sequelae
- typical EEG: repetitive spikes in centrotemporal area with normal background
- treatment: frequent seizures controlled by carbamazepine, no medication if infrequent seizures

Treatment
- anticonvulsants often initiated if >2 unprovoked afebrile seizures within 6-12 months
  1. initiate: treatment with drug appropriate to seizure type
  2. optimize: start with one drug and increase dosage until seizures controlled
  3. if no effect, switch over to another before adding a second anticonvulsant
  4. continue anticonvulsant treatment until patient free of seizures for 2 years or more, then wean medications over 6-12 months
- ketogenic diet (high fat diet) – used in patients who do not respond to polytherapy or who do not wish to take medication (valproic acid contraindicated in conjunction with ketogenic diet because may increase hepatotoxicity)
- education for patient and parents
- privileges and precautions in daily life (e.g., buddy system, showers instead of baths)
- legal obligation to report to Ministry of Transportation if patient wishes to drive, Ministry will determine if driver’s license is permitted

Generalized and Partial Seizures
- see Neurology, p8
Benign Febrile Seizures

Epidemiology
- most common cause of seizure in children
- 3-5% of all children, M>F
- age 6 months-6 years

Clinical Presentation
- thought to be associated with initial rapid rise in temperature
- no neurologic abnormalities or developmental delay before or after seizure
- no evidence of CNS infection/inflammation before or after seizure
- no history of non-febrile seizures
- duration <15 minutes (95% <5 minutes)
- generalized tonic-clonic, symmetric
- does not recur in a 24-hour period

Complex Febrile Seizure
- any one of the following features
  - focal onset, focal features during the seizure, or neurological deficit after
  - duration >15 minutes
  - recurrent seizures (>1 in 24-hour period)
  - previous neurological impairment
  - these seizures are not the benign, simple type, and require further investigations

Risk Factors for Recurrence
- 33% chance of recurrence, 75% recur within 1 year
- 50% chance of recurrence if <1 year of age
- 28% chance of recurrence if >1 year of age
- family history of febrile seizures or epilepsy
- risk factors include developmental or neurological abnormalities of child prior to seizures, family history of non-febrile seizures, and an atypical initial seizure, multiple simple febrile seizures

Workup
- history: determine focus of fever, description of seizure, meds, trauma history, development, family history
- exam: LOC, signs of meningitis, neurological exam
- septic work-up including LP if suspected meningitis (if child <12 months, strongly consider doing an LP; if child is 12-18 months, consider including an LP; if child >18 months, do LP if meningeal signs)
- EEG not warranted unless complex febrile seizure or abnormal neurologic findings
- if simple febrile seizure, investigations unnecessary except for determining focus of fever

Management
- counsel and reassure patient and parents (febrile seizures do not cause brain damage, very small risk of developing epilepsy; 9% in child with multiple risk factors 2% in child with febrile simple seizures compared to 1% in general population)
- antipyretics (e.g. acetaminophen) and fluids for comfort (neither prevent seizure)
- prophylaxis not recommended
- if high risk for recurrent or prolonged seizures, have rectal or sublingual lorazepam at home (danger of lorazepam is that it may hide signs of a CNS infection)
- treat underlying cause of fever, (e.g. otitis media)

Recurrent Headache
- see Neurology

Assessment
- if unremarkable history, and neurological and general physical exam is negative, likely diagnosis is migraine or tension-type headache
- obtain CT or MRI if history or physical reveals red flags
- inquire about level of disability, academic performance, after-school activities

Differential Diagnosis
- primary headache: tension, migraine, cluster
- secondary headache: see Neurology

MIGRAINE
- 4-5% of school aged children
- prevalence F:M = 2:1 after puberty
- heterogeneous autosomal dominant inheritance with incomplete penetrance (majority of patients have a positive family history)
Types
- common (without aura) – most common in children, associated with intense nausea and vomiting
- classic (with aura)
- complicated: e.g. basilar, ophthalmoplegic, confusional, hemiplegic

Clinical Features
- in infancy, symptoms include spells of irritability, sleepiness, pallor, and vomiting
- in a young child, symptoms include periodic headaches with nausea and vomiting; relieved by rest
- usually unilateral throbbing headaches in kids with photophobia or phonophobia

Prognosis and Treatment
- over 50% of children undergo spontaneous prolonged remission after 10 years of age
- early anaesthesia (ibuprofen) and rest in quiet, dark room
- non-pharmacological treatment and prophylaxis: avoid triggers (poor sleep, stress, cheese, chocolate, caffeine), biofeedback techniques, exercise
- pharmacological prophylaxis: beta-blockers (propranolol), antihistamines, antidepressants (e.g. amitriptyline), calcium-channel blockers, anticonvulsants (e.g. divalproex sodium)
- children >12 years can use sumatriptan nasal spray, other tryptans

TENSION HEADACHES
- usually consists of bilateral pressing tightness anywhere on the cranial or suboccipital region, usually frontal, hurting or aching quality, non-throbbing
- last 30 minutes to days, waxes and wanes, may build in intensity during the day
- no nausea/vomiting, not aggravated by routine physical activity
- most children have insight into the origin of headache: poor self-image, fear of school failure
- red flag: sudden mood changes, disturbed sleep, fatigue, withdrawal from social activities, chronic systemic signs (e.g. weight loss, fever, anorexia, local neurological signs)
- treatment
  - reassurance and explanation about how stress may cause a headache
  - rule out refractory errors in eyesight as cause of headache
  - mild analgesia (NSAIDs, acetaminophen)
  - supportive counselling

ORGANIC HEADACHES
- organic etiology often suggested with occipital headache and red flags below
- with increased ICP
  - etiology: brain tumors, hydrocephalus, meningitis, encephalitis, cerebral abscess, pseudotumor cerebri, subdural hematoma
  - characteristics: diffuse early morning headaches, early morning vomiting, headache worsened by increased ICP (cough, sneeze, Valsalva); as ICP increases, headache is constant and child is lethargic and irritable
- without increased ICP
  - etiology: cerebral arteriovenous malformation (AVM), aneurysm, collagen vascular diseases, subarachnoid hemorrhage, stroke

Hypotonia
- decreased resistance to movement – “floppy baby”
- proper assessment of tone requires accurate determination of gestational age
- evaluate
  - spontaneous posture (spontaneous movement, movement against gravity, frog-leg position) important in evaluation of muscle weakness
  - joint mobility (hyperextensibility)
  - muscle bulk, presence of fasciculations
  - postural maneuvers
    - traction response – pull to sit, look for flexion of arms to counteract traction and head lag
    - axillary suspension – suspend infant by holding at axilla and lifting; hypotonic babies will slip through grasp because of low shoulder girdle tone
    - ventral suspension – infant is prone and supported under the abdomen by one hand; infant should be able to hold up extremities; inverted “U” posturing demonstrates hypotonia, i.e. baby will drape self over examiner’s arms
  - investigations will depend on history and physical exam
    - rule out systemic disorders
    - blood glucose
    - enhanced CT of brain
    - peripheral CK, EMG, muscle biopsy
    - chromosome analysis, genetic testing
  - treatment: counsel parents on prognosis and genetic implications; refer patients for specialized care, refer for rehabilitation, OT, PT, assess feeding ability

Differential Diagnosis
- central
  - chromosomal (e.g. Down syndrome, Prader-Willi, Fragile X)
  - metabolic (e.g. hypoglycemia, kernicterus)
Treatment

- perinatal problems (e.g. asphyxia, ICH)
- endocrine (e.g. hypothyroidism, hypopituitarism)
- infections (e.g. TORCH)
- CNS malformations
- dysmorphic syndromes
- peripheral
  - motor neuron (e.g. spinal muscular atrophy, polio)
  - peripheral nerve (e.g. Charcot-Marie-Tooth syndrome)
  - neuromuscular junction (e.g. myasthenia gravis)
  - muscle fibres (e.g. mitochondrial myopathy, muscular dystrophy, myotonic dystrophy)

Cerebral Palsy (CP)

- a symptom complex, not a disease
- nonprogressive central motor impairment syndrome due to insult to or anomaly of the immature CNS, extent of intellectual impairment varies, presentation of the impairment changes with age
- incidence: 1.5-2.5:1,000 live births (developing countries)
- life expectancy is dependent on the degree of mobility and intellectual impairment, not on severity of CNS lesion

Etiology

- often obscure, no definite etiology identified in 1/3 of cases
  - only 10% related to intrapartum asphyxia
  - 10% due to postnatal insult (infections, asphyxia, prematurity with intraventricular hemorrhage and trauma)
  - association with low birth weight babies

Clinical Presentation

Table 48. Types of Cerebral Palsy

<table>
<thead>
<tr>
<th>Type</th>
<th>% of Total CP</th>
<th>Characteristics</th>
<th>Area of Brain Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spastic</td>
<td>70-80%</td>
<td>Truncal hypotonia in 1st year</td>
<td>UMN of pyramidal tract</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased tone, increased reflexes, clonus</td>
<td>Diplegia associated with periventricular leukomalacia (PVL) in premature babies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Affects one limb (monoplegia), one side of body (hemiplegia), both legs (diplegia), both arms and legs (quadriplegia)</td>
<td>Quadriplegia associated with HIE (asphyxia), associated with higher incidence of MRI</td>
</tr>
<tr>
<td>Athetoid</td>
<td>10-15%</td>
<td>Athetosis (involuntary writhing movements)</td>
<td>Basal ganglia (may be associated with kernicterus)</td>
</tr>
<tr>
<td>Dyskinetic</td>
<td></td>
<td>Athetosis (involuntary jerky movements)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Can involve face, tongue (results in dysarthria)</td>
<td></td>
</tr>
<tr>
<td>Ataxic</td>
<td>&lt;5%</td>
<td>Poor coordination, poor balance (wide based gait)</td>
<td>Cerebellum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Can have intention tremor</td>
<td></td>
</tr>
<tr>
<td>Atonic</td>
<td>&lt;5%</td>
<td>Marked hypotonia, hyperreflexia, severe cognitive delay</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>10-15%</td>
<td>More than one of the above motor patterns</td>
<td></td>
</tr>
</tbody>
</table>

Other Signs

- swallowing: incoordination – aspiration
- microcephaly (25%)
- seizures
- mental retardation, learning disabilities
- delay in motor milestones

Investigations

- may include metabolics, chromosome studies, serology, neuroimaging, EMG, EEG (if seizures), ophthalmology, audiology

Treatment

- maximize potential through multidisciplinary services; important for family to be connected with various support systems
- orthopaedic management (e.g. dislocations, contractures, rhizotomy)
- management of symptoms: spasticity (baclofen, botox), constipation (stool softeners)

Neurocutaneous Syndromes

- characterized by tendency to form tumours of CNS, PNS, viscera and skin

Neurofibromatosis Type I (NF-1)

- autosomal dominant but 50% are the result of new mutations
- also known as von Recklinghausen disease
- incidence 1:3000, mutation in NFI gene on 17q11.2 (codes for neurofibrin protein)
- learning disorders, abnormal speech development, and seizures are common

In neurocutaneous syndromes, the younger the child at presentation, the more likely they are to develop mental retardation.
• diagnosis of NF-1 requires 2 or more of
  • >6 café-au-lait spots (>5 mm if prepubertal, >1.5 cm if postpubertal)
  • >2 neurofibromas of any type or one plexiform neurofibroma
  • >2 Lisch nodules (hamartomas of the iris)
  • optic glioma
  • freckling in the axillary or inguinal region
  • a distinctive bony lesion (e.g. sphenoid dysplasia, cortical thinning of long bones)
  • a first degree relative with confirmed NF-1

Neurofibromatosis Type II (NF-2)
• autosomal dominant
• incidence 1:33,000
• characterized by predisposition to form intracranial, spinal tumours
• diagnosed when either bilateral vestibular schwannomas found, or a first-degree relative
  with NF-2 and either a neurofibroma, meningioma, glioma, or schwannoma
• also associated with posterior subcapsular cataracts
• treatment consists of monitoring for tumour development and surgery

Sturge-Weber Syndrome
• port-wine nevus syndrome in V1 distribution with associated angiomatic malformations
  of brain causing contralateral hemiparesis and hemiatrophy, also associated with seizure,
  glaucoma and mental retardation

Tuberous Sclerosis
• autosomal dominant inheritance; 50% new mutations
• adenoma sebaceum (angioikeratomas on face, often in malar distribution), Shagreen patch
  (isolated raised plaque over lower back, buttocks), “ash leaf” hypopigmentation seen with
  Wood’s lamp (UV light)
• cardiac rhabdomyomas, kidney angiomyolipoma, mental retardation and seizures
• cerebral cortex tubers (areas of cerebral dysplasia); subependymal nodules (SEN) may
  evolve into giant cell astrocytomas (may cause obstructive hydrocephalus)
• calcifications within the SEN are seen on CT, MRI (especially around the foramen
  of Munro); these may obstruct the foramen and cause hydrocephalus

Acute Disseminated Encephalomyelitis (ADEM)

Epidemiology
• median age of onset 5-8 years
• male predominance (F:M — 0.6:1)
• annual incidence in North America is estimated to be 0.4 per 100,000 children <20 yrs of age

Pathophysiology
• Acute Disseminated Encephalomyelitis (ADEM) is an immune-mediated inflammatory
  disorder of the central nervous system, seen in children
• characterized by a widespread demyelination that predominantly affecting the white
  matter of the brain and spinal cord (similar to Multiple Sclerosis)
• usually preceded by a viral infection or vaccination, and is therefore commonly categorized
  as either post-vaccination or post-infectious
• absence of clear precedent event has been reported in 26% of patients

Clinical Presentation
• often occurs 2 days to 4 weeks after a clinically evident infection or vaccination
• headache, nausea, vomiting
• pyrexia/malaise
• rapid onset encephalopathy
• multifocal deficits
• seizures
• pyramidal syndrome
• cerebellar ataxia
• brainstem involvement
• clinical course is rapidly progressive and usually develops over hours to maximum deficits
  within days

Investigations
1. Lumbar puncture → CSF showing variable pleocytosis and oligoclonal banding
2. MRI → large, multifocal, poorly marginated regions of demyelination affecting bilateral
  subcortical white matter, and deep grey matter (thalamus, basal ganglia); lesions show
  complete or partial resolution on follow-up, with absence of new clinically silent lesions

Treatment
• high dose corticosteroids and supportive measures

Prognosis
• favourable, though some residual deficits often exist
Oncology

- cancer is second most common cause of death in children after 1 year of age (injuries are first)
- cause is rarely known, but increased risk with
  - chromosomal syndromes
  - prior malignancy
  - neurocutaneous syndromes
  - immunodeficiency syndromes
  - family history
  - exposure to radiation, chemicals, biologic agents
- leukemias are the most common type of pediatric malignancy (40%), followed by brain tumours (29%), and lymphomas (15%)
- some malignancies are more prevalent in certain age groups
  - newborns: neuroblastoma, other embryonal tumours e.g. Wilms' tumour (nephroblastoma), retinoblastoma
  - infancy and childhood: leukemia, neuroblastoma, Wilms' tumour, retinoblastoma
  - adolescence: lymphoma, gonadal tumours, bone tumours
- unique treatment considerations because radiation, chemotherapy, and surgery can impact growth and development, endocrine function and fertility
- most children do survive – treatments have led to remarkable improvements in overall survival and cure rates for many pediatric cancers

Leukemia

- see Hematology

Epidemiology
- mean age of diagnosis 2-5 years but can occur at any age
- heterogenous group of diseases:
  - acute lymphoblastic leukemia (ALL) (75%)
  - acute myeloblastic leukemia (AML) (10%)
  - chronic myelogenous leukemia (CML) (5%)
  - unclear type (10%)
- children with Down syndrome are 15 times more likely to develop leukemia

Etiology
- mostly unknown; retrovirus (HTLV) may be associated with T-cell leukemia

Clinical Presentation
- infiltration of leukemic cells into bone marrow results in bone pain, and subsequent bone marrow failure (anemia, neutropenia, thrombocytopenia, purpura, petechiae)
- infiltration into tissues results in: lymphadenopathy, hepatosplenomegaly, CNS manifestations
- fever, fatigue, weight loss

Prognosis
- 80-90% 5-year event-free survival for ALL, 50% for AML

Lymphoma

- see Hematology

Hodgkin's Lymphoma
- incidence is bimodal–peaks at age 15-34 and 50+
- similar to adult Hodgkin’s
- most common presentation is persistent, painless, firm, cervical or supraclavicular lymphadenopathy
- can present as persistent cough (secondary to mediastinal mass) or less commonly as splenomegaly, axillary or inguinal lymphadenopathy
- constitutional symptoms (B symptoms) in 30% of children

Non-Hodgkin's Lymphoma
- incidence peaks 7-11 years
- generally categorized into lymphoblastic, large cell, and Burkitts/Burkitts-like lymphoma
- rapidly growing tumour with distant metastases which differs from adult non-Hodgkin lymphoma
- signs and symptoms related to disease site, most commonly abdomen, chest (mediastinal mass), head and neck region

Etiology
- mostly unknown; EBV associated with African Burkitt lymphoma
Treatment
- aggressive multidrug chemotherapy with radiation and surgery to debulk large tumour masses
- 80-90% 5-year survival in Hodgkin’s; 50-75% in non-Hodgkin’s

Brain Tumours
- see Neurosurgery
- classified by location and histology
- location: 60% infratentorial (cerebellum, midbrain, brainstem) versus supratentorial
- histology: glial (cerebellar astrocytomas most common), primitive neuroectodermal (medulloblastoma), neuronal, pineal

Clinical Presentation
- infratentorial: increased ICP (obstruction of 4th ventricle), vomiting, morning headache
- increased head circumference, VI nerve palsy, upward-gazing eyes, ataxia, cranial nerve palsies
- supratentorial: focal deficits, seizures, long tract signs, visual field defects
- evaluation
  - history, physical exam including complete neurological exam
  - CT and/or MRI of head

Wilms’ Tumour (Nephroblastoma)
- usually diagnosed between 2 and 5 years of age
  - most common primary renal neoplasm of childhood
  - M:F
  - 5-10% of cases both kidneys are affected (simultaneously or in sequence)
- differential diagnosis
  - hydroureter, polycystic kidney disease, renal cell carcinoma, neuroblastoma

Clinical Presentation
- 80% present with asymptomatic, unilateral abdominal mass
- may also present with hypertension, gross hematuria, abdominal pain, vomiting
- may have pulmonary metastases at time of primary diagnosis (respiratory symptoms)

Associated Congenital Abnormalities
- WAGR syndrome (Wilms’ tumour, Aniridia, Genital anomalies, mental Retardation) with 11p13 deletion
- Beckwith-Wiedemann syndrome
  - characterized by enlargement of body organs, hemihypertrophy, renal medullary cysts, and adrenal cytomegaly
  - also at increased risk for developing hepatoblastoma, adrenocortical tumours, rhabdomyosarcomas, and pancreatic tumours
- Denys-Drash syndrome
  - characterized by gonadal dysgenesis and nephropathy leading to renal failure

Management
- nephrectomy
- staging, chemotherapy, radiation

Prognosis
- 90% long-term survival

Neuroblastoma

Epidemiology
- most common cancer occurring in first year of life
- neural crest cell tumour arising from sympathetic tissues (neuroblasts)
  - adrenal medulla (45%)
  - sympathetic chain (25% retroperitoneal, 20% posterior mediastinal, 4% pelvis, 4% neck)

Clinical Presentation
- can originate from any site in sympathetic nervous system, presenting as mass in neck, chest or abdominal mass (most common site is adrenal gland)
- signs and symptoms of disease vary with location of tumour
  - thoracic: dyspnea, Horner’s syndrome
  - abdomen: palpable mass
  - spinal cord compression
- metastases are common at presentation (>50% present with advanced stage disease)
  - usually to bone or bone marrow (presents as bone pain, limp)
• can also present with periorbital ecchymoses, abdominal pain, emesis, fever, weight loss, anaemia, hepatomegaly, “blueberry muffin” skin nodules
• paraneoplastic: hypertension, palpitations, sweating (from excessive catecholamines), diarrhoea, FTT (from VIP secretion), opsomyoclonus

**Investigations**
- CBC, electrolytes, LFTs, renal function tests, LDH, Ca, Mg, serum ferritin
- urine VMA, HVA levels
- CT scan of chest, abdomen and pelvis, bone scan
- bone marrow analysis - neuroblastoma cells in “rosettes”
- tissue biopsy

**Good Prognostic Factors**
- “age and stage” are important determinants of better outcome
  - <1 year old
  - stage I, II, IV-S disease (“S” designates a “Special” classification only pertaining to infants)
- primary site: posterior mediastinum and neck
- serum ferritin
- specific histology
- tumour cell markers
  - aneuploidy
  - absent N-myc oncogene amplification

**Management**
- depends on prognostic factors and may include any of the following alone or in combination: surgery, radiation, chemotherapy, bone marrow transplantation
- prognosis is often poor as it is found at an advanced stage

### Rhabdomyosarcoma

- third most common extracranial solid tumour of children (after neuroblastoma and Wilms' tumour)
- no clear predisposing risk factors
- common sites of origin are structures of the head and neck, GU tract and extremities
- presentation: firm, painless mass
- metastases to lung, bone marrow and bones
- evaluation: MRI or CT scan of primary site, CT chest, bone scan, bilateral bone marrow aspirates and biopsies
- treatment: multidrug chemotherapy and surgery

### Generalized Lymphadenopathy

- features of malignant lymphadenopathy (LAD): firm, discrete, non-tender, enlarging, no associated erythema, warmth, fluctuance, ± suspicious mass/imaging findings, ± B symptoms

**Differential Diagnosis**
- infection:
  - viral – URTI, EBV, CMV, Adenovirus, HIV
  - bacterial – S. aureus, GAS, anaerobes, Mycobacterium, cat scratch disease
  - other: fungal, protozoan, rickettsia
- auto-immune: rheumatoid arthritis, SLE, serum sickness
- malignancy: lymphoma, leukemia, metastatic solid tumours
- storage diseases: Niemann-Pick, Gaucher’s
- other: sarcoidosis, Kawasaki disease, histiocytes

**Investigations**
- generalized LAD
  - CBC & differential, blood culture
  - uric acid, LDH
  - ANA, RF, ESR
  - EBV/CMV/HIV serology
  - toxoplasma titre
  - fungal serology
  - CXR
  - PPD
  - biopsy
- regional LAD
  - period of observation in an asymptomatic child
  - trial of oral antibiotics
  - biopsy (especially if persistent >6 weeks and/or B symptoms)
Respirology

Approach to Dyspnea

- see Table 1 “Average Vitals at Various Ages”, P3

<table>
<thead>
<tr>
<th>Pulmonary</th>
<th>Cardiac</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Airway</td>
<td>Lower airway</td>
<td>Pleura</td>
</tr>
<tr>
<td>• Foreign body</td>
<td>• Tracheitis</td>
<td>• CHF</td>
</tr>
<tr>
<td>• Croup</td>
<td>• Bronchiolitis</td>
<td>• Cardiac tamponade</td>
</tr>
<tr>
<td>• Laryngeal edema</td>
<td>• Pneumonia</td>
<td>• Other</td>
</tr>
<tr>
<td>• Epiglottitis</td>
<td>• Atelectasis</td>
<td>• CHF</td>
</tr>
<tr>
<td>• Retropharyngeal abscess</td>
<td>• Asthma</td>
<td>• ICP</td>
</tr>
</tbody>
</table>

Figure 6. Approach to Dyspnea in Childhood

Upper Respiratory Tract Diseases

- see Otolaryngology
- disease above the thoracic inlet characterized by inspiratory stridor, hoarseness, and suprasternal retractions
- differential diagnosis of stridor
  - croup
  - bacterial tracheitis
  - epiglottitis
  - foreign body aspiration
  - subglotic stenosis congenital or iatrogenic
  - laryngomalacia/tracheomalacia – collapse or epiglottis cartilage on inspiration

Table 49. Common Upper Respiratory Tract Infections

<table>
<thead>
<tr>
<th>Anatomy</th>
<th>Group (Laryngotracheobronchitis)</th>
<th>Bacterial tracheitis</th>
<th>Epiglottitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subglottic laryngitis</td>
<td>Subglottic laryngitis</td>
<td>Rare</td>
<td>Supraglottic laryngitis</td>
</tr>
<tr>
<td>Common</td>
<td>Rare</td>
<td>All age groups</td>
<td>Rare</td>
</tr>
<tr>
<td>6 mo-4 yrs</td>
<td>Usually older (2-6 yrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak incidence: fall and early winter</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Etiology

Parainfluenza (75%)
Influenza A and B
RSV
Adenovirus

<table>
<thead>
<tr>
<th>Supraglottic laryngitis</th>
<th>S. aureus</th>
<th>H. influenzae</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha-hemolytic strep</td>
<td>Pneumococcus</td>
<td>beta-hemolytic strep</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical presentation

| Harse voice | Similar symptoms as croup but more rapid deterioration with high fever |
| Barking cough | Toxic appearance |
| Stridor | Does not respond to croup treatments |
| Worse at night | Clinical diagnosis |

Investigations

Clinical diagnosis
CXR in atypical presentation: “steeple sign” from subglottic narrowing

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Endoscopy; definitive diagnosis</th>
<th>Clinical diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid examining the throat to prevent further respiratory exacerbation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Treatment

Humidified O2
Dexamethasone: PO 1 dose
Racemic epinephrine: nebulized, 1-3 doses, q1-2 hours
Intubation if unresponsive to treatment

Lower Respiratory Tract Diseases

- obstruction of airways below thoracic inlet, produces more expiratory sounds
- classic symptom: wheezing
Differential Diagnosis of Wheezing

- **common**
  - asthma: recurrent wheezing episodes, identifiable triggers
  - bronchiolitis: first episode of wheezing
  - recurrent aspiration: often neurological impairment
  - pneumonia: fever, cough, malaise
- **uncommon**
  - foreign body: acute wheezing and coughing
  - cystic fibrosis: prolonged wheezing, unresponsive to therapy
  - bronchopulmonary dysplasia: often develops after prolonged ventilation in the newborn
- **rare**
  - congestive heart failure
  - mediastinal mass
  - bronchiolitis obliterans
  - tracheobronchial anomalies

Pneumonia

- inflammation of pulmonary tissue, associated with consolidation of alveolar spaces

Clinical Presentation

- incidence is greatest in first year of life
- viral cause is more common in children <5 years old
- **viral**
  - cough, wheeze, stridor
  - CXR - diffuse, streaky infiltrates bilaterally
- **bacterial**
  - cough, fever, chills, dyspnea
  - CXR - lobar consolidation, possibly pleural effusion

Etiology and Management

- supportive therapy: hydration, antipyretics, humidified O₂

Table 50. Common Causes and Treatment of Pneumonia at Different Ages

<table>
<thead>
<tr>
<th>Age</th>
<th>Bacterial</th>
<th>Viral</th>
<th>Atypical bacteria</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates</td>
<td>GBS</td>
<td>CMV</td>
<td>Mycoplasma hominis</td>
<td>ampicillin + gentamicin / tobramycin</td>
</tr>
<tr>
<td></td>
<td>E. coli</td>
<td>Herpes virus</td>
<td>Ureaplasma urealyticum</td>
<td>(add erythromycin if suspect Chlamydia)</td>
</tr>
<tr>
<td></td>
<td>Listeria</td>
<td>Enterovirus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3 months</td>
<td>S. aureus</td>
<td>CMV, RSV</td>
<td>Chlamydia trachomatis</td>
<td>cefuroxime OR ampicillin +</td>
</tr>
<tr>
<td></td>
<td>H. influenzae</td>
<td>Influenza virus</td>
<td>Ureaplasma</td>
<td>erythromycin OR clarithromycin</td>
</tr>
<tr>
<td></td>
<td>S. pneumoniae</td>
<td>Parainfluenza</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>B. pertussis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months - 5 years</td>
<td>S. pneumoniae</td>
<td>RSV</td>
<td>M. pneumoniae, TB</td>
<td>ampicillin OR cefuroxime</td>
</tr>
<tr>
<td></td>
<td>S. aureus</td>
<td>Adenovirus</td>
<td></td>
<td>Mild. PO amoxicillin</td>
</tr>
<tr>
<td></td>
<td>H. influenzae</td>
<td>Influenza virus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>GAS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 years</td>
<td>S. pneumoniae</td>
<td>Influenza virus</td>
<td>Mycoplasma pneumoniae</td>
<td>erythromycin OR clarithromycin</td>
</tr>
<tr>
<td></td>
<td>H. influenzae</td>
<td>Varicella</td>
<td>Chlamydia pneumonia</td>
<td>OR - ampicillin</td>
</tr>
<tr>
<td></td>
<td>S. aureus</td>
<td>Adenovirus</td>
<td></td>
<td>OR - cefuroxime</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Legionella pneumophila</td>
<td></td>
</tr>
</tbody>
</table>

Bronchiolitis

- defined as the first episode of wheezing associated with URTI and signs of respiratory distress

Epidemiology

- common, affects 50% of children in first 2 years of life
- peak incidence at 6 months, winter or early spring
- occurs in children prone to airway reactivity, increased incidence of asthma in later life

Etiology

- respiratory syncytial virus (RSV) (>50%)
- parainfluenza, influenza, rhinovirus, adenovirus, rarely M. pneumoniae

Clinical Presentation

- prodrome of URTI with cough and fever
- feeding difficulties, irritability
- wheezing, respiratory distress, tachypnea, tachycardia, retractions, poor air entry lasting for 5-6 days
- children with chronic lung disease, severe CHD and immunodeficiency have a more severe course of the illness

**Investigations**
- CXR (only needed in severe disease, poor response to therapy, chronic episode)
  - air trapping, peribronchial thickening, atelectasis, increased linear markings
  - nasopharyngeal swab
  - direct detection of viral antigen (immunofluorescence)
- WBC usually normal

**Treatment**
- mild distress
  - supportive: oral or IV hydration, antipyretics for fever
  - humidified O₂ (maintain O₂ sat >92%)
  - inhaled bronchodilator (Ventolin™) 0.03 cc in 3 ml NS by mask, q20 min, and then q1 hour – stop if no response
- moderate to severe distress
  - as above - rarely; intubation and ventilation
  - ipratropium (Atrovent™) and steroids are not effective
  - consider rebetol (Ribavirin™) in high risk groups: bronchopulmonary dysplasia, CHD, congenital lung disease, immunodeficient
- monthly RSV-Ig or palivizumab (monoclonal antibody against the F-glycoprotein of RSV) may offer some protection against severe disease in high risk groups
  - case fatality rate <1%
- antibiotics have no therapeutic value unless there is secondary bacterial pneumonia
- indications for hospitalization
  - hypoxia: O₂ saturation <92% on initial presentation
  - persistent resting tachypnea >60/minute and retractions after several salbutamol (Ventolin™) masks
  - past history of chronic lung disease, hemodynamically significant cardiac disease, neuromuscular problem, immunocompromised
  - young infants <6 months old (unless extremely mild)
  - significant feeding problems
  - social problem (e.g. inadequate care at home)

**Asthma**
- see Respirology
- characterized by airway hyperreactivity, bronchospasm and inflammation, reversible small airway obstruction
- very common, presents most often in early childhood
- associated with other atopic diseases such as allergic rhinitis or atopic dermatitis

**Clinical Presentation**
- episodic bouts of
  - wheezing
  - dyspnea
  - cough at night, early morning, with activity, with cold exposure
  - tachypnea
  - tachycardia
  - post-tussive emesis
- physical exam may reveal hyper-resonant chest, prolonged expiration, wheeze

**Triggers**
- URI (viral or Mycoplasma)
- weather (cold exposure, humidity changes)
- allergens (pets), irritants (cigarette smoke)
- exercise, emotional stress
- drugs (aspirin, beta-blockers)

**Classification**
- mild asthma
  - occasional attacks of wheezing or coughing (<2 per week)
  - symptoms respond quickly to inhaled bronchodilator
- moderate asthma
  - more frequent episodes with symptoms persisting and chronic cough
  - decreased exercise tolerance
- severe asthma
  - daily and nocturnal symptoms
  - frequent ER visits and hospitalizations
Management
- acute
  - O₂ to keep O₂ saturation >92%
  - fluids if dehydrated
  - beta₂-agonists: salbutamol (Ventolin™) 0.03 cc/kg in 3 cc NS q20 minutes by mask
    until improvement, then mask hourly if necessary
  - ipratropium bromide (Atrovent™) if severe: 1 cc added to each of first 3 salbutamol masks
  - steroids: prednisone (2 mg/kg in ER, then 1 mg/kg PO OD x 4 days) or
dexamethasone (0.3 mg/kg/day PO)
  - in severe disease, give steroids immediately since onset of action is slow (4 hours)
- indications for hospitalization
  - pre-treatment O₂ saturation <92%
  - past history of life-threatening asthma (ICU admission)
  - unable to stabilize with q4h masks
  - concern over environmental issues or family’s ability to cope
- chronic
  - education, emotional support, avoidance of environmental allergens or irritants,
    development of an “action plan”
  - exercise program (e.g. swimming)
  - monitoring of respiratory function with peak flow meter (improves compliance and
    allows modification of medication)
  - PFTs for children ≥6 years
  - patients with moderate or severe asthma will need regular prophylaxis in addition to
    bronchodilators (e.g. daily inhaled steroids, long-acting beta-agonists,
    anticholinergics, sodium cromoglycate, theophylline, leukotriene receptor antagonist)
- Canadian Paediatric Asthma Consensus Guidelines for assessing adequate control of
  childhood asthma:
  1. daytime symptoms <4 days/wk
  2. night time symptoms <1 night/wk
  3. normal physical activity
  4. no school/absenteeism
  5. need for beta agonist < 4 doses/wk

Cystic Fibrosis (CF)

- see Respirology
- autosomal recessive, CFTR gene found on chromosome 7 (ΔF508 mutation in 70%, over 800
  different mutations identified)
- 1 in 3,000 live births, mostly Caucasians
- mutation in transmembrane conductance regulator of chloride – causes cells to be
  impermeable to Cl which increases the reabsorption of Na
- leads to relative dehydration of airway secretions, resulting in impaired mucociliary
  transport and airway obstruction

Clinical Presentation
- neonatal
  - meconium ileus
  - prolonged jaundice
  - antenatal bowel perforation
- infancy
  - pancreatic insufficiency with steatorrhea and FTT (despite voracious appetite)
- childhood
  - anemia, hypoproteinemia, hyponatremia
  - heat intolerance
  - wheezing or chronic cough
  - recurrent chest infections (S. aureus, P. aeruginosa, H. influenzae)
  - hemoptysis
  - nasal polyps (associated with milder disease)
  - distal intestinal obstruction syndrome, rectal prolapse
  - clubbing of fingers
- older patients
  - chronic obstructive pulmonary disease (COPD)
  - infertility

Investigations
- sweat chloride test x 2 (>60 mEq/L)
  - false positive tests: malnutrition, celiac disease, adrenal insufficiency, anorexia
    nervosa, hypothyroidism, nephrogenic diabetes insipidus, nephrotic syndrome
  - false negative tests: peripheral edema, cloxacillin, glycogen storage disease,
    hypoparathyridism, atopic dermatitis, Klinefelter syndrome, hypogammaglobulinemia
- pancreatic dysfunction – determined by 3-day fecal fat collection
- genetics – useful where sweat chloride test is equivocal

Treatment
- nutritional counselling
  - high calorie diet
  - pancreatic enzyme replacements
  - fat soluble vitamin supplements
- management of chest disease
  - physiotherapy, postural drainage
  - exercise
  - bronchodilators
  - aerosolized DNAase
  - antibiotics: depends on sputum C&S (e.g. cephalosporin, cloxacillin, ciprofloxacin, inhaled tobramycin)
  - lung transplantation
- genetic counselling

Complications
- respiratory failure
- pneumothorax (poor prognostic sign)
- cor pulmonale (late)
- pancreatic fibrosis with diabetes mellitus
- gallstones
- cirrhosis with portal hypertension
- infertility
- early death (current median survival is 30 years)

Rheumatology

Evaluation of Limb Pain

| Table 51. Differential Diagnosis of Limb Pain |
|---|---|---|---|
| Cause | <3 years | 3-10 years | >10 years |
| **Trauma** | x | x | x |
| **Infectious** | | | |
| Septic arthritis | x | x | x |
| Osteomyelitis | x | x | x |
| **Inflammatory** | | | |
| Transient synovitis | x | x | x |
| JIA | x | x | x |
| Seronegative spondyloarthropathy | x | x | x |
| SLE | x | x | x |
| Dermatomyositis | x | x | x |
| HSP | x | x | x |
| **Anatomic/Orthopaedic** | | | |
| Legg-Calve-Perthes disease | x | x | x |
| Slipped capital femoral epiphysis | x | x | x |
| Osgood-Schlatter disease | x | x | x |
| **Neoplastic** | | | |
| Leukemia | x | x | x |
| Neuroblastoma | x | x | x |
| Bone tumour | x | x | x |
| **Hematologic** | | | |
| Hemophilia (hemarthrosis) | x | x | x |
| Sickle cell anemia | x | x | x |
| **Pain Syndromes** | | | |
| Growing pains | x | x | x |
| Fibromyalgia | x | x | x |
| Reflex sympathetic dystrophy | x | x | x |

Investigations
- CBC, differential, blood smear, ESR
- x-rays of painful joints/limbs
- as indicated: blood C&S, ANA, RF, PTT, sickle cell prep, viral serology, immunoglobulins, complement, urinalysis, synovial analysis and culture, TB test, ASOT, slit lamp
Septic Arthritis

- medical emergency
- hematogenous osteomyelitis spread seen most commonly in neonates and infants
- clinical presentation: acute monoarthritis with erythema, warmth, swelling, intense pain on passive movement (pain may be so severe that it causes pseudoparalysis of involved limb), fever and chills
- definitive test: joint aspirate and culture
- management: proper antibiotic selection requires knowledge of likely bacterial pathogen at various ages

Growing Pains

- age 2-12 years, M=F
- diagnosis
  - intermittent, well between episodes
  - poorly localized pain in the legs
  - usually bilateral
  - occurs in evening or awakens child at night
  - responds to reassurance, massage or analgesics
  - resolves completely in the morning
- no associated systemic symptoms (e.g. fever)
- possible family history of growing pains
- normal physical examination
- lab investigations not necessary if typical presentation

Transient Synovitis

- age 3-10 years, M>F
- benign, self limited disorder, usually occurs after upper respiratory tract infection, pharyngitis, bronchitis, otitis media

Clinical Presentation
- afebrile or low-grade fever, pain typically occurs in hips, knees, painful limp but still capable of ambulating
- symptoms resolve over 7-10 days

Investigations
- ESR, WBC within normal limits
- x-ray is typically normal
- U/S may show joint effusion
- must exclude septic arthritis, osteomyelitis, AVN, slipped capital femoral epiphysis (SCFE)

Treatment
- symptomatic and anti-inflammatory medications

Juvenile Idiopathic Arthritis (JIA)

- formerly known as Juvenile Rheumatoid Arthritis (JRA)
- a heterogenous group of conditions characterized by persistent arthritis in children under 16 years
- diagnosis: arthritis in ≥1 joints lasting ≥6 weeks in child <16 years with exclusion of other causes of arthritis
- classification defined by features/number of joints affected in the first 6 months of onset

Systemic Arthritis (Still's disease)
- high spiking fever (38.5°C) for at least 2 weeks
- extra-articular features: erythematous “salmon-coloured” maculopapular rash, lymphadenopathy, hepatosplenomegaly, leukocytosis, thrombocytosis, anemia, serositis (pericarditis, pleuritis)
- onset at any age, M=F
- arthritis may occur weeks to months later
- high ESR, CRP, WBC, hematocrit count

Oligoarticular Arthritis (arthritis of 1-4 joints in the first 6 months)
- persistent - affects no more than 4 joints during the disease course
- extended - affects more than 4 joints after the first six months
- onset 1-3 years of age, F>M
- typically affects large joints - knees > ankles, elbows, wrists, hip involvement unusual
- ANA positive ~80%, rheumatoid factor (RF) negative
Polyarticular Arthritis (arthritis of 5 or more joints)
- RF negative
  - often involves large and small joints of hands and feet, temporomandibular joint, cervical spine
  - patients, especially those who are ANA positive, are prone to chronic uveitis
- RF positive
  - similar to the aggressive form of adult rheumatoid arthritis
  - severe, rapidly destructive, symmetrical arthritis of large and small joints
- may have rheumatoid nodules at pressure points (elbows, knees)
- unremitting disease, persists into adulthood

Enthesitis-Related Arthritis
- arthritis or enthesitis or both with at least two of
  - sacroiliac tenderness and/or inflammatory spinal pain
  - HLA B27 positive
  - family history of confirmed HLA B27-associated disease in a 1<sup>st</sup> or 2<sup>nd</sup> degree relative
  - symptomatic (acute) anterior uveitis
  - onset of arthritis in a boy >8 years

Psoriatic Arthritis
- arthritis and psoriasis or arthritis and at least two of
  - dactylitis, nail abnormalities, or family history of psoriasis in a 1<sup>st</sup> degree relative

Unclassified
- arthritis of unknown cause that persists for 6 weeks and either does not fulfill criteria for any category or fulfills criteria for more than one category

Management
- children may complain very little about their pain and disability
- exercise to maintain range of motion (ROM) and muscle strength
- multidisciplinary approach with OT/PT, social work, orthopaedics, ophthalmology, rheumatology
- first line drug therapy: NSAIDs, intra-articular corticosteroids
- 2nd line
  - DMARDs - methotrexate, sulfasalazine
  - other corticosteroids - intra-articular, systemic for systemic onset of JIA, topical eye drops for uveitis
  - biologic agents - etanercept (Enbrel<sup>®</sup>); binds TNF and blocks its interaction with cell surface receptors

Systemic Lupus Erythematosus (SLE)
- see Rheumatology
- autoimmune illness affecting multiple organ systems
- incidence 1:1000; more commonly age >10, F:M = 10:1

Reactive Arthritis
- arthritis follows bacterial infection especially with <i>Salmonella, Shigella, Yersinia, Campylobacter, Chlamydia, and Streptococcus</i> (post-streptococcal reactive arthritis)
- prognosis:
  - typically resolves
  - may progress to chronic illness or Reiter’s syndrome (urethritis, conjunctivitis)

Lyme Arthritis
- see Infectious Diseases
- caused by spirochete <i>Borreli burgdorferi</i>
- incidence highest among 5-10 year olds
- arthritis begins months after initial infection (late Lyme disease)
- typically involves large joints, especially knees (affected in ~90% of cases)
- large, expanding erythematous macule with fever - erythema migrans of Lyme arthritis
- management: doxycycline or amoxicillin for 30 days; do not treat children <8 years old with doxycycline as it may cause permanent discoloration of teeth
Vasculitides

HENOC-SCHÖNLEIN PURPURA (HSP)
- most common vasculitis of childhood
- vasculitis of small vessels
- peak incidence 4-10 years, M:F = 2:1
- recurrence in about one third of patients
- often have history of URTI 1-3 weeks before onset of symptoms

Clinical Presentation
- skin: palpable, non-thrombocytopenic purpura in lower extremities and buttocks, edema, scrotal swelling
- joints: arthritis/arthralgia involving large joints
- GI: abdominal pain, GI bleeding, intussusception
- renal: IgA nephropathy, hematuria, proteinuria, hypertension, renal failure in <5%

Management
- symptomatic, corticosteroids may relieve abdominal pain
- monitor for renal disease, may develop late
- immunosuppressive therapy for severe renal disease

Prognosis
- self-limited disease in 90%

Kawasaki Disease

- acute vasculitis of unknown etiology
- mainly affecting medium-size arteries
- most common cause of acquired heart disease in children
- peak age <5 years; East Asians > Blacks > Caucasians

Diagnostic Criteria
- fever persisting 5 days or more AND
  - 4 of the following features:
    1. bilateral nonpurulent conjunctivitis
    2. red fissured lips, strawberry tongue, erythema of oropharynx
    3. changes of the peripheral extremities
       - acute phase: erythema, edema of hands and feet
       - subacute phase: peeling from tips of fingers and toes
    4. polymorphous rash
    5. cervical lymphadenopathy: >1.5 cm in diameter
- exclusion of other diseases (e.g. scarlet fever, measles)
- atypical Kawasaki disease: less than 5 of 6 diagnostic features but coronary artery involvement

Associated Features
- acute phase (as long as fever persists, about 10 days)
  - most of diagnostic criteria present
  - irritability, aseptic meningitis, myocarditis, pericarditis, CHF
  - diarrhea, gallbladder hydrops, pancreatitis, urethritis, arthritis
  - subacute phase (resolution of fever, peeling of skin, elevated ESR and platelets, usually days 11-21)
    - arthritis
    - beau’s lines seen on nail growth
  - convalescent phase (lasts until ESR and platelets normalize, >21 days)
    - coronary artery aneurysms, aneurysm rupture, myocardial infarction (MI), CHF

Management
- high (anti-inflammatory) dose of ASA while febrile
- low (anti-platelet) dose of ASA in subacute phase until platelets normalize or longer if coronary artery involvement
- IV immunoglobulin (2 g/kg) reduces risk of coronary aneurysm formation
- baseline 2D-echo and follow up periodic 2D-echocardiograms (usually at 6 weeks)

Complications
- coronary artery vasculitis with aneurysm formation occurs in 20-25% of untreated children,
  <5% if receive IVIG within 10 days of fever
- 50% of aneurysms regress within 2 years
- anticoagulation for multiple or large coronary aneurysms
- risk factors for coronary disease: male, age <1 or >9 years, fever >10 days
Juvenile Dermatomyositis

Pathophysiology
- activation of B and T cells → small vessel vasculitis of skeletal muscle with characteristic skin manifestations

Epidemiology
- more common in girls than boys
- typical age of onset 4-10 yrs

Clinical Characteristics
- insidious progressive fatigue, malaise
- muscle weakness
  - primarily affecting proximal muscles (hips and shoulders)
  - difficulty climbing stairs and getting up off of the floor (gower’s)
- low-grade fevers
- rash
  - on face and across cheeks
  - shawl sign (rash on shoulders/back)
  - heliotrope discolouration of eyelids
  - gottron papules (scaly red plaques on knuckles and extensor surfaces)
  - periungual erythema and dilated nail fold capillaries
- upper airway involvement may cause voice change (nasal voice) and dysphagia
- small joint arthritis

Treatment
- systemic corticosteroids, and methotrexate are the mainstays of treatment
- may also consider cyclophosphamide, IVIG, and hydroxychloroquine

Prognosis
- variable (note: unlike in adults, JDM is not associated with malignancy in children)

Common Medications

Table 52. Commonly Used Medications in Pediatrics

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Schedule</th>
<th>Indications</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>acetaminophen</td>
<td>10-15 mg/kg/dose PO PR q4-6h pm</td>
<td>Analgesic, antipyretic</td>
<td></td>
</tr>
<tr>
<td>amoxicillin</td>
<td>80-90 mg/kg/day PO divided q8h</td>
<td>Otitis media (severe)</td>
<td></td>
</tr>
<tr>
<td>dexamethasone</td>
<td>0.6 mg/kg IV x 1 OR 1 mg/kg PO x 1</td>
<td>Croup</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.3 mg/kg/day PO</td>
<td>Acute asthma</td>
<td></td>
</tr>
<tr>
<td>fluticasone</td>
<td>moderate dose – 250-500 μg/day divided bid</td>
<td>Asthma</td>
<td>Cautious use in patients with liver impairment, history of GI bleeding or ulcers</td>
</tr>
<tr>
<td>ibuprofen</td>
<td>5-10 mg/kg/dose PO q6-8h</td>
<td>Analgesic, antipyretic</td>
<td></td>
</tr>
<tr>
<td>iron</td>
<td>6 mg/kg/day elemental iron bid-tid</td>
<td>Anemia</td>
<td>Side effects: dark stool, constipation, dark urine</td>
</tr>
<tr>
<td>prednisone</td>
<td>1-2 mg/kg/day PO x 5 days</td>
<td>Asthma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3-4 mg/kg/day PO</td>
<td>ITP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 mg/m2/day PO</td>
<td>Nephrotic syndrome</td>
<td></td>
</tr>
<tr>
<td>salbutamol</td>
<td>0.01-0.03 mL/kg/dose in 3 mL normal saline via nebulizer q1/2-4h pm</td>
<td>Acute asthma</td>
<td>Maintenance treatment for asthma</td>
</tr>
<tr>
<td></td>
<td>100-200 μg/dose pm, max frequency q4h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Publicly Funded Immunization Schedules for Ontario - January 2009.


Neurology


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Respirology


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Rheumatology


Web-based Resources

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http://www.icondata.com/health/pedbase
http://www.cda-adc.ca