Paediatric Clinical Chemistry

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Paediatric biochemistry

The child is not a “miniature adult”
• Physiological development
  – Immature organ systems
  – Growing individual
• Different disease profile
  – Infectious diseases
  – Genetic disease
  – Inborn errors of metabolism
• Small body size
  – Specimen volume small
Developmental changes

- **Birth**
  - Adaptation from intrauterine to extrauterine life
- **Neonatal period**
  - Normal BW 3.2 kg – SGA 2.5 kg
  - Wt loss due to insensible fluid loss offset by gain due to feeding
  - BW will double in 4-6 mnths
  - Immature organ systems
    - Liver (2-3 mnths)
    - Kidney (1 yr)
  - Haemopoietic system changes: HbF to HbA
  - Premature infants may have respiratory distress, fluid and electrolyte abnormalities and excessive jaundice
- **Birth**
  - Bone growth in first few years and at puberty
  - Sexual maturation

Phlebotomy

- **Specimen collection**
  - Narrow gauge needles (↑ haemolysis)
  - Skin vs venipuncture (capillary vs venous blood)
  - Values often lower in skin puncture samples (dilution due to interstitial fluid); glucose higher

- **Specimen volume**
  - Premature babies: 115 mL blood/kg BW
  - Newborns: 80-110 mL blood/kg BW
  - Infants: 75-100 mL blood/kg BW
  - Hct ↑ in infants ∴ serum/plasma yield ↓
  - Evaporation
Recommended blood draw volumes

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Volume per draw (ml)</th>
<th>Volume per hospitalization (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 kg</td>
<td>1.0</td>
<td>8</td>
</tr>
<tr>
<td>1-2</td>
<td>1.5</td>
<td>12</td>
</tr>
<tr>
<td>2-3</td>
<td>2.0</td>
<td>17</td>
</tr>
<tr>
<td>3-4</td>
<td>2.5</td>
<td>23</td>
</tr>
<tr>
<td>4-5</td>
<td>3.5</td>
<td>30</td>
</tr>
<tr>
<td>5-7.5</td>
<td>5.0</td>
<td>40</td>
</tr>
<tr>
<td>&gt; 10.0</td>
<td>10.0</td>
<td>60</td>
</tr>
</tbody>
</table>

Choice of analyzer

- Small sample volume
- Small dead volume on analyzer
- Clot or bubble detection: sample salvage
- Random access
  - Select only required tests
Point-of-care analysis

• Immediate turnaround
• Cost-effective?
• Quality assurance (QA)
  – Lower precision
  – Linear range narrower
    • Example: Glucometer
• Laboratory evaluation
  – Lock out untrained users
  – QA procedures before patient sample analysis
  – Data download to laboratory information system

Reference values

• Ranges adjusted for sex and age
• Transferability of ranges
• Terminology
  – Neonate – first 4 weeks
  – Infant – 4 weeks to 2 years
  – Child – 2 years to puberty
  – Adolescent – puberty to adulthood
• Premature vs full-term infants
Reference values (cntd)

- Important differences – routine chemistry
  - Electrolytes and acid-base
  - Urea, and creatinine
  - Uric acid
  - Cholesterol
  - Calcium, Phosphate
  - Immunoglobulins
  - Bilirubin
  - ALP
  - TFT’s
  - Gonadal hormones
  - AFP (several thousand µg/L in neonates)

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Neonate</th>
<th>Infant</th>
<th>Child</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium (mmol/L)</td>
<td>3.7-5.9</td>
<td>4.1-5.3</td>
<td>3.4-4.7</td>
<td>3.5-5.1</td>
</tr>
<tr>
<td>HCO₃⁻ (mmol/L)</td>
<td>13-22</td>
<td>20-28</td>
<td>20-28</td>
<td>22-28</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>1.4-4.3</td>
<td>1.8-6.4</td>
<td>1.8-6.4</td>
<td>2.1-7.1</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>27-88</td>
<td>18-35 (5d)</td>
<td>27-62</td>
<td>44-88</td>
</tr>
<tr>
<td>Uric acid (mmol/L)</td>
<td>0.12-0.32</td>
<td>0.12-0.32</td>
<td>0.12-0.32</td>
<td>0.21-0.42</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>1.90-2.60</td>
<td>2.25-2.75</td>
<td>2.20-2.70</td>
<td>2.15-2.55</td>
</tr>
<tr>
<td>Phosphate (mmol/L)</td>
<td>1.45-2.91</td>
<td>1.45-2.16 (10d)</td>
<td>1.45-1.78</td>
<td>0.87-1.45</td>
</tr>
<tr>
<td>Immunoglobulins</td>
<td>See figure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilirubin (mmol/L)</td>
<td>24-149</td>
<td>26-205 (3-6d)</td>
<td>6.8-34.2</td>
<td>6.8-34.2</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>75-316</td>
<td>82-383</td>
<td>82-383</td>
<td>52-171</td>
</tr>
<tr>
<td>Ammonia (mmol/L)</td>
<td>100-200</td>
<td>40-80 (from 10d)</td>
<td>11-35</td>
<td>11-35</td>
</tr>
</tbody>
</table>
Foetal lung maturity

- Respiratory distress syndrome (RDS)
  - Hyaline membrane disease
  - ↓ Pulmonary surfactant
  - Premature delivery
    - Amniotic fluid: phosphatidyl glycrol (PG)
    - Lamellar body count
    - L:S ratio (Lecithin: Sphingomyelin)
    - Cervicovaginal fluid: Fibronectin

Liver function

- Physiological jaundice
  - Polycythaemia
  - Immature bilirubin UDP-glucuronyl transferase
  - Breast milk
  - Unconjugated hyperbilirubinaemia after day 1, baby appears healthy, bilirubin up to 250 µmol/l, normalizes within 10-14 days
  - Distinguish from other causes of neonatal jaundice
  - Crigler-Najjar disease
    - Absent bilirubin UDP-glucuronyl transferase
Neonatal hypoglycaemia

- Premature / Dysmature (IUGR)
- Septicaemia
- Asphyxia
- Infant of a diabetic mother
- Hypopituitarism
- Inborn errors of metabolism
  - Galactosaemia
  - Disordered gluconeogenesis
  - Disorders of fatty acid oxidation

Changes in TSH and Thyroxine (T4) at term

From: www.endotext.org
Immunoglobulin levels in children

From: www.ncbi.nlm.nih.gov/books/NBK27109/

Genetic disease

- Inheritance of most genetic diseases presenting in childhood is:
  - autosomal recessive (CF, CAH)
  - X-linked recessive (haemophilia)
- Mitochondrial DNA only from the maternal side
Metabolic disease

• Large molecule disease
  – Intracellular accumulation of abnormal chemical, small excretion in body fluids
  – Storage disease
    • Glycogen storage
    • Mucopolysaccharidoses
    • Lipid storage diseases
  – Diagnosis
    • Tissue biopsy for measurement of specific enzyme’s activity
    • Some enzymes’ activity can be measured in white blood cells
    • Few urine tests: some storage diseases associated with unusual metabolites

Metabolic disease

• Small molecule diseases
  – Defects in intermediary metabolism
  – Accumulation of low MW compounds, excreted in body fluids (urine)
  – Organic acidurias, urea cycle defects, amino acidurias, defects in fatty acid metabolism
• Diagnosis
  – ABG, anion gap, LFT, muscle markers, lactic acid, ammonia
  – Urine GC/MS (organic acids)
  – Serum ion exchange chromatography (amino acids)
Neonatal screening

- Detection of disease before it manifests clinically
- Prenatal, in neonatal period or later
- Criteria for selection of disorders for screening
  - Condition either fatal or leads to severe morbidity if untreated
  - Effective and acceptable treatment is available
  - Condition is relatively common in the population to be screened
  - Screening method is reliable (high sensitivity and acceptable specificity) and cost-efficient
  - Confirmatory diagnostic tests available
  - Resource implications not prohibitive

Drug metabolism and pharmacokinetics

- Absorption
  - Syrup: rapid release
  - Gastric pH higher in infants
- Distribution
  - Relatively little adipose tissue
- Elimination
  - Immature hepatic and renal function
References