The child with abnormal liver function tests

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Contents

• Over view of liver anatomy, histology and pathophysiology

• What is meant by liver function tests

• Liver diseases that occur in childhood

• How to investigate a child with abnormal liver function tests

• Patterns of abnormal biochemistry
The normal liver
The normal liver

- Liver right Lobe
- Liver left lobe
- Esophagus
- Falciform ligament
- Stomach
- Common Hepatic duct
- Pancreatic duct
- Gall bladder
- Cystic duct
- Duodenum
- Pancreas
- Common bile duct
- Right & Left Hepatic duct
The normal liver

- Central vein
- Hepatic artery
- Portal vein
What is the function of the normal liver?

• The liver is very complex and has hundreds of functions
• Interacts with all other systems / organs
• In summary
  – Processing of digested food from the intestine
  – Control levels of proteins, fats and glucose
  – Combat infection
  – Manufacture and excretion of bile
  – Store iron and vitamins
  – Excretion of drugs and toxins
  – Regulation of hormones
  – Regulation of blood clotting
Liver investigations

• Biochemical liver function tests:
  – Hepatic or biliary damage
  – Liver dysfunction

• Specific investigations for cause of liver disease
Liver biochemistry: bilirubin

- A breakdown product of heme (part of the haemoglobin in red blood cells)
- The hepatocytes takes up bilirubin, conjugates it to make it more water soluble and secretes it onto the bile ducts for excretion via the intestine

- Increased bilirubin causes jaundice
  - Prehepatic: too much red cell break down (unconjugated)
  - Hepatic: unable to metabolise the bilirubin (mixed)
    - Reduced conjugation
    - Unable to secrete bilirubin
  - Post hepatic: obstruction to the excretion of bile (conjugated)
Liver transaminases

- Aspartate aminotransferase (AST) and alanine aminotransferase (ALT): intracellular enzymes

- Raised if hepatocytes are damaged (often measured as multiples of upper limit of normal)
  - ALT more liver specific but longer half life
  - AST is an early marker of liver damage
Liver biochemistry: bile ducts

• Alkaline phosphatase (alk phos) elevated in bile epithelium damage
• Also found in kidney, bone and intestine

• γ-Glutamyltransferase (GGT) found in biliary epithelium and elevated in many forms of liver disease
  – If normal despite high bilirubin it is diagnostic of specific intrahepatic cholestasis syndromes
Liver function

• Clotting factors: prothrombin (PT) – very specific for liver dysfunction / liver failure

• Albumin: low in chronic liver disease

• Glucose: hypoglycaemia indicates severe hepatic dysfunction
Liver pathology

Normal liver

Cirrhotic liver

Acute hepatic necrosis
Causes of liver disease

European transplant registry; 2006. Available at: www.eltr.org
Types of liver disease

- **Cholestasis**: Biliary atresia, PFIC, Alagille syndrome, parenteral nutrition
- **Infection**: hepatitis A, B, C, E, EBV, CMV
- **Chemical damage**: drugs, chemotherapy
- **Hereditary**: Wilsons disease, haemochromatosis
- **Vascular damage**: Budd-Chiari
- **Autoimmunity**: autoimmune hepatitis, primary sclerosing cholangitis
- **Congenital anomalies**: biliary atresia, Caroli’s disease
- **Metabolic disease**: galactosemia, fatty liver disease
How to investigate a child with abnormal liver biochemistry

- History
- Examination
- Biochemistry
- Liver function
- Specific investigations
- Liver imaging
- Histology
- Endoscopy/ERCP
- MRI
- Bone marrow
- Ophthalmology
Investigating the cause of liver disease

- FBC
- Culture
- TORCH screen
- Infection hepatitis A, B, C, E, EBV
- Alpha 1-antitrypsin
- Copper, ceruloplasmin
- C3, C4, ANA, SMA, LKM
- Immunoglobulins

- Serum iron and ferritin
- Amino acids
- Organic acids
- Cholesterol & triglycerides
- Lactate, free fatty acids
- Ketones
- Ammonia
- Acyl carnitines
- Alpha fetoprotein
- DNA
Case 1: patterns of abnormal biochemistry

• 4/52 female
  – Term (3.4kg), thriving, cannabis during pregnancy
  – Well baby jaundiced with pale stool
  – Bottle fed
• **Initial blood investigations**
  – FBC - normal
  – Electrolytes - normal
  – Liver function tests -

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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<tbody>
<tr>
<td>Bilirubin (0-24)</td>
<td>203µmol/l</td>
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<tr>
<td>Conjugated (0-17)</td>
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<tr>
<td>Alkaline phosphatase (Alkphos) (250-1000)</td>
<td>469 IU/l</td>
</tr>
<tr>
<td>Alanine transferase (ALT) (5-45)</td>
<td>246 IU/l</td>
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<td>Aspartate transferase (AST) (0-80)</td>
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<td>Gamma glutamyl transferase (GGT) (0-115)</td>
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<tr>
<td>Prothrombin time (PT) (8-15)</td>
<td>12 seconds</td>
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<tr>
<td>Albumin (34-42)</td>
<td>40 g/l</td>
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Imaging
- ultrasound
- radionucleotide excretion scan
Diagnosis case 1

• Biliary atresia
• Kasai operation at 6 weeks
  – Bile flow established

• Nutrition
• Vitamins
• Cholangitis prophylaxis
Case 2: patterns of abnormal biochemistry

• 13 years old boy
  – Tired
  – Weight loss of 1 Kg
  – Abdominal discomfort and stools 4x per day
  – Intermittent jaundice
• **Initial blood investigations**
  - Iron deficient anaemia
  - Electrolytes - normal
  - Liver function tests -

<table>
<thead>
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<td>Alanine transferase (ALT) (5-45)</td>
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<td>Aspartate transferase (AST) (0-80)</td>
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<td>Gamma glutamyl transferase (GGT) (0-115)</td>
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<td>Prothrombin time (PT) (8-15)</td>
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<td>Albumin (34-42)</td>
<td>31 g/l</td>
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</table>
• ANA 1:340
• TTG: 33.8 U/ml (0-15)
• IgG: 34
• Imaging:
  – Nodular liver, hilar lymphadenopathy
• Histology:
Case 2

• Type 1 autoimmune hepatitis

• Treatment
  – Immunosuppression
    • Steroids
    • Azathioprine
  – Support with vitamin supplementation (vitamin K)

• Look for other autoimmune entities
  – Coeliac disease
  – Diabetes
  – Thyroid function
Case 3: patterns of abnormal biochemistry

- 2/52 boy
  - Not feeding well, irritable
  - Blood in nappy

- 2\textsuperscript{nd} baby, normal pregnancy and antenatal scans

- Normal delivery

- Mother well and no family history
• **Initial blood investigations**
  – Haemoglobin & white cell count: normal
  – Platelets low
  – Electrolytes - normal

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<td>Alkaline phosphatase (Alkphos) (250-1000)</td>
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<td>Aspartate transferase (AST) (0-80)</td>
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<td>Gamma glutamyl transferase (GGT) (0-115)</td>
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Investigations

- Lactate 5mmol/l (0.6-2.6)
- Ferritin 3478 µg/l (32-233)
- Amino & organic acids normal
- Ammonia 128 µmol/l (<125)
- Acyl carnitines normal
- Serology negative including herpes simplex
- Lip biopsy: iron in salivary glands
Case 3: diagnosis

• Neonatal haemochromatosis
  – Intensive care
  – Antioxidant therapy
  – Exchange transfusion
  – Super urgent liver transplant

• Alloimmune disease and therefore could occur in subsequent pregnancies
  – Maternal immunoglobulin infusions from 18 weeks gestation
Summary

• Acute and chronic liver disease

• Early referral and recognition of liver disease

• Referral to Specialist centre
  – Early diagnosis
  – Consideration of Treatment
  – Improve outcomes for children