JAUNDICE AND LIVER FAILURE
Patrick Nee and John McLindon

BACKGROUND
Condition caused by raised bilirubin in the plasma. Yellowing of the skin and sclera becomes apparent at levels >35mcmol/L. Isolated hyperbilirubinaemia may be seen in Gilbert's disease (mild, worse on fasting), haemolysis or GI bleeding. The common pathological causes are divided into Hepatic (predominantly raised transaminases) and Obstructive (predominantly raised ALP and GGT). In Shock liver there is a non-specific elevation of all liver enzymes.

Common causes of jaundice in adults include:
- Viral Hepatitis (Hepatitis A,B,C. EBV, CMV)
- Alcoholic hepatitis
- Late stage cirrhosis
- Obstruction (gallstones, tumour)
- Drug induced (hepatic or obstructive)
- Metabolic Eg.Wilson's disease
- Chronic active hepatitis, Primary Biliary Cirrhosis
- Other; sepsis, heart failure, multiple hepatic metastases

HISTORY
Search for evidence of:
- Flu-like antecedent illness of viral hepatitis, EBV, CMV
- Biliary Obstruction (dark urine, pale stools, itching, biliary colic)
- Chronic malaise and weight loss suggesting malignancy
- Recent anaesthetic, surgery or blood transfusion
- Foreign travel, alcohol history, illicit drugs or unsafe sexual practice
- Prescription drugs (anticonvulsants, testosterone, rifampicin etc)
- Relevant family history
- Contact with other unwell persons

EXAMINATION
Search for evidence of:
- Vital signs, Respiratory distress, Circulatory shock, GCS,
- Flapping tremor
- Chronic liver disease
- Liver, spleen enlargement, oedema, ascites
- Bleeding, bruising
- Depth and colour of jaundice

INVESTIGATIONS:
In the undifferentiated jaundiced patient all specimens must be considered High Risk. Routine investigations include bloods for FBC, clotting, U&E, Glucose, blood cultures and ABG, CXR and ECG as indicated. Only send haemolysis screen (Haptoglobins, reticulocyte count, Coomb’s test or
conjugated/unconjugated bilirubin, urinary urobilinogen) if falling Hb suggests acute haemolysis. If an autoimmune hepatitis (PBC, CAH) is anticipated send blood for autoantibody screen.

An ultrasound of the liver will be required in all cases of jaundice with abnormal LFTs

**LIVER FUNCTION TESTS; NORMAL VALUES**

<table>
<thead>
<tr>
<th>Test</th>
<th>Normal Values</th>
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<tbody>
<tr>
<td>Albumin</td>
<td>35-50 g/L</td>
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<tr>
<td>Alkaline phosphatase (adult)</td>
<td>30-110 u/L</td>
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<tr>
<td>Alpha-1 antitrypsin</td>
<td>1.1-2.1 g/L</td>
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<tr>
<td>Alanine aminotransferase (ALT)</td>
<td>5-32 u/L</td>
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<tr>
<td>Aspartate aminotransferase (AST)</td>
<td>5-40 u/L</td>
</tr>
<tr>
<td>Ammonia</td>
<td>&lt;47 mcmol/L</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>0-17 mcmol/L (Direct 0.5 mcmol/L)</td>
</tr>
<tr>
<td>Caeruloplasmin (males)</td>
<td>0.18-0.34 g/L; 0.14-0.46 g/L</td>
</tr>
<tr>
<td>Ferritin (male)</td>
<td>14-179 mcg/L</td>
</tr>
<tr>
<td>Ferritin (female)</td>
<td>5-146 mcg/L</td>
</tr>
<tr>
<td>Gamma glutamyl transferase (GGT)</td>
<td>6-40 u/L</td>
</tr>
<tr>
<td>Globulin</td>
<td>17-35 g/L</td>
</tr>
<tr>
<td>Immunoglobulin A</td>
<td>0.8-4.0 g/L</td>
</tr>
<tr>
<td>Mean Corpuscular Volume (MCV)</td>
<td>86-96 fl</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>9-12 s</td>
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<tr>
<td>APTT</td>
<td>20-30 s</td>
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**TREATMENT**

Depends on the cause
Supportive measures are set out below

**ALCOHOLIC HEPATITIS**

Acute inflammation of the liver due to alcohol, may be against a background of normal or fatty liver, or cirrhosis. Variable severity, may be relatively benign and reversible or progress to fatal complications; variceal bleeding, hepatorenal syndrome, sepsis, encephalopathy, multiple organ failure.

**DIAGNOSIS**

Clinical diagnosis:
Jaundice, malaise, pyrexia, weight loss, stigmata of chronic liver disease.

Laboratory tests:
Neutrophilia, prolonged clotting studies
Moderately elevated transaminases. AST>ALT. More severe elevation suggests hepatocellular necrosis and FHF, see below
Raised Bilirubin, GGT, IgA and Ferritin (does not necessarily indicate haemochromatosis)

Liver Biopsy:
Required for the definitive diagnosis, often omitted because of hazards (bleeding). Transjugular biopsy available in some settings.
PROGNOSIS
Discriminant Function (DF) is the serum bilirubin (mcmol/L) divided by 17 plus the difference between the prothrombin time and the control (seconds) multiplied by 4.6.

\[
DF = \frac{[\text{Bili}]}{17} + (\text{PT-Control}) \times 4.6
\]

It maps to outcome as follows:
Mild disease (DF <24) 15% mortality at three months post presentation; moderate disease (DF 24-31) 20% mortality, severe disease (DF>32) 55% mortality.

TREATMENT
Stop alcohol
Treat withdrawal effects with Diazepam, lorazepam or chlordiazepoxide
Pabrinex IV twice daily for five days
Thiamine 100mg IV twice daily for two weeks or 100mg oral tds
Enteral or parenteral nutrition (1.5 g/kg ideal bwt/day protein and 35-40 kcal/kg/day non-protein)
Screen and treat for bacterial/fungal infections
Corticosteroids may be used in the absence of infection, bleeding or encephalopathy

Hepatorenal syndrome: ARF for which liver failure is the only identifiable cause. Low urine sodium (<10mmol/L) is usual. Grave prognosis, 95% mortality. Give terlipressin 1-2mg tds and 2 units 20% HAS each day.
HF/HD is not indicated in hepatorenal syndrome since the prognosis is hopeless. However, it is important to exclude other causes of renal failure before diagnosing hepatorenal syndrome.

Referral for liver transplantation is sometimes appropriate in patients who have abstained from alcohol for some time.

ACUTE (FULMINANT) HEPATIC FAILURE
See next chapter