Inflammation of liver with abnormal LFTs and various histological changes noted on biopsy.
Acute = self-limited liver inj <6/12
Chronic = diagnosed on pathological criteria, >6/12
Incubation - pre-icteric - icteric - convalescent
ALT > AST (AST > ALT in cirrhosis); ALP normal or mild incr

**Causes**
1. Drugs and toxins - EtOH, paracetamol, aspirin [Reyes], paraquat, carbon tetrachloride [dry cleaning], idiosyncratic - fluclox, halothane, amiodarone
2. Infection
   - viral (Hep A, B+/D, C, E, G, CMV, HSV, yellow fever)
   - post-viral (Reye’s)
   - non-viral (lepto, toxo, Q fever, mycoplasma)
3. Vascular - shock, portal vein thrombosis, Budd Chiari, veno-occlusive disease
4. Depositions - Fe, Cu, fatty liver, NASH (resembles alcoholic hepatitis but no hx alcohol abuse)
5. Malignancy - primary or secondary
6. Autoimmune
7. CHF

Investigations: FBC, U&E, LFT, INR, serology. USS/CT/MRI to assess presence of cirrhosis/other causes.

**Acute Hepatitis**
Features: Fever, liver tenderness, jaundice, N+V; may develop acute liver failure, ascites, hepatic encephalopathy. Hepatomegaly (10%), splenomegaly (5%), and LN (5%).

**Viral Hepatitis**
Responsible for ~50% of all cases of acute hepatitis. Hep viruses A–E, CMV, EBV, adenovirus, herpes simplex
Hepatitis A–E account for about ≥95% of cases of acute viral hepatitis
### Acute = HBsAg and HBeAg, IgM-anti HBCAg
Symptomatic acute infection in 30%; Arthritis, fever, skin eruption in preicteric phase; most common hepatitis cause of ALF; mortality higher in ALF caused by Hep B than Hep A

- **HBsAg** = acute, detectable 1st in preicteric phase; may have normalized if late presentation; carrier if present on 2 occasions >6/12 apart
- **IgM-anti HBCAg** = acute; high infectivity
- **HBeAg** = acute and phase 2 chronic (usually decreases in 3-4/52); high infectivity; marker of viral replication

### Fulminant
- 0.1-0.5% (mortality rate 80%)

### Chronic
- 5-10% (1-3% healthy adults, 5-10% immunocomp, 90% neonates) = HBsAg >6/12, IgG-anti HBCAg, maybe HBeAg, anti-HBeAg
  - cirrhosis and hepatocellular Ca; shortens life span in 45% men, 15% women

**Phase 1:** immune tolerance; 20-40yrs; normal ALT; high levels viral replication; no trt

**Phase 2:** immune clearance with immune response; symptomatic in 30%; hepatitis, incr ALT 0 fibrosis with repeated episode; cirrhosis in 30-40%

**Phase 3:** immune control 0 immune response suppresses replication 0 decr inflamm, ALT normalises; 5-10%/yr phase 2 become phase 3; assoc with HBeAg seroconversion (anti-HBeAg develops, decr HBeAg); hepatitis stops; may reactivate at any time

**Phase 4:** immune escape; recurrence of hepatitis, fibrosis; virus mutates and stops making HBeAg; incr ALT; 8-10%/yr develop cirrhosis

- **IgG-anti ABCAg** = chronic, previous infection
- **Anti-HBeAg** = phase 3 chronic; low infectivity

### HBV DNA: high infectivity, used for monitoring response to trt

### Carrier: 1-10% = HBsAg
Accounts for 90% chronic infections

- **IgG-anti HBsAg** = immunity and recovery

<table>
<thead>
<tr>
<th>Current acute infection:</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
</tr>
<tr>
<td>HBeAg</td>
</tr>
<tr>
<td>IgM-anti HBCAg</td>
</tr>
<tr>
<td>Hep B DNA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Co-infection:</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
</tr>
<tr>
<td>HBeAg</td>
</tr>
<tr>
<td>IgM-anti HBCAg</td>
</tr>
<tr>
<td>Hep B DNA</td>
</tr>
<tr>
<td>Anti-D virus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chronic active Hep B:</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
</tr>
<tr>
<td>HBeAg</td>
</tr>
<tr>
<td>IgG-anti ABCAg</td>
</tr>
<tr>
<td>Hep B DNA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous resolved Hep B:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti HBsAg</td>
</tr>
<tr>
<td>Anti-HBeAg</td>
</tr>
<tr>
<td>IgG-anti ABCAg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccine available (HBsAg):</th>
</tr>
</thead>
<tbody>
<tr>
<td>If non-immune exposed, give anti-HBsAg within 1/52 (75% effective)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Supportive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trt if infected and abnormal LFT's or high HBV DNA levels (likely in acute, phase 2 + 4 chronic) – entecavir, lamivudine, tenofovir etc...</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anti-HBsAg</th>
</tr>
</thead>
</table>

**www.shakEM.co.nz**
<table>
<thead>
<tr>
<th>Letter</th>
<th>Table</th>
<th>Description</th>
</tr>
</thead>
</table>
| C | 2/12 | Parenteral
80% prevalence in IVDU
15% rate of transmission with sex (rare)
10% unknown source
<2% seroconvert with needlestick
Single stranded RNA virus
**Acute** = HCV RNA: Pre-icteric non-specific; usually asymptomatic (Sx in 15-20%) ◊ icteric phase for 1-2/52; Extrahepatic Sx in 75%: arthralgia, paraesthesia, myalgia, pruritis, sicca ◊ spontaneous resolution in 30-50%
**Chronic** = IgG-anti HCV: 75-85% adults; 55% children
25% develop cirrhosis over 20-30yrs; 20% cirrhotics develop hepatocellular Ca
**Carrier:** 0.2-1%
**HCV RNA** = acute, detectable 1st within 1-2/52 exposure
**IgG-anti HCV** = chronic; +ive by 3/12 usually

| D | 4-7/52 | Parenteral
Sexual rare
Usually IVDU Only occurs in patients with acute/chronic HBV
5% HBV carriers have HDV
circular ssRNA virus. Reqs HBV for replication
**Acute** = HDV RNA, Ig-anti HDV: in 2-20%
**Co-infection** = hepatitis with resolution in 80-95%
**Fulminant** = 2-20% if super-infection
**Chronic** = Ig-anti HDV: 5-10% if co-infection; 80% if super-infection
**Carrier:** Low
1-10% IVDU and haemophiliacs are carriers
**HDV RNA** = acute
**Co-infection** = IgM-anti HDAg + IgM antiHBcAg
**Super-infection** = IgM-anti HDV + HBsAg
**IgM/G-anti HDV** = acute / chronic

| E | 2-8/52 | Faecal-oral, water-bourne
**Acute** = HEV Ag, IgM-anti HEV: Self-limited; 1-3% overall fatality; 5-25% mortality in pregnancy
**Fulminant** = 20% if pregnant
**Chronic** = No
**Carrier:** No
**HEV Ag** = acute
**IgM-anti HEV** = chronic
**IgG-anti HEV** = immunity

---

**Drug-Induced Hepatitis & Liver Disease**
- Up to 25-50% of all cases of hepatitis:
  - Acute hepatocellular damage:
    - dose-unrelated, e.g. antituberculous drugs, halothane, anticonvulsants
    - dose-related, e.g. alcohol, paracetamol, amiodarone, methotrexate
  - Chronic active hepatitis, e.g. isoniazid, nitrofurantoin
  - Cirrhosis, e.g. alcohol, methotrexate
  - Hepatic tumours, e.g. anabolic steroids, combined oral contraceptives
  - Intrahepatic cholestasis:
    - dose-unrelated, e.g. carbimazole, erythromycin, phenothiazines
    - dose-related, e.g. anabolic steroids, azathioprine, oestrogens
  - Gallstones, e.g. clofibrate, oestrogens
Risk factors: Race (Afrocaribbeans & isoniazid), age, EtOH, liver disease, P450 genetics, malnourished

Pathogenesis:
- Predictable or direct: usually promptly follows an exposure to a new medication. Direct toxicity or a toxic metabolite, e.g. paracetamol.
- Unpredictable or idiosyncratic: may be related to immune hypersensitivity; rash, fever and eosinophilia are typically present. These reactions follow exposure by a few weeks e.g. Augmentin.
- Late (many months) onset idiosyncratic reactions are difficult to recognise and usually do not display features of hypersensitivity, e.g. isoniazid.

Clinical patterns:
- Hepatitis: elevated AST/ALT; e.g. paracetamol poisoning, thiazolidinediones, statins
- Cholestasis: elevated ALP; e.g. chlorpromazine, erythromycin, oestrogens
- Mixed picture: biliary canaliculi and hepatocytes damage: elevations in liver enzymes e.g. Augmentin

Investigations: LFTs, paracetamol level, viral serology, ANA, Cu & Fe levels, abdo USS/CT/MRI scan, liver biopsy.

Management: N-acetylcysteine for paracetamol poisoning. Supportive care or even transplant for liver failure.

Chronic Hepatitis
- Chronic Hepatitis B, C or D infection
- Autoimmune hepatitis
- Alcoholic liver disease
- Sarcoidosis
- Drug induced hepatitis, e.g. isoniazid, methyldopa, nitrofurantoin, etc
- Metabolic, e.g. Wilson's disease, alpha-1 antitrypsin deficiency, haemochromatosis

Leptospirosis (Weil's Disease)
Spirochaete infection. Principal source of human infection is the rat but includes dogs & livestock. Contracted via contact with contaminated water, soil, or urine/tissues.

Epidemiology
- Most widespread zoonosis in the World
- Significant in Belize and Vietnam, eastern/southern Europe, Australia & New Zealand.
- Most often affects teenagers and adults and is more common in men.
- Risk factors include sewage workers, swimming in contaminated water, farmers, veterinarians, abattoir workers, rodent control workers, animal workers.

Presentation
- Incubation period is usually 7-14 days (range from 2-25 days). Onset is usually abrupt.
- Infection may be anicteric (self-limiting) or icteric leptospirosis (Weil's disease).
- Often mild with flu-like symptoms, but may cause pneumonitis, arthritis, orchitis, cholecystitis, myocarditis, coronary arteritis, aortitis, aseptic meningitis and uveitis.
- Approximately 10% become jaundiced (with hepatocellular necrosis) and have a severe and rapidly progressive form of the disease with liver failure and renal failure.
- The jaundice appears during days 5-9 of illness and lasts ~1 month. The degree of jaundice itself is not prognostic but leptospirosis without jaundice is rarely fatal.
- Purpura, petechiae, epistaxis, minor haemoptysis and other signs of bleeding are common.
Other symptoms include fever, vomiting, abdominal pain, hepatomegaly, skin rashes, conjunctival haemorrhage, uveitis. There is often a severe headache, retro-orbital pain, and photophobia. (aseptic meningitis). A severe myalgia (lower back, and legs) is common.

Resp sympts vary from cough, SOB, and haemoptysis to ARDS and massive haemorrhage.

Leptospiral nephropathy is usual, sometimes → life threatening renal failure.

Investigations

- Bloods: LFT (↑Bili, ↑AST&ALT), ↑INR, FBC (↓Hb, ↑WCC, ↓plts), renal impairment, ↑CK (rhabdo), coags (↑PT)
- MSU usually shows sediment and proteinuria.
- CXR: may be normal or show patchy shadowing in alveolar haemorrhage.
- Dx based on serology (paired), either using microscopic slide agglutination test or ELISA

Management

- Oral doxycycline or amoxicillin (Jarisch-Herxheimer reaction possible).
- Intravenous penicillin G or chloramphenicol for severely ill patients
- Supportive care and treatment of the hypotension, haemorrhage, RF and liver failure
- Vitamin K should be administered for hypoprothrombinaemia
- Usually self-limiting.