

## Viral Hepatitis

Viral hepatitis is inflammation of the liver as a result of viral infection. Whilst hepatitis can be due to infection it is important to remember there can be other causes, such as therapeutic drugs, alcohol and drug misuse, autoimmune and metabolic diseases. Treatment varies between the different infectious causes and whether the infection is acute or chronic.

### Clinical Features

Acute (<6 months)	<ul style="list-style-type: none"><li>• Can be asymptomatic</li><li>• Anorexia</li><li>• Malaise</li><li>• Right upper quadrant pain</li><li>• Jaundice</li><li>• Liver failure</li></ul>
Chronic (>6 months)	As for acute plus: <ul style="list-style-type: none"><li>• Weight loss</li><li>• Abdominal distension</li><li>• Confusion</li><li>• Signs of liver failure</li></ul>

### Causes

Acute	<ul style="list-style-type: none"><li>• <i>Hepatitis A Virus</i></li><li>• <i>Hepatitis B Virus (+/- Hepatitis D Virus)</i></li><li>• <i>Hepatitis C Virus</i></li><li>• <i>Hepatitis E Virus</i></li><li>• <i>Epstein Barr Virus (EBV)</i></li><li>• <i>Cytomegalovirus (CMV)</i></li></ul>
Chronic	<ul style="list-style-type: none"><li>• <i>Hepatitis B Virus (+/- Hepatitis D Virus)</i></li><li>• <i>Hepatitis C Virus</i></li><li>• <i>Hepatitis E Virus</i></li></ul>

### Warning

If your patient did not have hepatitis on admission and now has symptoms it is unlikely that they have acquired an infectious cause as an inpatient. It is more likely that they have been given a therapeutic drug that has caused the hepatitis. Many drugs such as pain killers, anticonvulsants, statins and even the oral contraceptive pill can do this as well as antibiotics.

### Investigations

- Biochemistry
  - Raised ALT and AST
  - Often raised bilirubin
- Serology
  - *Hepatitis A Virus* (anti-HAV IgM)
  - *Hepatitis B Virus* (HBsAg, anti-HBs, anti-HBc and IgM anti-HBc)
  - *Hepatitis C Virus* (anti-HCV)
  - EBV (IgM and IgG)
  - CMV (IgM and IgG)

An IgM antibody positive test for Hepatitis A, Hepatitis C, EBV and CMV indicates that the patient has an acute infection (see section – Microbiology, How to Interpret Microbiology Results – Serology and Virology). Hepatitis B serology, however, can be confusing because there are four different antibody and antigen tests. It is important to be able to interpret these results in combination in order to establish if there is acute infection, chronic infection, evidence of past infection or immunity due to vaccination.

### Interpretation of Serology for Hepatitis B

Test	Result	Interpretation
HBsAg Anti-HBc Anti-HBs	Negative Negative Negative	No evidence of infection <b>OR</b> immunity
HBsAg Anti-HBc Anti-HBs	Negative Positive Positive	Evidence of past infection with subsequent immunity
HBsAg Anti-HBc Anti-HBs	Negative Negative Positive	No evidence of infection but immune due to vaccination
HBsAg Anti-HBc IgM Anti-HBc Anti-HBs	Positive Positive Positive Negative	Acute infection
HBsAg Anti-HBc IgM anti-HBc Anti-HBs	Positive Positive Negative Negative	Chronic infection
HBsAg Anti-HBc Anti-HBs	Negative Positive Negative	Discuss with Gastroenterologist or Microbiologist  4 possible interpretations: <ul style="list-style-type: none"> <li>• Resolved infection (most common)</li> <li>• False positive anti-HBc therefore susceptible to infection</li> <li>• Low level chronic infection</li> <li>• Resolving acute infection</li> </ul>

**HBsAg** = Hepatitis B surface antigen (evidence of acute or chronic hepatitis, patient is infectious).

**Anti-HBc** = Total Hepatitis B core antibody (appears at the onset of symptoms and persists for life, evidence of active or past infection).

**IgM anti-HBc** = IgM specific Hepatitis B core antibody (evidence of acute infection **NOT** positive in chronic infection).

**Anti-HBs** = Hepatitis B surface antibody (part of the normal immune response to Hepatitis B or the vaccine; evidence of immunisation or past infection. **NOT** positive in acute or chronic infection, as the infection has now resolved).

## Treatment

There is no specific treatment for viral hepatitis caused by Hepatitis A, E, CMV and EBV. The treatment of Hepatitis B and C requires specialist advice from a Gastroenterologist. Treatment courses last for months and are generally poorly tolerated due to side effects.

<b>Hepatitis B</b>	
Acute	No treatment 90% of acute hepatitis resolves spontaneously, reactivation can occur but is rare and usually triggered by immunosuppressive therapy
Chronic and asymptomatic	No treatment Treatment may start when there is evidence of liver damage (raised ALT) to prevent cirrhosis and hepatocellular carcinoma
Chronic with raised ALT	PO Nucleoside inhibitors <b>PLUS</b> SC PegIFN

<b>Hepatitis C</b>	
Mild / Early	No treatment
Moderate / Severe	PO Telepravir <b>OR</b> PO Bosepravir <b>PLUS</b> Ribavirin <b>PLUS</b> SC PegIFN
<ul style="list-style-type: none"><li>• Hepatitis C is divided into six genotypes with many subtypes. Most infections in the UK are genotypes I, II, III</li><li>• Each genotype contains closely related viruses which have the ability to mutate and become immune to current treatments. This is why chronic Hepatitis C is difficult to treat</li><li>• Different genotypes respond differently to treatment</li></ul>	

## Prognosis and Complications

- Hepatitis B - 10% of acute infections become chronic
- Hepatitis C - 85% of acute infections become chronic
- Treatment of HCV results in 70-80% cure but side effects can lead to problems with compliance

## Prophylaxis and Prevention

- Vaccination against Hepatitis A and Hepatitis B
- Avoid exposure through sexual intercourse or IV drug abuse
- See management of needlestick injuries (see section – Infection Control, Needlestick Injuries)

## Hints and Tips

Hepatitis C can become resistant to antivirals during treatment. However, on stopping treatment this reverses back to sensitive "wild-type". Restarting treatment does not trigger resistance again because HCV is an RNA virus and cannot store the resistance genes.

### On the Horizon

The treatment of Hepatitis C is likely to change dramatically within the next year with the expected licensing in the UK of a new RNA polymerase inhibitor, Sofosbuvir (Solvadi®).

Treatment regimens including Sofosbuvir lead to a cure in HCV Genotypes 1-4 in almost all patients who have not been previously treated with other antivirals. There are still potential issues with side effects, but these are primarily related to the Ribavirin or PegIFN with which it is combined.

### Proposed Treatment of Hepatitis C with Sofosbuvir

Genotype 1 or 4	PO Sofosbuvir <b>PLUS</b> Ribavirin <b>PLUS</b> SC PegIFN	12 weeks
Genotype 2	PO Sofosbuvir <b>PLUS</b> Ribavirin	12 weeks
Genotype 3	PO Sofosbuvir <b>PLUS</b> Ribavirin	24 weeks

**The main drawback is the cost.** It is estimated that 12 weeks of treatment with Sofosbuvir will be approximately £35,000 per person. However, this is a clinically superior drug and compares favourably long-term when calculating the current cost of treatment including blood tests, side effect management and hospital visits.