Clare Hawley
GPwSI and associate specialist in cardiology, Chesterfield, Derbyshire

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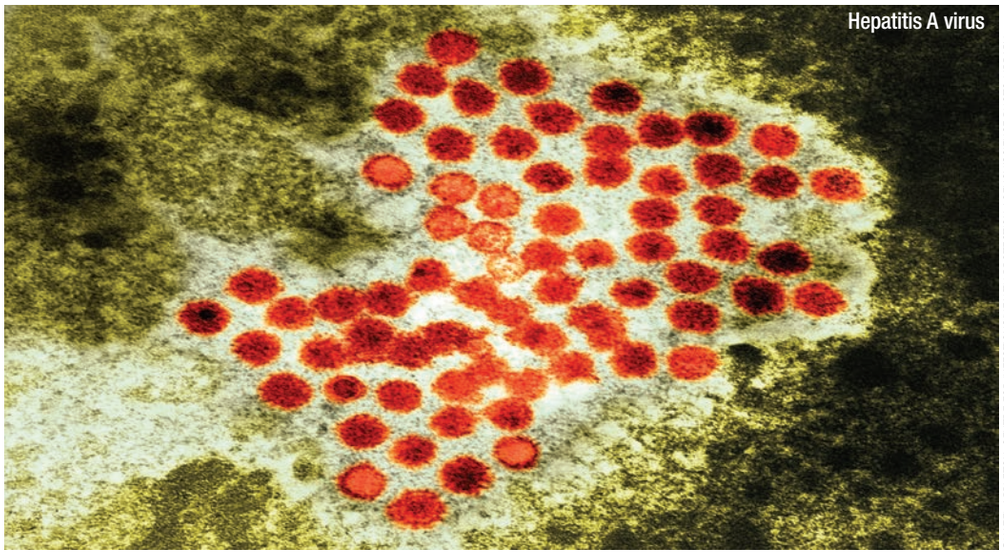
Disease Focus 2

UNDERSTANDING VIRAL HEPATITIS: AS EASY AS A, B, C

Viral hepatitis is one of the three main causes of liver disease. We review the different types of viral hepatitis and the key steps in prevention, diagnosis and treatment.



Hepatitis A virus

Key points:

- Viral hepatitis is becoming a major health problem as a result of drug misuse and silent transmission between individuals who are unaware they are infected
- It is largely preventable and effective treatments are available
- Primary care has a key role in identifying those at risk, detecting hepatitis B and C infection and offering infected individuals effective treatments and support
- Lifestyle change in respect of safe sex, safe drug use and alcohol consumption is key to prevention of transmission and progression

Hepatitis simply means inflammation of the liver, for which there are many causes but viral infection is one of the most important. There are at least six specific hepatitis viruses: A, B, C, D, E and G, but no F! Of these, hepatitis A, B and C are most common. Each virus is different in the way it is transmitted from person to person, causes damage to the liver and its long-term effects on health. Hepatitis viruses come in different strains or genotypes (with different genetic makeup), which respond differently to treatment.

ACUTE OR CHRONIC INFECTION?

Acute viral hepatitis is a sudden inflammation or infection lasting no more than a couple of months. Symptoms vary in severity from mild and hardly noticed to severe and requiring hospital admission. Symptoms of acute infection are similar for hepatitis A, B and C and include fever, fatigue, and nausea and vomiting (see Table 1).

Chronic hepatitis is where inflammation of the liver lasts for longer than six months. Hepatitis B and C infection are the commonest causes of chronic viral hepatitis and have the most serious long-term effects on health. Over time, continuous inflammation causes liver cell damage with scarring and fibrosis and healthy tissue is eventually replaced by irreversible scarring (cirrhosis). The liver becomes unable to function normally and if untreated, chronic hepatitis may progress to liver failure and primary liver cancer (hepatocellular carcinoma). Signs and symptoms of chronic infection are often absent until liver damage is advanced.

Hepatitis A, B and C are notifiable diseases and screening should be offered to people with unexplained abnormal liver function tests (LFTs) or who are identified as being at high risk.

Table 1: Symptoms of acute viral hepatitis

- Fever
- Fatigue
- Loss of appetite
- Nausea and vomiting
- Abdominal pain
- Pale-coloured bowel movements
- Joint pain
- Jaundice

“Hepatitis B and C infection are the commonest causes of chronic viral hepatitis and have the most serious long-term effects on health”

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Basic immunology: a reminder

WHAT ARE VIRUSES?

Viruses are tiny micro-organisms made up of a central core of genetic material (DNA or RNA) surrounded by a protein shell, occasionally with an extra outer envelope (as in hepatitis B). Each virus has a number of different strains or genotypes.

HOW DO VIRUSES REPRODUCE?

Viruses can live outside the body in an inactive form for long periods. In order to reproduce or replicate, they need to break in to body cells and take over their internal workings to become factories for making new virus particles. This triggers an immune reaction and inflammatory response, which damages the cells, causing scarring and fibrosis. Infected cells may burst, releasing millions of virus particles to cause further problems around the body.

HOW DOES THE BODY PROTECT AGAINST VIRUSES?

The immune system is designed to protect the body from viruses by detecting foreign proteins and eliminating them.

When a virus invades the body the immune system spots the foreign protein or **antigen** on its surface. Specialist white blood cells (B lymphocytes) then produce proteins, called **antibodies** or **immunoglobulins**, which lock onto the antigen, identifying it as harmful. T lymphocytes then spot the antibody and move in to kill the infected cells.

IgM antibodies are first responders and indicate recent infection.

IgG antibodies are produced later on in the course of infection.

IMMUNITY AND IMMUNISATION

Active immunity is where the surface protein of a virus has been identified and tagged as harmful by antibodies, which then stay in the system and are able to recognise the virus and fight it off if it invades again.

Passive immunity is where antibodies (immunoglobulins) are given directly to help a patient fight off an acute infection.

Immunisation is a form of active immunity and involves introducing a weakened or killed form of the virus that won't cause illness but will allow the body to produce antibodies and protect the body from future attack.

TREATMENTS FOR VIRAL INFECTION

Antiviral drugs – affect the genetic material inside the core of the virus so that the viral genetic material is unable to replicate so no new viruses are produced.

Interferons – are immune system proteins that 'interfere' with viral replication, making infected cells easier to spot and protecting healthy cells from becoming infected. Interferons can be used as treatments in the management of hepatitis B and C. Pegylated interferons incorporate chemicals that enable interferons to work for longer in the body.

TESTING FOR HEPATITIS INFECTION

Acute infection is confirmed by testing for the presence of the viral surface antigen.

A past infection, ongoing infection and current immunity is confirmed by testing for the presence of antibodies.

The viral load gives a measure of the number of virus particles in the blood and is used as a measure of response to treatment (with the aim of reducing viral load).

Testing methods available include:

- venous blood sample testing
- dried blood spot testing
- single kits are available for hepatitis B and hepatitis C
- buccal swab

HEPATITIS A

Hepatitis A is an acute, self-limiting illness transmitted directly from person to person or through ingestion of food or drinks contaminated with the hepatitis A virus (HAV). It is common where there is poor personal or food hygiene. Testing is based on a blood test for antibodies (see Table 2). There is no specific treatment and illness may last several weeks, but it cannot be caught again after recovery. There is no chronic phase and there are usually no long-term effects from hepatitis A.

Table 3: People at risk of hepatitis A infection

- travellers to high risk areas or people who live in the UK who were born in those areas, *eg* South and East Europe, Africa, parts of Middle and Far East
- high risk occupations, *eg* sewage workers
- close contacts of a person with acute infection

Table 2: Tests for hepatitis A

The test	What it tests for	What it tells us
HAV- total antibodies	IgM and IgG immune response to HAV infection or immunisation	• previous infection or vaccination • person immune to further infection
Hepatitis A IgM antibodies	Antibodies produced in the early stages of acute HAV infection	Recent acute HAV infection

Hepatitis B and C

Hepatitis B and C cause both acute and chronic infection. The two most important consequences of chronic infection are cirrhosis and primary liver cancer (hepatocellular carcinoma) so it is essential to try to prevent infection in the first place, and to detect and treat early in patients who are infected. Primary care has a key role in detecting hepatitis B and C and supporting patients through treatment and necessary lifestyle change.

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HEPATITIS B

Hepatitis B (HBV) is the commonest form of viral hepatitis and is highly infectious: one hundred times more than HIV. It is estimated that 350 million people around the world are infected with hepatitis B. In the UK, the prevalence of hepatitis B is three cases in every 1,000 people and is rising rapidly due to increasing immigration of infected people from parts of the world where prevalence is high. It is estimated that 6-7,000 people with chronic HBV move to this country each year and that most are undiagnosed.

HBV is found in the body fluids, such as blood, vaginal fluid, semen and saliva, of infected people. In the UK infection is spread primarily during **sexual contact or sharing needles and other drug-taking equipment**. HBV infection can also be passed between an infected mother and her baby during delivery – so-called **vertical transmission** – which is how the infection tends to be spread in parts of the world where prevalence is high.

HBV causes an acute, often asymptomatic illness and most people are able to clear it naturally within the first six months. However, 25% will go on to develop chronic hepatitis B that, if undiagnosed and untreated, can lead to cirrhosis and liver cancer. An important consideration for patient care is that 10% of people with HIV are also infected with HBV.

TESTS FOR HEPATITIS B

There are a number of tests used in the diagnosis of HBV infection. They look for the presence of viral antigens and evidence of immune response and can help establish:

- if there is current infection
- if the person was infected or vaccinated in the past and is now immune
- the likelihood of an acute infection clearing naturally
- the likelihood of developing chronic hepatitis B infection

TREATMENT

The treatment of chronic hepatitis B infection includes:

- Interferon or long-acting pegylated interferon injections which mimic the body's own defences against infection
- Antiviral drugs given orally to reduce the amount of virus in the blood. Examples include lamivudine, tenofovir, entecavir and adefovir. Response to treatment varies in different individuals

Table 4: People at risk of hepatitis B infection

- people who inject drugs (PWID)
- sexual contacts of infected or high-risk people
- men who have sex with men
- sex workers (male and female)
- people with HIV and other sexually transmitted infections
- people receiving haemodialysis
- babies born to infected mothers
- healthcare workers
- people living in prison
- victims of sexual assault or needle stick injury
- travellers to or from areas of the world where infection is common, *ie* >2% population, *eg* sub-Saharan Africa, Asia and Pacific Islands

Table 5: Testing for hepatitis B

The test	What it tests for	What it tells us
Hepatitis B surface antigen (HBsAg)	Protein on the outer surface of the virus	Positive result indicates: ● current hepatitis B infection ● infection may be acute or chronic ● the person is infectious **Action: refer to specialist for further tests** Negative result: ● Shows the person never had the virus or has recovered from infection
Hepatitis B surface antibodies (Anti-HBs)	Antibodies that appear during recovery from HBV infection or in response to immunisation	Positive result shows the person is immune to hepatitis B and is not infectious
Hepatitis B e-antigen (HBeAg)	Shows a highly infectious stage of HBV infection	The person is highly infectious until antibodies develop **Action: refer to specialist for further tests**
Hepatitis B e-antibody (anti-HBe)	Antibodies to HBV e-antigen have developed	Shows an immune response to HBV-e The virus is inactive but remains in the liver
Anti-hepatitis B core antigen (Anti-HBc) IgM	Shows a recent early IgM immune response to the core antigen	Indicates infection within the last 6 months
Hepatitis B DNA – viral load (HBV-DNA)	A measure of the amount of virus in the blood	Low or negative result indicates a good response to treatment
Hepatitis B virus genotype	The strain of HBV present	Used to inform treatment decisions

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HEPATITIS C

Acute hepatitis C infection is usually asymptomatic and remains undiagnosed while being passed on, unknowingly, to others. One in four people infected with hepatitis C will clear the virus naturally and have no long-term effects. However, three out of four become chronically infected and 20% of these will develop cirrhosis and some will develop liver cancer. There is a 5% risk of vertical transmission from mother to baby.

Hepatitis C virus (HCV) is found in the blood of infected people and spreads by blood-to-blood contact. The virus can remain infectious in blood outside the body for several weeks, *eg* blood on razors and toothbrushes. People at highest risk are those who inject drugs (PWID) and share needles and other drug-taking paraphernalia – 90% of hepatitis C infection is transmitted by this route. It is estimated that 0.6% of the UK population is chronically infected with HCV, with 70% of these being completely unaware.

TEST FOR HEPATITIS C

The tests used for the diagnosis of hepatitis C look for the presence of viral genetic material, the quantity of virus in the body and evidence of an immune response.

Hepatitis C antibody test (anti-HCV) is the primary screening test and shows if a person has ever been infected. It does not confirm current infection.

- **A negative test** should be repeated in three months if exposure was within the last three months because it can take this long for antibodies to become detectable
- **A positive test** should be confirmed by a repeat test in three months because 25% of people will clear the infection naturally

If the antibody test remains positive a second test is required to establish if the infection is currently active.

Hepatitis C RNA (HCV-RNA) detects HCV genetic material and confirms current active infection.

Polymerase chain reaction (PCR) gives a measure of the number of viral particles or viral load and can be used to monitor response to treatment.

Genotyping is carried out before starting treatment. Knowing the genotype helps in making decisions about duration of treatment and its likelihood of success.

TREATMENT

Treatment with pegylated interferon and ribavirin can successfully clear the virus in over half of cases, depending on genotype. However, some people can get re-infected after showing an initial success so long-term monitoring is required. Excessive alcohol consumption significantly accelerates liver damage in HCV infection and lifestyle changes can significantly slow disease progression.

PREVENTION OF HEPATITIS A, B AND C: IMMUNISATION AND LIFESTYLE MEASURES

Vaccination is available for hepatitis A and B. It is recommended for people at risk and can be given individually or as a combined vaccine. There is currently no vaccination available for HCV.

Table 6: People at risk of HCV infection

People who:

- inject drugs or have ever shared equipment to inject drugs, no matter how rarely or how long ago
- have received medical or dental treatment in countries where infection control and sterilisation procedures are poor
- received a blood transfusion before 1991 or blood products before 1986
- are regular sexual partners of someone with HCV
- live in prison
- are born to a mother with HCV
- have accidental exposure to blood from a high-risk person – *eg* needle stick
- have tattoos, piercings, acupuncture or electrolysis where infection control procedures are poor

Table 7: Tests for hepatitis C

The test	What it tests for	What it tells us
Anti-HCV	Antibodies that become present 3-9 months after exposure to HCV. It is positive in acute, chronic or resolved infection	If the person has ever been infected with HCV. Negative result – the test might have not become positive if exposure was within the last 3 months **Action: retest in 3 months** Positive result – confirm the diagnosis and also test for active infection **Action: repeat anti-HCV in 3 months and check HCV-RNA**
HCV-RNA	Hepatitis C genetic material	Positive result confirms current infection **Action: refer to a specialist** Negative and anti-HVC positive means there was infection in the past but it has cleared It does not mean the patient will have lifelong immunity **Action: repeat after 6-8 weeks to confirm negative status**
HCV-RNA PCR (polymerase chain reaction) viral load	The number of viral particles in the blood	Used by specialists to monitor response to treatment If undetectable 6 months after treatment this is sustained viral response (SVR) and indicates treatment success
Viral genotyping	Identifies which of the six types of HCV is present	Helps with decisions about duration of treatment

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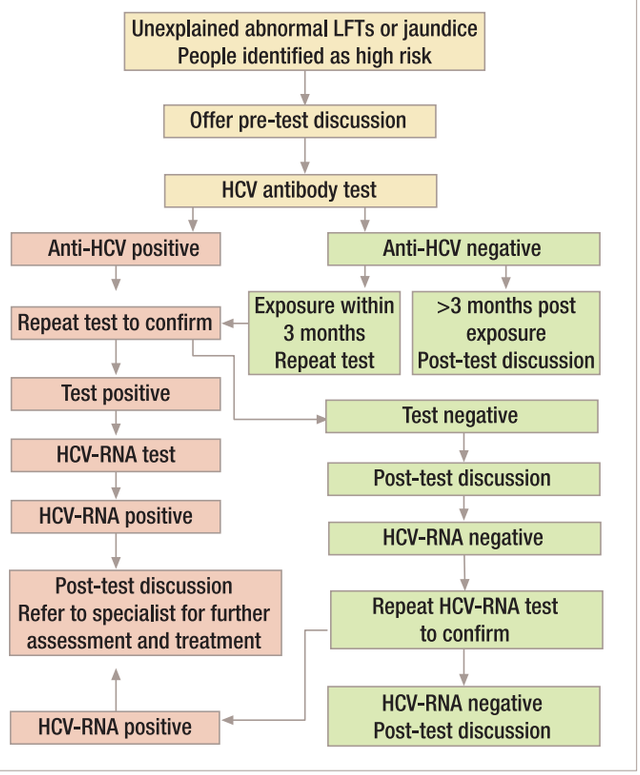
Hepatitis B immunoglobulin can be given to people who may have been exposed to infection, including healthcare professionals who sustain a needle stick injury and newborn babies of infected mothers. Since 2000 all pregnant women are screened for hepatitis B. Transmission to their babies can be prevented in over 95% of cases if vaccination is given immediately.

Hepatitis B and C can be prevented by avoiding risky behaviour in respect of injecting drugs, safe sex, taking care when receiving tattoos or piercings, medical or dental treatment overseas and by not sharing toothbrushes and razors with an infected person.

KEEPING PATIENTS INFORMED

Before testing for hepatitis it is good practice to discuss with the patient why the test is being done and the benefits and potential challenges of knowing the results. Verbal consent should be obtained and clear arrangements made for giving patients the results with appropriate counselling and support. Once results are available further discussion about the implications for the person affected and those closest to them should be arranged, together with follow-up and support.

Figure 1: Flow chart for diagnosis of viral hepatitis C



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Hepatitis A, B and C: pre-test discussion

Before testing for hepatitis A, B or C discussion with patient should include:

- what is being tested and why
- the benefits of knowing the results
- the potential challenges of knowing the results
- what the test involves and assurance of confidentiality
- assessment of risk and timing of possible exposure
- arrangements for receiving results
- advice not to do donate blood until results are known

Hepatitis A, B and C: post-test discussion

When the results are back :

- share the results and confirm or exclude the diagnosis
- discuss the need for repeating tests to confirm or exclude the diagnosis
- offer referral to a specialist if indicated
- provide information about
  - hepatitis
  - implications of a positive result
  - implications for close contacts and partners
  - implications for life insurance and mortgage
  - implications for employment
- give lifestyle advice to prevent transmission and deterioration
- advise that alcohol accelerates disease progression
- promote safe sex and use of condoms
- promote safe drug use - including support to quit
- direct to needle exchange schemes

more information

Resources www.britishlivertrust.org.uk www.hepc.nhs.uk

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Summary: Viral hepatitis key facts

	Hepatitis A	Hepatitis B	Hepatitis C
Caused by	hepatitis A virus (HAV)	hepatitis B virus (HBV)	hepatitis C virus (HCV)
Route of transmission	Faeco-oral spread • ingestion of infected food or drink • close contact with an infected person	Contact with infected body fluids • sharing drug-taking equipment • sexual contact with an infected person • during delivery of a baby to an infected mother • needle stick injury	Contact with infected blood • sharing drug-taking equipment Less commonly: • sexual contact with an infected person • babies during delivery to an infected mother • needle stick injury
Who is at risk	• travellers to areas of high risk – S & E Europe, Africa, parts of Middle and Far East • high-risk occupations, *eg* sewage workers • close contacts of infected people	• people who inject drugs • sexual contacts of infected people • babies of infected mothers • healthcare workers • people with HIV and other sexually transmitted diseases • men who have sex with men • sex workers • people in prison • people on haemodialysis • immigrants from parts of the world where prevalence is >2% of the population	• people who inject drugs • recipients of blood before 1991 or blood products before 1986 • healthcare workers exposed to needle stick • people with HIV • babies born to infected mothers • people who received medical or dental treatment in countries where infection control and sterilisation procedures are poor • people having tattoos, piercings, acupuncture or electrolysis where infection control procedures are poor • people in prison
Symptoms of acute infection	• Fever, fatigue, joint pain, pale stools, jaundice • Loss of appetite, nausea and vomiting, abdominal pain		
Likelihood of chronic infection	none	90% of infected infants up to 10% of adults	75% develop chronic infection 25% clear the virus naturally
Long-term complications	rare	20% develop cirrhosis, liver failure or liver cancer	up to 20% develop cirrhosis 1-5% die of cirrhosis or liver cancer
Tests for acute infection	IgM anti-HAV	• HBsAg • HBV core antigen • HBeAg • Anti-HBcAg	none
Tests for chronic infection	N/A	• anti-HBs • anti – HB-e • HBV-DNA • viral load • genotyping	• initial test – Anti-HCV • HCV-RNA • HCV-PCR viral load • genotyping
Screening for chronic infection	N/A	• unexplained abnormal LFTs • pregnant women • blood and organ donors • people in at-risk groups	• unexplained abnormal LFTs • people in at-risk groups • pregnant women • blood and organ donors
Treatment of chronic infection		• antiviral drugs • interferon • regular monitoring	• pegylated interferon and ribavirin • regular monitoring
Vaccination	travellers to countries at high-risk, effective for 10 years	• at-risk groups • healthcare professionals • children of infected parents • effective in 95%	• no vaccine available