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Hepatitis A

This is a notifiable disease in the UK. See the **Notifiable Diseases** article for more detail.

What is hepatitis A?

Hepatitis A virus (HAV) is a small, unenveloped, symmetrical RNA virus (picornavirus). The HAV was first isolated by Purcell in 1973. Since the 1980s, specific antibody tests have helped reveal the epidemiology, clinical manifestations and natural history of HAV infection. Infection with the virus ranges from mild symptoms of nausea to, in very rare cases, liver failure. Symptoms are usually worse and the illness more often severe in older patients.

Spread is normally by the faecal-oral route although there are occasional outbreaks through food sources. Hand washing and good hygiene around food and drink prevent spread of infection. Active and passive immunisation are used in those at risk of infection. Travellers to certain countries, injecting drug users and those in contact with infected individuals are at risk of infection.

The most important determinant of illness severity is age and there is a direct correlation between increasing age and morbidity and mortality. Most deaths from acute HAV infection occur in those over the age of 50 years, even though infection is uncommon in this age group.

Pathophysiology[1]

- Humans appear to be the only reservoir for the HAV.
- The incubation period usually lasts 2-6 weeks. The time to onset of symptoms may be dose-related.

- Viral replication depends on hepatocyte uptake.
- After uptake, the viral RNA is uncoated and host ribosomes bind to form polysomes.
- Viral proteins can then be synthesised with the viral genome being copied by a viral RNA polymerase.
- Assembled virus particles are then shed through the biliary tree into the faeces.
- Shedding of the HAV is greatest during the anicteric prodrome of infection (between 14 days and 21 days after infection). This corresponds to the time when transmission is highest.

How common is hepatitis A? (Epidemiology)

- The anti-HAV seroprevalence rate is presently decreasing in many parts of the world; however, in less developed regions and in several developing countries, HAV infection is still very common in the first years of life and seroprevalence rates approach 100%[2] .
- Hepatitis A is the most common form of acute viral hepatitis worldwide.
- The highest risk areas of the world for HAV infection include the Indian subcontinent (in particular India, Pakistan, Bangladesh and Nepal), Africa, parts of the Far East (except Japan), South and Central America and the Middle East.
- It is estimated that about 1.4 million cases of HAV infection occur every year worldwide but the true incidence is likely to be 3-10 times higher.[3]
- The incidence rate is strongly related to socio-economic indicators and access to safe drinking water.
- During 2019, there were 503 confirmed laboratory reports of HAV infection in England and Wales.[4] This number is likely to be an underestimate.
- In developed countries, reduced encounters with HAV in the young have resulted in a decline in herd immunity.

Risk factors[5]

Most people acquiring HAV infection do not have risk factors but these include:

- Personal contact.
- Certain occupations (for example, staff of large residential institutions, sewage workers).
- Travel to high-risk areas.
- Men who have sex with men and risky sexual behaviours, such as anonymous sex or group sex.
- Intravenous drug misuse.
- People with clotting factor disorders who are receiving factor VIII and factor IX concentrates.

Clinical features[6]

- The incubation period is 2-6 weeks with a mean of four weeks.
- There is a prodrome of mild flu-like symptoms (anorexia, nausea, fatigue, malaise and joint pain) preceding the jaundice. Smokers often lose their taste for tobacco. Diarrhoea can occur, particularly in children.
- Fever is not usually common.
- This can progress to the icteric phase with:
    - Dark urine (appears first).
    - Pale stools (not always).
    - Jaundice occurring in 70-85% of adults with acute HAV infection.
    - Abdominal pain occurring in 40% of patients.
    - Itch or pruritus (usually with jaundice but can occur without).
    - Arthralgias and skin rash. These occur less often (lower limbs and with a vasculitic appearance).

- Tender hepatomegaly, splenomegaly, and lymphadenopathy may occur.
- Young children are usually asymptomatic and the likelihood of symptoms tends to increase with age.[7]
- 70% of infections in children aged under 6 months are asymptomatic.
- Complete clinical recovery may take up to six months after the onset of the illness.
- Anorexia, malaise and weakness may persist for some weeks after biochemical recovery.
- The average age at infection has increased in developing countries, resulting in more severe hepatitis occurring.[8]

Differential diagnosis

- Other forms of viral hepatitis.
- Acute HIV infection.
- Drugs (hypersensitivity and toxicity).
- Cytomegalovirus.

Diagnosing hepatitis A (investigations)[6]

Specific antibody tests

- IgM antibody to HAV is positive with onset of symptoms (usually about 3-4 weeks after exposure but up to six weeks). The test is sensitive and specific. It remains positive for between 3-6 months (up to 12 months). It remains positive in relapsing hepatitis.
- IgG antibody to HAV appears soon after IgM and persists for many years. In the absence of IgM it indicates past infection or vaccination rather than acute infection. IgG remains detectable for life.

Liver enzymes

- Alanine aminotransferase (ALT) rises more than aspartate aminotransferase (AST) again with onset of symptoms, about four weeks after exposure. Levels usually return to reference ranges over several weeks but can remain elevated for months.
- Alkaline phosphatase rises with ALT and AST.

Other test results

- Bilirubin rises soon after rises in ALT and AST levels. Levels may be very high and remain elevated for several months. Older patients have higher bilirubin levels.
- Modest falls in serum albumin level may occur.
- Prothrombin time (PT) usually remains normal and estimation is necessary only in unusual cases or with complications. PT prolongation by more than five times is a sign of severe infection.[9]
- Indices of low-grade haemolysis may be detected.
- Mild lymphocytosis is common.
- Pure red cell aplasia and pancytopenia may very rarely occur.

Imaging
Ultrasound may, rarely, be needed to exclude other diseases.

Management of hepatitis A[10] [11]

- Mainly supportive with treatment of symptoms (fluids, antiemetics, rest).
- Avoid alcohol until liver enzymes are normal.
- Admit patients with severe systemic upset or intractable vomiting for rehydration and observation.
- Pregnant women should be advised of the increased risk of miscarriage and premature labour and the need to seek medical advice if symptoms develop.[9]

- Employment history should be obtained so the patient can be advised appropriately. Until patients become non-infectious, they should be advised to avoid food handling and unprotected sexual intercourse.[9]
- Advice on managing any outbreaks should be sought from UK regional public health organisations.

Complications of hepatitis A[5]

These rarely occur but include:

- Cholestatic hepatitis. This can occur in around 8% of people. Features may include severe pruritus, diarrhoea, weight loss and malabsorption. However, they usually fully recover.
- Fulminant liver failure. This occurs in less than 0.4% of people and usually manifests during the first four weeks of illness. It is more common in those with concurrent chronic hepatitis B or C.[12]
- The overall mortality is <0.1%, although this rises to 40% in those with actue liver failure.[9]
- Relapsing HAV infection can occur in up to 15% of people, at an interval of 4-15 weeks after the original illness. It can occur more than once.
- Other very rare complications (for example, acute kidney injury, red cell aplasia, Guillain-Barré syndrome, pancreatitis).
- Symptomatic hepatitis, severe disease, and death are more likely to occur when infection occurs at an older age.[13]

Prevention of hepatitis A[14]

Hepatitis A is the most frequent vaccine-preventable disease in travellers.

It can be a serious illness, particularly in the elderly. With proven means of prevention, it is important to pursue prevention actively. After infection and active immunisation, immunity is probably lifelong.

- Control of infection at source is needed. This requires notification and contact tracing.

- Good hygiene and sanitation are of fundamental importance. Tap water should be avoided in high-risk areas.
- Public education about transmission and prevention are needed, particularly in communities where HAV is endemic.
- Immunisation is effective and should be appropriately used. See the separate Hepatitis A Vaccination article.

Prognosis[5]

- Excellent. It is usually self-limiting with no long-term sequelae.
- There is no carrier state and chronic liver disease does not occur.

Outbreaks of hepatitis A

Advice on managing these should be sought from UK regional public health organisations.

Further reading

- Health Protection Scotland
- Public Health Agency Northern Ireland
- Public Health Wales

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