10

Hepatitis A Virus and Infectious Hepatitis

MUCH OF THE WORK on poliovirus and other enteroviruses in the environment described in chapter 9 was inspired by an interest in other excreted viruses that cause major public health problems but cannot be routinely isolated at the present time. Foremost among these other excreted viruses is hepatitis A virus, which is a common and important cause of disease throughout the world.

The study of the hepatitis viruses is a rapidly moving field of research—hepatitis A virus was not identified in fecal extracts until 1973, although the disease it causes has been recorded by civil and military historians since the fifth century BC. This chapter is brief, because little is known at the time of writing about hepatitis A virus in the environment, and tentative, because the rate of scientific progress is rapid, and much new information will come to light in the next few years. A recent and comprehensive account of the hepatitis viruses is given by Zuckerman and Howard (1979).

Description of Pathogen and Disease

Two distinct forms of viral hepatitis have been recognized: hepatitis A (also known as infectious hepatitis, epidemic hepatitis, or epidemic jaundice) and hepatitis B (also known as serum hepatitis). They differ in etiology and in some epidemiological, immunological, clinical, and pathological characteristics. From the environmental viewpoint, the primary distinction between them is that hepatitis A is transmitted by the fecal-oral route, whereas hepatitis B is normally transmitted by infected blood or tissue fluid (for instance, during blood transfusion, injection, immunization, tattooing, and acupuncture) but may also rarely be transmitted by saliva, semen, breastmilk, other body fluids, and feces if contaminated with blood. Because of these differences in mode of transmission, the approaches to prevention and control of hepatitis A and B are very different. Recently a third form of viral hepatitis has been described: non-A:non-B hepatitis. This new form of hepatitis is now known to be the most common type of post-transfusion hepatitis in some areas. Non-A:non-B hepatitis may prove to be divisible into more than one form. As far as is known, only hepatitis A is primarily an excreted infection, and therefore it alone will be discussed in this chapter.

Identification

The clinical picture of viral hepatitis varies in its presentation from inapparent or subclinical infection, to slight malaise, mild gastrointestinal symptoms and the anicteric (without jaundice) form of the disease, to acute icteric illness, severe prolonged jaundice, and chronic liver disease. The anicteric form is characterized by malaise, anorexia, various gastrointestinal disturbances, an enlarged and tender liver, and perhaps a fever. In acute icteric infections these symptoms may be more pronounced and may be followed after 5–10 days by dark urine, clay-colored stools, and jaundice, which persists commonly for 1–2 weeks. Typically, the disease is especially mild in children, for whom the ratio of anicteric to icteric illness may be 10 or more to 1. Convalescence usually is prolonged. In general, severity increases with age, but complete recovery without sequelae or recurrences is the rule. Many mild cases without jaundice, especially in children, are recognizable only by liver-function or serum-enzyme tests.

Occurrence

Viral hepatitis type A occurs endemically in all parts of the world, with frequent reports of minor and major outbreaks. The exact incidence is difficult to estimate because of the high proportion of subclinical infections and infections without jaundice, differences in surveillance, and differing patterns of disease. The degree

of underreporting is very high; even in developed countries with compulsory notification, it is doubtful whether more than 50 percent of cases of jaundice are actually reported.

Because serological tests for hepatitis A antibody are now available, it has become possible to study the incidence and distribution of hepatitis A infections in different populations and in various geographical areas. A recent survey of sera for hepatitis A antibody by immune adherence hemagglutination from samples of healthy adults, mostly volunteer blood donors, from seven geographical populations has shown that the age-standardized prevalence of hepatitis A antibody was 29 percent in Switzerland, 45 percent in the USA, 76 percent in Senegal, 81 percent in Belgium, 89 percent in Taiwan, 95 percent in Israel, and 97 percent in Yugoslavia (Szmuness and others 1977). This survey confirmed that infections with hepatitis A virus are widespread throughout the world.

Infectious agent

Small cubic particles measuring 27 nanometers have been seen by electron microscopy in infective feces of human subjects (see figure 10-1). The virus contains single-stranded RNA and has the biochemical and biophysical properties of a picornavirus.

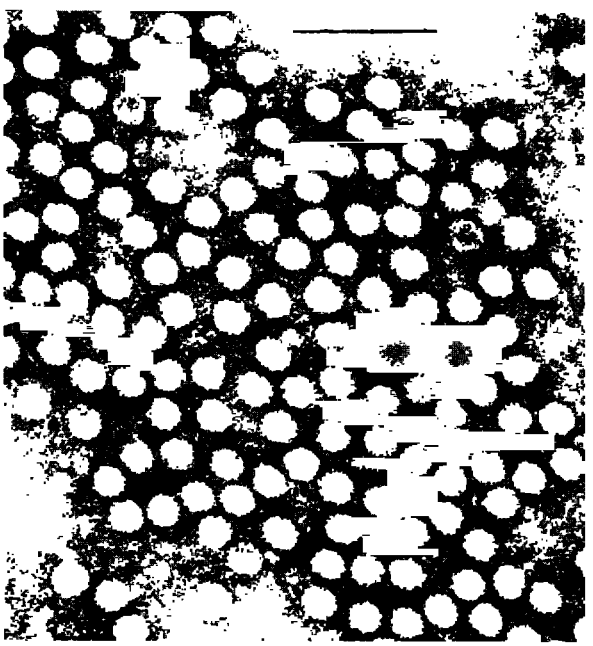

Figure 10-1. *Hepatitis A viruses under transmission electronmicroscopy.* Scale bar = 0.1 micrometers. (Photo: A. J. Zuckerman and A. Thornton, London School of Hygiene and Tropical Medicine, London, UK)

Reservoirs

Man is almost certainly the important reservoir for human hepatitis A infection. However, cases have been reported that suggest transmission to man from chimpanzees, gorillas, Celebes apes, gibbons, and woolly monkeys. Antibodies to hepatitis A virus are found in nonhuman primates, and susceptible chimpanzees and marmosets are readily infected in the laboratory.

Transmission

Hepatitis A virus is spread by the fecal-oral route, most commonly by person-to-person contact, and infection occurs readily in conditions of poor sanitation and overcrowding. Common-source outbreaks are most frequently initiated by fecal contamination of water and food, but waterborne transmission is not a major factor in the maintenance of this infection. Ingestion of shellfish cultivated in polluted water is associated with a high risk of acquiring hepatitis A.

Incubation period

The incubation period of hepatitis A is between 3 and 5 weeks, with a mean of 28 days.

Period of communicability

Hepatitis A virus is shed in the stools primarily during the period from 2 weeks before, to 2 weeks after, the onset of symptoms; in other words, for up to 4 weeks commencing 1–3 weeks after infection. Persistent carriage or excretion of hepatitis A virus in humans does not occur.

Resistance

Susceptibility is general. Low clinical incidence in infants and preschool children suggests that mild and anicteric infections are common. The degree and duration of homologous immunity after attack are unknown but presumed to be long lasting.

Epidemiology

All age groups are susceptible to hepatitis. Until recent years the highest incidence in the civilian population was observed in children of school age, but

in a number of countries, including Sweden and the USA, as many as 60–70 percent of notified cases now occur in adults. This shift in age incidence in the developed countries is reminiscent of the changing pattern of poliomyelitis (see chapter 9) and may reflect reduced transmission, caused by improved socioeconomic conditions, which defers infection to an older age group when the clinical consequences are usually more severe.

In conditions of poor hygiene, it is probable that transmission of hepatitis A virus occurs among children by direct fecal-oral routes. This leads to a high incidence of subclinical or very mild infections that confer substantial immunity. Moritsugu and others (1979) found that 92 percent of children under 9 years old in Colombo (Sri Lanka) had evidence of antibodies to hepatitis A virus. In Costa Rica (Villarejos and others 1976), age-specific antibody prevalences reached 80 percent by the age of 9 years. In Liberia, 90 percent of children over 5 years old in both urban and rural areas had hepatitis A antibodies (Willcox and others 1980). Similar results have been obtained from Kenya (Wankya and others 1979) and from Fiji, Tuvalu (formerly Ellice Islands), Niue, Cook Islands, and Western Samoa (Gust, Lehmann and Dimitrakakis 1979).

In developed countries, improved hygiene reduces the incidence of hepatitis A infection in the young, but many people become infected at some time in life. Gust, Lewis and Lehmann (1978) examined the sera (collected in 1954–55) of 959 people (mainly of low socioeconomic status) in Melbourne (Australia) and found that the prevalence of those having hepatitis A antibodies as 38 percent in the 6 to 10 year olds, 56 percent in the 20 year olds, and over 97 percent in those over 40 years old. The sera were collected prior to mass poliomyelitis vaccination campaigns, and it was found that the age-related acquisition of poliovirus antibodies was extremely similar to hepatitis A antibodies. This strengthens the possibility that the epidemiology and transmission of polio and hepatitis A infections may be similar and that they share a common response to improved hygiene. A repeat survey in Melbourne in 1975 found antibody prevalences of 23 percent in 6 to 10 year olds, 45 percent in 20 year olds, and 66 to 97 percent in those over 40 years old (Gust and others 1978). The decrease in antibody prevalence presumably reflects an improvement in economic and environmental conditions between the mid-1950s and the mid-1970s.

Villarejos and others (1976) found low prevalence of hepatitis A antibody among people of high socioeconomic status in the Philadelphia area (Pennsylvania, USA). Antibody was not detected in any individual under 20 years old, and the highest age-specific prevalence for hepatitis A antibody was 59 percent in the 40–49 age group. Antibody prevalences were higher among institutionalized individuals in Philadelphia. Szmuness and others (1976) studied 947 randomly selected individuals in New York City (USA) and found an overall prevalence of hepatitis A antibody of 45 percent. Lower social classes had significantly higher prevalences (72–80 percent) than higher social classes (18–30 percent). Jews had a significantly lower prevalence (7 percent) than other whites (39 percent), but sex and homosexuality did not affect prevalence. Antibody prevalence was closely related to age in all groups; for instance, among Chinese the prevalence rose to over 90 percent by the age of 40 years. For both blacks and whites, antibody prevalence was 2.5 to 4 times lower among individuals with postgraduate education than among those without.

These various studies show clearly that transmission of hepatitis A virus is more common, and thus the prevalence of antibodies among children is higher, among people of lower socioeconomic and educational status. This relationship can be detected both between and within countries. These and other aspects of hepatitis A epidemiology, as revealed by serological surveys, have been reviewed by Dienstag and others (1978). Recent investigations of hepatitis A outbreaks in day care centers in the USA have highlighted the major role of children who are not toilet trained (those under 2 years old) in spreading the infection (Hadler 1980; Vernon 1980).

In temperate zones the characteristic seasonal trend has been for a marked rise in incidence in the autumn and early winter months, with a progressive fall to a minimum in midsummer.

Control Measures

The spread of infection is reduced by simple hygienic measures and the sanitary disposal of excreta. Normal human immunoglobulin may prevent or attenuate a clinical illness but may not always prevent the infection. The use of normal immunoglobulin is of value in the control of outbreaks of infection in specific circumstances, such as in institutions and nursery schools. Following the recent development of a tissue culture technique for hepatitis A virus, hopes of developing a specific vaccine are high. The epidemiology of hepatitis A infection, and approaches to its control, would be altered considerably by the widespread use of such a vaccine.

Occurrence and Survival in the Environment

There is no direct evidence of the behavior or occurrence of hepatitis A virus in the environment because the virus has never been isolated from an environmental sample. Such isolations must await the development of sensitive and specific serological techniques for detecting small amounts of hepatitis A antigen or routine tissue culture techniques. The recent successful propagation of hepatitis A virus in marmoset liver, fetal rhesus monkey kidney, and other cells gives hope that tissue culture techniques will become available soon.

The available evidence on hepatitis A virus in the environment is indirect. The knowledge that hepatitis A incidence is high in some communities leads to the assumption that hepatitis A virus may be present where fecal pollution is present, and especially where high concentrations of enteroviruses are present (see chapter 9). However, far too little is known about the prevalence of hepatitis A virus excretion, or the numbers of virus particles excreted, to predict at what concentration hepatitis A virus might be found in, for instance, sewage. Some evidence is provided by outbreaks of hepatitis A infection that can be traced by epidemiological analysis to a particular source, such as contaminated water or food or shellfish.

Many outbreaks of hepatitis have been linked to polluted drinking water. An explosive outbreak occurred in New Delhi in December–January 1955–56 (Viswanathan 1957). About 30,000 cases were reported (presumably many cases were subclinical or went unreported) when sewage contaminated the city water supply after heavy rain. This outbreak produced evidence that this presumed hepatitis A virus-like strain is more resistant to chlorination than some enteric bacteria, and this is predictable from the data on the effect of chlorination on enteroviruses (see chapter 9). A more recent report from India (Newaskar, Vidwans and Vachha 1978) also suggests a link between sewage contamination of water supplies and an outbreak of hepatitis in Maharashtra.

Numerous small outbreaks attributed to water pollution are reported from North America and Europe (see Craun 1978). These outbreaks typically are associated with contamination of the water distribution system by cross-connection or back-siphonage or with the use of small untreated rural water supplies that are contaminated by sewage discharges or leaks. Neefe and Stokes (1945) reported an outbreak of 350 cases over 13 weeks at a summer camp in the USA. The outbreak was attributed to seepage from cesspools traveling a horizontal distance of 23–55 meters through fissured red shale and limestone to pollute a well 67 meters deep. Similarly, 24 cases of hepatitis A occurred among 180 residents of holiday cottages near Pilsen (Czechoslovakia) when their well was contaminated by seeping sewage (Vilim and others 1977). However, there is no evidence that water conforming to conventional bacteriological criteria has ever caused hepatitis A, and the disease occurs under conditions similar to those which lead to other waterborne, fecal-oral outbreaks of disease (Grabow 1976).

Known waterborne cases of hepatitis A in the USA range between 35 and 120 year, which is only about 0.4 percent of total reported cases. Recent studies have sought to associate hepatitis incidence in the USA with raw water quality, water treatment practices, or old distribution systems. However, many of these physical parameters are associated with socioeconomic status in the area, and it is well established that hepatitis A incidence is higher in poor and deprived communities. To clarify the situation, Batik and others (1980) compared hepatitis incidence with water supply factors among a sample of nearly 3 million people who experienced 11,633 reported cases of hepatitis A during 1965–77. The comparisons were controlled for age distribution, educational levels, population density, and poverty. None of the water supply source or treatment variables were significantly correlated with hepatitis A incidence.

Another source of circumstantial evidence of hepatitis A virus behavior in the environment are the many documented accounts of hepatitis outbreaks associated with contaminated shellfish (Gerba and Goyal 1978; Hughes, Merson and Gangarosa 1977; Levin 1978). As many as 8.6 percent of reported hepatitis A cases in the USA are associated with shellfish consumption (Levin 1978), usually with consumption of raw oysters and raw or steamed clams. Koff and others (1967) interviewed 270 adult hepatitis patients in Boston (Massachusetts, USA) hospitals and concluded that ingestion of raw or steamed shellfish was as common a source of infection as contact with jaundiced persons, even during a nonepidemic period.

An outbreak of hepatitis A (278 cases) that occurred in Louisiana during October and November 1973 was investigated and shown to be related to simultaneous outbreaks in Texas and Georgia (USA). The outbreak was attributed to the consumption of contaminated oysters harvested from approved growing areas on the east Louisiana coast. The oysters were probably polluted when contaminated river water was discharged into the area during floods earlier in the year.

Oyster fishing was prohibited while the counts of coliform bacteria were in excess of 70 per 100 milliliters. Oysters harvested some 4 weeks after the coliform counts fell below this limit led to the disease outbreak. The evidence suggests that the oysters concentrated the hepatitis virus and retained it for a period of 1.5–2 months. A more severe outbreak was probably avoided because oysters in heavily contaminated areas were killed by changes in salinity (Mackowiak, Caraway and Portnoy 1976; Portnoy and others 1975).

On the basis of the epidemiological evidence, there is good reason to believe that shellfish accumulate and retain hepatitis A virus from polluted waters in the same way that they accumulate and retain poliovirus (chapter 9). There is also good epidemiological evidence that cooking of shellfish does not necessarily inactivate all hepatitis A virus, just as it does not necessarily inactivate all poliovirus. Recent confirmation of this was provided by Peterson and others (1978), who reported that hepatitis A virus injected into oysters and treated at 60°C for 19 minutes could still induce acute disease and seroconversion when fed to fasted marmosets.

Inactivation by Sewage Treatment Processes

The lack of isolation techniques for hepatitis A virus has prevented any direct studies on the inactivation of the virus by sewage treatment. Indirect evidence on the reaction of hepatitis A virus to chlorination is provided by the work of Neefe and others (1947), who contaminated water with feces known to contain hepatitis A virus, subjected the water to various treatment regimes, and then asked volunteers to drink it. The results indicated that coagulation and filtration reduced but did not eliminate hepatitis A virus but that coagulation, filtration, and chlorination (to provide 0.4 milligrams per liter of free residual chlorine after 30 minutes) eliminated the virus. However, direct chlorination of the contaminated water (to provide a total chlorine residual after 30 minutes of 1 milligram per liter) did not prevent infection in the volunteers, whereas heavier chlorine doses applied to the contaminated water (15 milligrams per liter of total chlorine after 30 minutes) rendered the water noninfective to all volunteers. These results suggest that hepatitis A virus, like the enteroviruses (see chapter 9), is insensitive to combined chlorine and may only be inactivated in sewage disinfection by the application of heavy chlorine doses to highly purified effluents.

It is to be expected that isolation and enumeration techniques for hepatitis A virus will become available over the next few years and will be followed by a surge of investigations into the inactivation of the virus by sewage treatment processes. In the meantime, it is reasonable to assume that hepatitis A virus behaves in a way similar to the enteroviruses (chapter 9). This assumption will become more plausible if it is confirmed that hepatitis A virus is an enterovirus.

Inactivation by Night Soil and Sludge Treatment Processes

As with sewage treatment processes, no direct evidence is available on the inactivation of hepatitis A virus by night soil or sludge treatment processes. A study by Raška and others (1966) provided indirect evidence of hepatitis A virus survival in cesspool sludge applied to farm land. During the winter months of December and January (1962–63), cesspool sewage was spread on farmland near a small stream used as the source of water for a dairy near Jablonec (Czechoslovakia). On March 11–13 a thaw combined with rain led to the contamination of the stream. The organic content of the water was sufficient to overwhelm the chlorination of the supply, and contaminated water was used by the dairy. The water treatment process included chlorination followed by sand filtration. An epidemic of hepatitis A spread by dairy products occurred during April–June. There were 424 cases, with the highest incidence in the 15–20 age group. Relatively few contact cases occurred possibly due to the mass administration of gamma globulin, particularly to children. The average incubation period was 45 days. There was no increase in other enteric infections, and the authors attribute this either to a lack of the disease organisms in the sewage or to the marginal chlorination having been sufficient to inactivate bacterial pathogens. It is evident from the information supplied that under cold weather conditions hepatitis A virus survived at least 5 to 6 weeks in sewage spread on farmland.

There is some evidence that hepatitis A virus may be more resistant to heat than the enteroviruses discussed in chapter 9. Krugman, Giles and Hammond (1970) found that hepatitis A virus was rendered noninfectious and nonimmunogenic by treatment at 98°C for 1 minute. Deinhardt (1976) reported that some hepatitis A virus survived treatment at 60°C for 1 hour. However, ability to withstand fairly high temperatures (>60°C) for short times (<1 hour) may not be

indicative of the ability of the virus to withstand cooler temperatures for longer periods (see figure 9-2).

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