

Infection with HAV may produce a wide spectrum of outcomes from silent or subclinical hepatitis at one end, through typical acute hepatitis with jaundice, to fulminant hepatitis at the other. The single most important factor in determining the outcome of HAV infection appears to be age. Whereas greater than 90% of infections acquired before the age of 5 years are silent, the proportion of infected individuals with symptoms increases steadily, reaching approximately 25% by 15 years and 90% or above in adults.²² The duration of illness varies but most patients feel better, have lost their hepatomegaly, and have nearly normal liver function test results within 3 weeks. In the large 1989 Shanghai outbreak, 90% of a subset of 8647 hospitalized patients observed carefully had completely recovered in 4 months and all had recovered in 1 year.^{20, 23} Relapse consisting of renewed symptoms, elevated liver function test results, and possibly detection of virus in stools has been found in up to 10% of cases, but recovery is universal.^{24, 25} Hepatitis A never becomes chronic.

A cholestatic form of hepatitis A has been reported in which the patient experiences persistent jaundice usually accompanied by itching. A short course of corticosteroids may reduce these symptoms and hasten recovery, but even without treatment, recovery is universal. Clinical relapses that may include jaundice after initial resolution of illness have also been reported, but again, total recovery is the rule.^{26, 27}

Fulminant hepatitis, the most severe form of the disease, is fortunately rare, but special caution should be observed in elderly patients. Case-fatality rates are usually obtained from hospital series that are self-selected for patients with more severe disease. Even so, it is apparent that fulminating hepatitis, liver failure, and death are rare especially among children and young adults but become significant in older adults (Table 26-3). In a large hospital-based series from Fairfield Hospital in Melbourne, only three deaths occurred among more than 2000 patients with serologically confirmed hepatitis A, a case-fatality rate of 0.14%.²⁸ In the 1988 Shanghai epidemic that involved primarily adolescents and young adults, there were only 47 deaths recorded among the 310,746 diagnosed (0.015%) cases. Twenty-five of the deaths were due to fulminant hepatitis, and 15 were related to exacerbations of underlying chronic hepatitis B infections.²⁹

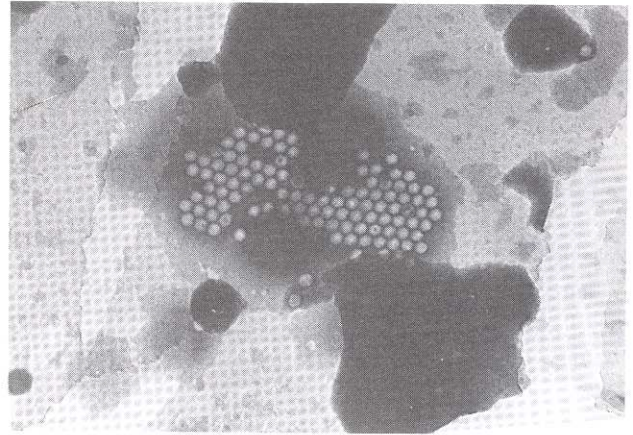


Figure 26-1. Electron micrograph of purified hepatitis A particles. Magnification $\times 125,000$.

Virology

HAV is a member of the *Picornaviridae* family, which includes both the enteroviruses and rhinoviruses of humans. Because of several unique features, HAV has been placed into its own genus, *Hepatavirus*.²⁹⁻³⁴ There are four recognized human genotypes of HAV based on primary sequence variability, but there is only one known serotype.^{35, 36} Many strains of HAV have been described on the basis of different growth characteristics, nucleotide sequence, or geographical origin.³⁷⁻³⁹ Polyclonal and monoclonal antibodies directed against the major antigenic determinant appear to be capable of detecting strains of HAV isolated in different parts of the world, suggesting that there is only one serotype.⁴⁰⁻⁴²

HAV is a nonenveloped, 27- to 28-nm-diameter spherical virus (Fig. 26-1) with a surface structure that suggests icosahedral symmetry, although fine resolution of the virus structure by x-ray crystallography has not yet been achieved.¹⁹ Mature HAV virions purified from feces collected from infected humans or chimpanzees band at 1.32 to 1.34 g per cm³ in CsCl and sediment at approximately 160 S.⁴³⁻⁴⁵ A lower density fraction can often be detected that bands at about 1.27 g per cm³ in CsCl and sediments at 70 to 80 S, which consists primarily of empty capsids. In addition, a high-density fraction (1.4 g/cm³) that may represent particles with a more open virion structure (allowing increased penetration and binding of CsCl into the viral particle) may also be found. These high-density particles have been shown to contain HAV RNA but tend to be less stable than mature virions.⁴⁵⁻⁴⁷

Resistance to Physical and Chemical Agents. HAV is more resistant to heat than other picornaviruses are.^{48, 49} Whereas HAV may be incompletely inactivated (depending on the conditions) by exposure to 60°C for 10 to 12 hours,⁴⁹ complete inactivation is attained after exposure to 100°C for 5 minutes, after heating for 4 minutes to 70°C, after 5 seconds at 80°C, and virtually instantly at 85°C.⁵⁰ HAV may survive for days to weeks in shellfish, water, soil, or marine sediment.⁵¹ Outbreaks of hepatitis A have been reported after ingestion of partially cooked shellfish, suggesting that the usual

Table 26-3. AGE-SPECIFIC MORTALITY DUE TO HEPATITIS A

AGE GROUP (yr)	NO. OF CASES (%)	NO. OF DEATHS (%)	CASE-FATALITY PER 1000
<5	6,165 (5.3)	9 (2.4)	1.5
5-14	22,548 (19.5)	1 (0.3)	0.004
15-29	49,642 (43)	28 (7.3)	0.57
30-49	26,961 (23.3)	67 (17.6)	2.5
≥49	10,235 (8.8)	276 (27.4)	27
Total	115,551	381	3.3

From Centers for Disease Control. Viral Hepatitis Surveillance Program, 1983-1989.