Hepatitis A and E in Hong Kong

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Acute viral hepatitis is one of the most prevalent infectious diseases in Hong Kong and hepatitis A accounts for two thirds or more of reported cases. Improved sanitation has led to a decline in hepatitis A infection in childhood but more clinically overt adult cases now occur. Shellfish ingestion and recent travel are important risk factors. A highly immunogenic and effective inactivated hepatitis A vaccine is available. Hepatitis E is of emerging importance as a cause of acute hepatitis. Large outbreaks have occurred in China and other developing countries; sporadic cases occur in Hong Kong. High mortality is associated with hepatitis E complicating late pregnancy. Serological diagnosis by enzyme immunoassay for anti-HEV is available. The education of travellers to endemic areas is advised with special caution being given to pregnant women. A vaccine for hepatitis E is not yet available.

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Introduction

Acute viral hepatitis is one of the most common notifiable infectious diseases in Hong Kong, ranking next to tuberculosis and food poisoning in importance.1 In a prospective study of the cases of acute hepatitis A to E treated by the Infectious Disease Team of the Princess Margaret Hospital, Hong Kong, from January 1993 to December 1993, data from 648 patients was collected.2 This represents 51% of all cases of viral hepatitis notified to the Department of Health in the same year. The episodes due to hepatitis A to E are shown in the Table. While hepatitis B, C, and D cause chronic liver disease, hepatitis A and E only cause acute hepatitis without chronic sequelae. The following review focuses on current aspects of epidemiology and the prevention of hepatitis A and E in Hong Kong.

Hepatitis A

Hepatitis A remains the most common type of acute hepatitis in Hong Kong. From 1990 to 1995, it represented from 67% to 83% of all notified cases of viral hepatitis reported to the Department of Health. An epidemic of hepatitis A occurred in Hong Kong in 1992, with a recorded peak of 3626 cases.

Improved sanitation has led to a decline in hepatitis A infection in childhood, as reflected by a comparison of the prevalence of antibodies to the hepatitis A virus (anti-HAV) in two studies conducted 10 years apart.3 The prevalence of anti-HAV in 1987 to 1989 was significantly lower than it was in 1978 to 1979 in every age group from 0 to 30 years (Fig). The study in 1987 to 1989 revealed that the prevalence of anti-HAV was 24% for subjects below age 30 and 89.2% for those above age 30.

The shift from high endemicity to intermediate endemicity does not necessarily result in a lower incidence of hepatitis A. Less exposure to the infection in childhood means that the average age of infection moves to early adulthood and then to older age groups. While infection in childhood is predominantly subclinical, adult infection is often clinically overt and icteric. It is to be expected that more clinical cases of hepatitis A will need medical treatment or even hospitalisation. Prevention thus becomes all important, to avoid clinical illness in an economically-active age group with a lower herd immunity.

In a survey of 950 hepatitis A patients in 1990, recent shellfish intake was found in 55% of patients and travel to endemic areas outside of Hong Kong occurred in 17% of patients.4 Shellfish, raw or under-cooked, were often implicated in outbreaks of hepatitis A. In Shanghai, China, in 1988 more than 300 000 clinical cases of hepatitis A were caused by the ingestion of under-cooked contaminated clams.5 In a study of viral
contamination in shellfish sold in markets in Hong Kong conducted by the Chinese University of Hong Kong (Tam JS, personal communication). HAV RNA detection by reverse transcriptase-polymerase chain reaction (RT-PCR) were positive in 6% of clams, 14% of mussels, and 30% of oysters during the winter period (November to March). In summer (June to September), HAV contamination was 0% in clams and 26.6% in mussels. No oysters were available in summer. The peak season for outbreaks of hepatitis A in Hong Kong occurs in late spring to early summer, the months of February to May. This may be related both to the seasonal habit of eating “hot-pots” in colder months and the heavier HAV contamination of shellfish in winter. The complete inactivation of HAV at a water boiling temperature of 100°C requires a duration of five minutes. Such a level of heating is seldom adhered to locally in the cooking of shellfish.

Although improvements in sanitary conditions and personal hygiene have largely been achieved, changing the culinary habits of local people remains difficult. Active immunisation with a HAV vaccine may be the most effective means of prevention. The currently licensed inactivated HAV vaccine (strain HM175) has been shown to be highly immunogenic and effective. Seroconversion rates are more than 95% after the first dose and 100% after two doses. The mean persistence of antibody after three doses of vaccine is at least 10 years. Following a good immunological prime, circulating memory cells are capable of inducing an anamnestic response to viral exposure and may extend protection for even longer periods.

For the immediate protection of contacts of hepatitis A patients or immediately departing travellers to endemic areas, human normal immunoglobulin (HNIG) can be administered simultaneously with the HAV vaccine at separate injection sites. This may result in a slight reduction in immunogenicity of the vaccine but adequate concentrations of anti-HAV are induced. If necessary, for rapid achievement of active immunity, the second dose of HAV vaccine may be administered two weeks following the first dose. Vaccination is more effective than HNIG in interrupting community-wide outbreaks of hepatitis A because vaccination reduces the shedding of virus.

While universal vaccination is an ideal, the cost of doing this is prohibitive at present. Other than contacts of hepatitis A patients, vaccination is recommended for travellers to endemic areas, health care workers, child day-care staff, food handlers, the armed forces, sewage workers, male homosexuals, intravenous drug abusers, haemophiliacs, patients with chronic liver disease, and the staff and inmates of institutions for the mentally handicapped. In Hong Kong, in 1989 to 1990, 80% of hepatitis A cases were in the 11 to 30 year age group, while in 1987 to 1989, only 5.3% of children in the 0 to 10 age group were anti-HAV positive. In terms of logistics and priority, it would be easier to offer HAV vaccine to all school children as part of a school health programme.

Looking ahead, additional licensing of inactivated HAV vaccines may somewhat reduce the cost of existing vaccine through competition. Already there are promising candidates either of a different strain of HAV or of a different adjuvant system. Also, combining the HAV vaccine with other childhood vaccines should reduce the cost of delivery. Live attenuated vaccines may induce even longer periods of protection and require only a single-dose inoculation and the cost of production is also substantially cheaper. A few have been produced, including one from China, and initial clinical evaluation has confirmed their safety and immunogenicity. Genetically-engineered vaccine is another strategy for producing vaccine at a lower cost. The prospects for universal vaccination appear optimistic.

Table. Prevalence of acute hepatitis A to E in Hong Kong based on data collected from January 1993 to December 1993 at a regional hospital

<table>
<thead>
<tr>
<th>Acute hepatitis</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>A</td>
<td>470 (72.5)</td>
</tr>
<tr>
<td>B</td>
<td>66 (10.2)</td>
</tr>
<tr>
<td>C</td>
<td>9 (1.4)</td>
</tr>
<tr>
<td>D</td>
<td>0</td>
</tr>
<tr>
<td>E</td>
<td>57 (8.8)</td>
</tr>
<tr>
<td>non-ABCDE</td>
<td>46 (7.1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>648</strong></td>
</tr>
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**Hepatitis E**

With the availability of effective vaccines for hepatitis A and B, and the use of reliable screening tests for hepatitis C in blood donors, hepatitis E virus (HEV) will become the causative agent of a relatively greater proportion of cases of acute viral hepatitis.

Formerly called enterically transmitted non-A, non-B hepatitis, the disease is frequently spread by faecally-contaminated drinking water. Outbreaks of hepatitis E
involving several thousand people have been reported in developing countries, such as in the Indian subcontinent, Asia, and Africa.\textsuperscript{1} Epidemics are frequently observed after the rainy season or after flooding. Sporadic cases occur in endemic areas and in developed countries in individuals returning from visits to endemic areas.

Outbreaks of hepatitis E have been described in north-western and north-eastern parts of China\textsuperscript{2}; it is likely that the disease also occurs in other provinces. While the sanitary conditions and clean water supply in Hong Kong may not be conducive to outbreaks of hepatitis E, the frequency of travel between China and Hong Kong may account for many sporadic cases in returning travellers.

Modes of transmission in endemic regions include water-borne transmission, food-borne transmission, and person-to-person transmission. In an epidemic in Xinjiang, China, in 1986 to 1988, 119 280 cases were reported.\textsuperscript{4} Nearly 78\% of patients were aged 15 to 49 years, with a relative excess of male cases. The incubation period ranged from 15 to 75 days and ALT levels usually normalised within six weeks from the onset of illness. Mortality increased during late pregnancy and reached 21\% in the third trimester of pregnancy with a high incidence of disseminated intravascular coagulation. Pregnant women should be warned particularly of this risk when they travel to endemic areas.

The cloning of HEV\textsuperscript{5} allowed the development of an enzyme immunoassay (EIA) to detect IgG and IgM antibodies to recombinant expressed HEV antigen (anti-HEV).\textsuperscript{6} A seroepidemiological survey of HEV in Hong Kong was conducted in 1991 using recombinant-based EIA.\textsuperscript{7} The prevalence of IgG anti-HEV was 16\%, and was higher in subjects older than 20 than it was in younger individuals (24\% vs 4\%). Among patients with acute non-A, non-B, non-C hepatitis, one third were positive for IgM anti-HEV. Co-infection of HAV and HEV was also noted. Six percent of patients with acute hepatitis A were also IgM anti-HEV positive, while 26\% of subjects with past hepatitis A infection were also IgG anti-HEV positive. In a study in Taiwan, where sporadic or subclinical hepatitis E occurs, the prevalence of IgG anti-HEV was about 10\% in normal subjects older than 20, and persistence of IgG anti-HEV may be for more than eight years.\textsuperscript{8}

In the prevention of hepatitis E, sanitary measures and personal hygiene standards similar to those outlined to prevent hepatitis A apply. Education for travellers to endemic areas is important and the risk to pregnant women should be emphasised. A safe and effective vaccine against HEV needs to be developed.

References

1. Hong Kong Government Department of Health, Public Health


