

Does Hong Kong need hepatitis A vaccine?

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The inactivated hepatitis A vaccine available in Hong Kong is efficacious and useful in preventing hepatitis A. Incorporating hepatitis A vaccination as part of the childhood immunisation programme would require that it be extremely safe and effective. The vaccine needs to have a long duration of protection and be able to be combined with other antigens to minimise the cost of delivery. Most importantly, it should be available to the public sector at low cost. A hepatitis A immunisation programme as a public health preventive measure is cost-beneficial, but the programme itself is expensive. As booster doses are probably required for prolonged protection, difficulties in giving booster doses above the Expanded Programme of Immunisation age limit of 15 years would render a universal immunisation programme impractical at this stage in Hong Kong.

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Introduction

Hepatitis A virus (HAV) infection, if symptomatically manifested, is clinically indistinguishable from other types of acute hepatitis. Its self-limiting course and the lack of long term sequelae such as chronic hepatitis, cirrhosis, and hepatocellular carcinoma distinguish it from other types of hepatitis which follow a more sinister course, namely, hepatitis B and C. As HAV infection is rarely fatal, the introduction of hepatitis A vaccination as a public health measure would have to meet certain stringent criteria.

One of the most important factors affecting disease severity with HAV is age. Young children are less likely than are adults to exhibit the classic pattern of clinical HAV symptoms when infected.¹ The frequency and severity of symptoms increase with age. Almost all infected adults suffer from the overt disease and the older adult patient is more likely to develop serious complications. Immunity following infection is for life and there is no chronic carrier state.

The most common mode of transmission of HAV infection is by the faeco-oral route. Person-to-person spread is important in places where there is overcrowding and where poor standards of hygiene exist, such as in day-care centres, junior schools, and within families.² Consumption of contaminated shellfish, particularly bivalves—which have the ability to concentrate HAV—is responsible for many outbreaks. Raw clams, oysters, cockles, and mussels are the commonest culprits.³

The situation in Hong Kong

In Hong Kong, with improvements in sanitation having occurred over the last two decades, the age at which HAV occurs has shifted from early childhood to adolescence and early adulthood. Between 1979 and 1989, there was a drop in anti-HAV antibody prevalence in the general population.⁴ For instance, anti-HAV antibody prevalence among the 11- to 20-year age group dropped from 42.8% in 1979 to 11.2% in 1989.⁵ However, the number of clinical cases has increased. Epidemics occurred in 1988 and 1992.⁶ The number of notifications in recent years has ranged from 600 to 3600 cases annually (an average of 1500 annually). Of these cases, approximately 90% were notified by hospitals. The corresponding notification rates ranged from 10 to 62 per 100 000 population.⁶ Of these, approximately 80% were in the 11- to 30-year age group.⁵ It is apparent that there is a certain degree of under-notification. The actual scale of the problem is likely to be much greater.

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Shellfish—raw, semi-cooked, or cooked—are commonly eaten by the local population. Fresh shellfish, ranging from the inexpensive to expensive, are widely available in the territory. There is no restriction, health-related or otherwise, on shellfish importation. Some of the shellfish—notably oysters—require cultivation in local waters.

Current control measures

Experience in other countries shows that improvements in sanitation may increase the number of clinical cases in the short term, due to deferment of infection to older age groups which are more likely to manifest the disease clinically. Despite improved standards of hygiene, disease can still be contracted by eating contaminated shellfish.

Most of the shellfish imported into the territory do not require cultivation in local waters and are from surrounding regions, which have a higher endemicity of infection. Consequently, improving the quality of local waters only provides part of the answer. Additional control measures such as restricting importation is likely to be difficult to implement due to the number of sources of supply. Changing the culinary habits of the population also presents a considerable challenge as raw or semi-cooked shellfish are regarded as delicacies. Unfortunately, HAV is resistant to heat; gentle steaming may be sufficient to open the shell but not to destroy the virus.⁷

Although passive immunisation with immune serum globulin has approximately 90% efficacy, it only provides a short duration of protection, varying from three to six months depending on the dose.⁸ Hence, passive immunisation has never been an integral part of the preventive strategy in Hong Kong at a population level.

Hepatitis A vaccine

An inactivated HAV vaccine is available in Hong Kong. It has been shown to attain over 90% seroconversion and produces much higher antibody titres than does passive immunisation. In a trial conducted during an epidemic, protection was found to be conferred within 21 days of vaccination and was effective during the epidemic.⁹ In Thailand, it has also been shown to be efficacious in children aged from one to 16 years.¹⁰ However, the duration of protection of this vaccine is not known, although it is likely to exceed 10 years.¹¹⁻¹³

The inactivated HAV vaccine—though free from the live attenuated vaccine's potential problem of over-attenuation or under-attenuation—has the disadvantage that more than a single dose is probably required to achieve prolonged protection. The current recommended immunisation schedule consists of two doses spaced two weeks to one month apart, which provides immunity for at least one year. A booster dose is recommended between six and 12 months following the initial dose, to give immunity for up to 10 years.¹⁴

Live attenuated HAV vaccines offer the greatest hope for development of a product capable of inducing lifelong immunity following administration of a single dose. One such vaccine is currently being developed in China.¹⁵ Initial studies show that it is efficacious and produces few side effects. No live attenuated HAV vaccine is available in Hong Kong.

The way ahead

Immunisation against hepatitis A would benefit many groups, including employees of child-care centres, international travellers, military personnel, food handlers, prisoners, health care workers, and consumers of raw shellfish.¹⁶ A high-risk approach focusing on these groups is probably sufficient for its control in places of relatively low endemicity.¹⁷

In Hong Kong, HAV is distributed widely in the community and no particular group is exempt (Department of Health, unpublished data). To achieve effective control, phased introduction of immunisation with ultimate universal childhood vaccination should be the target. However, routine use of HAV vaccine should only be considered if the vaccine is extremely safe and effective, has a long duration of protection, can be combined with other antigens to minimise its cost of delivery, and is available to the public sector at low cost.

It has been shown that HAV vaccine can be given together with hepatitis B vaccine,¹⁸ and can probably be incorporated into the Expanded Programme of Immunisation (EPI) with minimal additional cost of delivery, especially when only a single dose is required. However, the vaccine's duration of protection is crucial in determining whether or not it is a suitable candidate for EPI. Unless the duration of protection is sufficiently long, the immunisation programme may only delay the age of infection and convert asymptomatic early childhood infection into symptomatic disease later in life. To provide lifelong protection, booster doses may be required. In addition to the extra cost incurred by giving booster doses, difficulty in reaching the at-risk population arises when

they are beyond the age of the EPI (older than 15 years) as many adolescents then leave school. This is a group at high risk of symptomatic disease, which can be severe. It is also necessary to determine whether the vaccine will be effective in infants who have circulating maternal antibodies. Although the vaccine has been shown to be effective against the disease, it is still not clear whether it is effective in preventing HAV infection and subsequent transmission.

The current market price in Hong Kong of a single dose of inactivated HAV vaccine is HK\$200. According to the recommended immunisation schedule, it can be estimated that it would cost HK\$42 million annually to introduce this programme for infants. Based on surveillance statistics and estimated disease under-reporting of 50%, an estimated 2250 HAV cases will require hospitalisation annually. The average length of stay for a patient with HAV is 10 days, and the daily cost of hospitalisation in an acute general hospital amounts to HK\$2105.¹⁹ The resultant burden on health care amounts to HK\$47 million annually. In addition to the time lost from work (an average of 20 days), and costs borne by patients and their families, this crude cost analysis shows that the cost of the disease outweighs the cost of the intervention, despite the fact that the vaccine is costly and several doses are required. However, the programme is intrinsically expensive. With its relatively low position on the list of health priorities, unless there is a substantial reduction in cost or change in priorities, it is probably not yet timely to introduce a universal immunisation programme against HAV.

It is evident that Hong Kong needs the HAV vaccine, but the currently available vaccine has yet to fulfil implementation criteria. While we are waiting for more information on the long term efficacy of the vaccine and a reduction in its price, existing control measures should be reinforced. Those people who can afford the vaccine privately (e.g. expatriates and the growing middle class) can gain extra protection through private means. Nevertheless, the protection conferred by the vaccine does not remove all the risks associated with eating shellfish, as other enteric organisms, such as hepatitis E, may also be transmitted in this way. Some 25% of the adult population have evidence of previous hepatitis E infection.²⁰

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