

# HEPATITIS A VIRUS: DECLINING SEROPREVALENCE IN CHILDREN AND ADOLESCENTS IN SOUTHEAST ASIA

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**Abstract.** The prevalence of hepatitis A virus (HAV) in a country largely reflects its standards of hygiene and socioeconomic conditions. Countries which undergo socioeconomic development show major change in HAV prevalence from high to low endemicity, and this is largely reflected in patterns of age-related seroprevalence. This paper presents age-related HAV seroprevalence patterns of SE Asian countries, and highlights how these patterns have changed over recent decades. Singapore, Thailand and Malaysia have experienced a decline in childhood and adolescent HAV seroprevalence, typical of countries which undergo socioeconomic development. By contrast, India has remained a country of high endemicity, with almost universal seroconversion in childhood. The Philippines and Vietnam show age-related seroprevalence patterns typical of high to moderate endemicity, while Indonesia shows significant regional variation in HAV seroprevalence.

Populations within countries which exhibit major improvements in endemicity and age related HAV seroprevalence patterns are at risk of HAV epidemics, and a paradoxical increase in incidence tends to occur as seroconversion shifts from children to adults. The residents of these countries, a significant number of whom are at-risk, would benefit from a program of vaccination, as would non-infected individuals visiting high-risk areas.

## INTRODUCTION

The hepatitis A virus (HAV) is a major cause of hepatitis throughout the world, causing significant morbidity in many countries. HAV endemicity varies from country to country, and within individual countries. Although the Southeast Asian region currently shows endemicity which ranges from high to low, many countries in the region have experienced dramatic changes in age-related HAV seroprevalence over the past one or two decades as a result of socioeconomic development.

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Countries undergoing socioeconomic development generally experience improvements in public health measures, such as the provision of clean water and improved sanitary practices. These improvements lead to a reduction in childhood prevalence of HAV, and as the prevalence of anti-HAV diminishes in children, adolescents and adults become increasingly susceptible to HAV infection.

This article reviews the age-related seroprevalence of HAV in a number of SE Asian countries which are categorized according to endemicity. Changes which have occurred over recent decades are identified, and a case is made for vaccination in countries which experience significant morbidity as a result of shifting seroprevalence patterns.

## WORLDWIDE OVERALL AND AGE-RELATED SEROPREVALENCE

Worldwide, the prevalence of HAV varies with geographical location and socioeconomic status. Almost universal endemicity occurs in poor countries, compared with low endemicity - less than 30% seroprevalence - in developed countries (Szmunes *et al*, 1977). Several authors have identified age-related seroprevalence patterns which correlate with the socioeconomic status of a country (Szmunes *et al*, 1977; Shapiro and Margolis, 1993; Hadler, 1991; Gust and Feinstone, 1989).

- In poor countries with poor sanitary and hygienic conditions, there is high endemicity, and every child is infected by the age of 5-10 years.

- Developing countries, where sanitation and hygiene are improved, are characterized by moderate endemicity. Seroconversion occurs predominantly in adolescents or young adults, and most adults have been infected.

- In developed countries, with good sanitation and hygiene, seroprevalence increases steadily with age, although the general adult population has low seroprevalence.

- Differences in age-related seroprevalence patterns may occur between geographically distinct communities within individual countries.

Countries such as Ethiopia show high endemicity, with universal seroconversion in childhood, whereas countries such as the USA and Singapore (in the 1990s) show low endemicity, with high seroprevalence only in older age groups (Fig 1).

## CHANGING PATTERNS IN DEVELOPING COUNTRIES

Age-related HAV seroprevalence patterns change in poor countries as they undergo socioeconomic development (Shapiro and Margolis, 1993; Hadler, 1991; Gust and Feinstone, 1989; Forbes and Williams, 1990). Over time, HAV seroprevalence declines markedly in children, although a substantial proportion of the adult population remains seroconverted as a result of previous infection. The proportion of seroconverted adults gradually declines as uninfected children become adults,

and the overall population seroprevalence declines. In terms of age-related patterns, countries undergoing development have curves which shift to the right and downwards as fewer children, and eventually adults, have seroconverted (Fig 1).

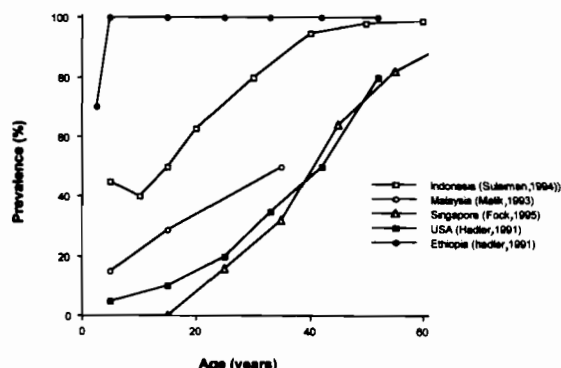


Fig 1—Age-related prevalence patterns in SE Asia, USA and Ethiopia.

Paradoxically, the incidence of clinical disease often increases in countries which undergo development, as largely subclinical infection in children is replaced with clinical infection in adolescents and adults (Shapiro and Margolis, 1993). As acute HAV infection produces illness in adults which is progressively more severe with age (Forbes and Williams, 1990), vaccination may be an appropriate strategy for developing countries to combat the greater morbidity associated with infection during adulthood.

Developing countries are also more susceptible to epidemics (Shapiro and Margolis, 1993), as their populations comprise a significant proportion of uninfected individuals, as well as a large reservoir of potentially contagious individuals living in communities of variable standards of hygiene and sanitation. An example of this susceptibility was recently seen in the Philippines when an outbreak of acute viral hepatitis A in the University of Santo Tomas failed to be controlled by conservative measures, and the institution had to be closed. Vaccination of at-risk populations in developing countries—school children, students, factory workers and the mentally handicapped (Poovorawan *et al*, 1994), as well as travellers to these countries (Shapiro and

Margolis, 1993) – would help prevent the occurrence of such epidemics.

## SINGAPORE

In Singapore, age-related seroprevalence has changed significantly since 1975. Childhood and adolescent seroprevalence has declined markedly, and the impact of this decline has been shown in the adult and overall population, although older adults retain a relatively high seroprevalence of antibodies.

The seroprevalence of HAV has decreased from 60% of 10-19 year olds in 1975 to 5.7% in 10-14 year olds in 1985 (Goh *et al*, 1987), and to less than 1% in 10-19 year olds in 1991 (Yap and Guan, 1993) (Fig 2).

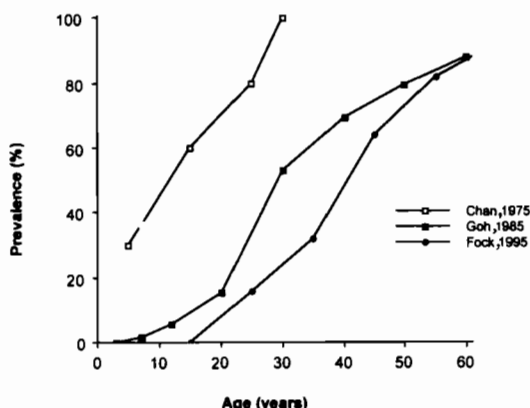


Fig 2—Age-related prevalence in Singapore by decade, 1975-1995.

A seroprevalence of 80% first occurred in the 20-29 year age group in 1975 compared with the 45-54 year age group in 1985 (Goh *et al*, 1987), and the 51-60 year age group in 1991 (Fock *et al*, 1995). Similar patterns for all levels of seroprevalence have also been shown, although the change is minimal in older adults, who have retained consistently high seroprevalence.

Overall population seroprevalence of HAV has declined from 31.8% in 1985 (Goh *et al*, 1987), to 21.4% in 1991 (Yap and Guan, 1993). The latter study demonstrated a non-significant reduction

over 4 years from 33.1% in 1987 to 21.4% in 1991.

Clearly, the decline in the proportion of seroconverted children and adolescents, together with the increase in age at which specific seroprevalences were shown, indicate that seroconversion now occurs at an older age. The consistently high seroprevalence in older adults indicates high seroprevalence when these cohorts were younger. These changes have occurred in parallel with the continuing socioeconomic development in Singapore, and the associated improved standards of living and public health (Yap and Guan, 1993).

Age-related changes in seroprevalence correlate with age-related incidence. Statistics for 1994 show that 65% of all cases of acute HAV occurred in individuals aged 15-34 years, while only 10% occurred in individuals under 15 years of age (Communicable Disease Surveillance in Singapore, 1994). Clearly, greater seroconversion now occurs in late teenage and early adult years, rather than in childhood.

Age-related seroprevalence and incidence patterns in Singapore now reflect those of a developed country with low endemicity.

## THAILAND

Since the early 1970s there has been a marked change in age-related seroprevalence in Thailand which has paralleled socioeconomic development.

Two studies effectively chart the changes in age-related HAV seroprevalence from the early 1970s to the mid-1990s (Poovorawan *et al*, 1993; Innes *et al*, 1991). Direct comparisons between similar populations sampled over consecutive decades have shown significant reductions in seroprevalence in urban (Burke *et al*, 1981) and rural (Echeverria *et al*, 1983) primary school and adolescent populations, and in young adult medical students (Viranuvatti *et al*, 1982).

Major findings include changes in Bangkok primary school children, who showed 50% seroprevalence by 4 years of age in 1971-1972 (Echeverria *et al*, 1983), compared with 10-12 years in 1988 (Innes *et al*, 1991). Rural Thai children showed 50% seroprevalence at age 7 years in 1980 (Echeverria *et al*, 1983) compared with 12-14 years in 1989, and 18-20 years in 1992 (Poovorawan *et al*,

1993). Medical students aged 20-21 years showed 73% seroprevalence in 1981 (Viranuvatti *et al*, 1982), compared with 30% in 1992 (Poovorawan *et al*, 1993). The increase in age at which 50% seroprevalence was first attained in rural populations over the period 1980-1992 demonstrates a shift in seroconversion to older children and adolescents (Fig 3).

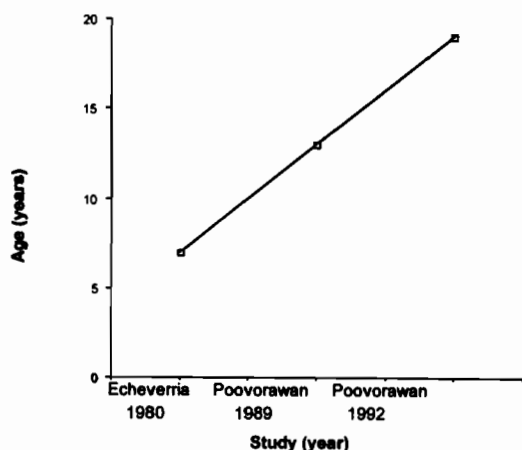


Fig 3—Age of 50% prevalence in rural Thailand, 1980-1992.

A significant reduction in seroprevalence was shown over a 4-year period in a rural population of children aged 6-11 years between 1985 and 1989, suggesting that major changes in age-related seroprevalence over a very short time frame are possible (Innes *et al*, 1991).

The overall seroprevalence in adult populations appears to have declined in Thailand since 1971. While almost universal seroconversion in adults was shown in 1971 and 1976 (Burke *et al*, 1981), and 90-100% seroprevalence in 1982 and 1983 (Echeverria *et al*, 1983), there was only 60-68% seroprevalence in 1991 (Poovorawan *et al*, 1991).

Clearly, age-related and overall seroprevalence in the Thai population has changed from the 1970s to the early 1990s. A marked decline in seroprevalence in children through to young adults has been shown, while the overall seroprevalence in adults has declined from almost universal endemicity to

levels of approximately 60%. Over the past 25 years, HAV seroprevalence in Thailand has changed from high to moderate endemicity, which is typical for a developing country.

## MALAYSIA

Over the last decade, the Malaysian population has seen changes in younger age groups, similar to those shown in Singapore and Thailand. A marked decrease in the seroprevalence of HAV has occurred in the 0-10 year age group—from 39% in 1985 to 15% in 1993, and in the 11-20 year age group—from 51% in 1985 to 29% in 1993 (Malik and Baharin, 1994; Tan *et al*, 1986). Only in adults over 30 years of age was 50% or more of the population seropositive in 1993, compared with 51% of the 11-20 year age group in the 1985 study. The age-related seroprevalence found in these studies clearly demonstrates a shift towards seroconversion at a later age (Fig 4).

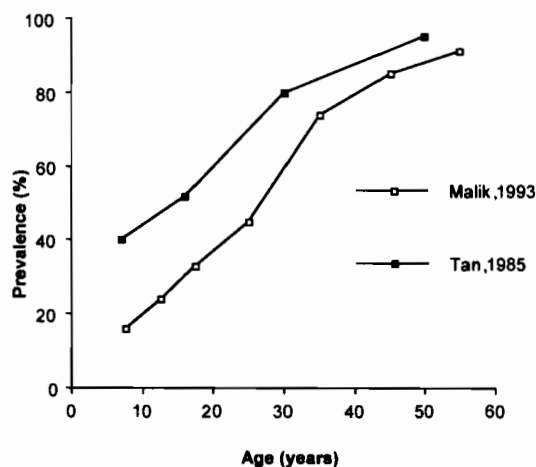


Fig 4—Age-related prevalence in Malaysia by decade, 1985-1993.

Although the adult 41-60 year old population showed a reduction in seroprevalence over this time from approximately 96% to 88%, the consistently high level suggests that the marked age-related improvements shown in younger ages have yet to

have an impact on older adult populations.

The age-related HAV seroprevalence has changed from 1985 to 1993 in Malaysia, which now has moderate endemicity. In line with the rapid development of SE Asia, seroprevalence in children and young adults has markedly decreased.

## INDONESIA

In contrast to Singapore, Thailand and Malaysia, Indonesia shows marked regional variations of age-related and overall seroprevalence which range from high to moderate endemicity.

High endemicity was identified on the island of Bali between the years of 1978 and 1981, with 93-98% seroconversion in individuals aged 9-29 years, and universal seroconversion in those aged 30 years and over (Brown *et al*, 1985). However, a 1994 survey of Jakarta hospitals by Sulaiman and Julitasari (personal communication) found a seroprevalence of 48% at age 5 years, progressively rising to a 97% or greater from age 50 years onwards - a pattern typical of moderate endemicity.

The differences shown by these age-related seroprevalence patterns are likely to be attributed to improvements over time, although it is noted the populations are geographically and socioeconomically distinct.

Further regional variation in individuals under 20 years of age was identified in a 1981 study, which found 49.4% seroconversion in a poor urban population of Jakarta, 47.5% in a rural population in Ujung Pandang region described as having poor sanitation, and 63.2% in a sub-urban population in Bandung region (Akbar *et al*, 1981). These populations also showed increasing age-related seroprevalence up to 20 years of age.

Over the period 1981-1994, a marked variation in age-related seroprevalence has occurred in a number of Indonesian populations. Most studies have shown increasing seroprevalence with age, and the patterns are indicative of high to moderate endemicity. The overall seroprevalence varies markedly from 40% to 98%, depending upon the population and the region (Sulaiman, 1993; Mulyanto, 1985; Sanjaya *et al*, 1990), further supporting the notion of marked regional variation.

Incidence studies also suggest that infection occurs predominantly in individuals under 30 years of age, with few cases in adults over 30 years of age (Noer *et al*, 1981).

The evidence clearly suggests that age-related seroprevalence in Indonesia varies from high to moderate endemicity, with marked variations between geographically distinct populations.

## VIETNAM

Only one 1995 study reports the seroprevalence of hepatitis A in Vietnam, and its findings suggest that Vietnam is a country of high endemicity.

Katellaris *et al* (1995) found 93% seroprevalence in children aged between 2 and 12 years, living in a rural commune approximately 100km from Ho Chi Minh city.

An earlier study in 1981 found a high seroprevalence in Vietnamese refugees resettling in Denmark (Skinhoj *et al*, 1981). Seroprevalence was approximately 50% at 5 years of age, 90% at 15 years, and almost universal in the adult population.

These findings suggest that the Vietnamese population shows an age-related seroprevalence typical of countries with high endemicity, although further studies are required to confirm this.

## PHILIPPINES

The age-related and overall seroprevalence in urban parts of the Philippines in the 1990s appears to reflect that of moderate endemicity, although there is little evidence identifying any change over preceding decades.

A 1992-1993 study demonstrated an overall seroprevalence of 62% in metropolitan Manila, with age-related seroprevalence which increased progressively with age. Less than 10% of children aged under 5 years had seroconverted, compared with 20% of children aged 5-10 years, and 42% of those aged 11-15 years. Progressive increments occurred in all sub-groups, and adults aged 40 years and over showed seroprevalence consistently above 90% (Barzaga *et al*, 1996).

An early 1980s study of rural populations demonstrated almost universal endemicity in those aged 5 years or older (Veronica Chan, personal communication), while Philippine dentists demonstrated 86% HAV seroprevalence in 1986 (Lim *et al*, 1986), and adult expatriate Philippine workers in Saudi Arabia demonstrated 91-95% seroprevalence in 1986 (Ramia *et al*, 1986).

The absence of longitudinal studies assessing similar populations prevents any comment on the change in seroprevalence over time. The current urban Philippine population is typical of a country with moderate endemicity, while data from the 1980s suggest that seroprevalence in rural areas was typical of high endemicity. These variations suggest that regional variation may occur, although further studies are clearly required to confirm either regional variation or age-related change over time.

## INDIA

The prevalence of HAV in India is typical of a country with high endemicity. Studies from 1982 onwards undertaken in different geographical regions of India have shown near universal seroconversion from a very young age.

A study from Pune, a city near Bombay, demonstrated no significant change in age-related seroprevalence from 1982 to 1992 (Arankalle *et al*, 1995). In 1982, 73% of children over 1.5 years of age had seroconverted, compared with 85% in 1992. Seroprevalence to 95% and over was found in children aged 6-10 years in both 1982 and 1992, and near universal seroprevalence occurred in all age-groups over 10 years of age.

Studies undertaken in other regions of India in 1990 demonstrated almost universal seroprevalence in children over the age of 10 years (Werner *et al*, 1990), and 98.2% seroprevalence in those aged 3-21 years (Graham *et al*, 1991).

India, therefore, has high HAV endemicity shown by near universal infection at an early age. There is no evidence that the age-related pattern has changed in the last decade.

## CONCLUSIONS

Age-related HAV seroprevalence has improved over the last two decades in Singapore, Malaysia

and Thailand, and each country has shown declining endemicity.

- The proportion of seroconverted children and adolescents has decreased in line with socioeconomic development of these countries.

- In some cases, reduced childhood and adolescent seroprevalence has made an impact on young and middle aged adult populations, and this trend is expected to continue with time.

- Relatively high seroprevalence still occurs in older adults, although this is expected to decline as the current cohort is replaced by younger adults.

Indonesia, Vietnam, the Philippines and India appear to show high to moderate endemicity, although there appears to be significant regional variation in Indonesia. There is no clear indication that age-related HAV seroprevalence has changed in association with socioeconomic development in these countries, although further studies could identify such trends.

Populations that show age-related seroprevalence changes in parallel with socioeconomic development are at risk of significant morbidity from active disease.

- Acute HAV illness in these populations is more likely to affect older individuals in whom the illness is more severe.

- Epidemics of HAV are more likely because of the significant number of individuals who are susceptible to infection, and variable conditions of sanitation which are conducive to water and food borne transmission.

- Individuals in high risk groups - school children, factory workers, the mentally handicapped, and travellers to surrounding countries of high endemicity - are at risk of infection.

Vaccination could prove to be a public health measure of considerable benefit for SE Asian countries experiencing improved age-related HAV seroprevalence patterns in parallel with socioeconomic development.

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## REFERENCES

- Akbar N, Sulaiman A, Effendi AT. Antibody to hepatitis A virus in young population in Indonesia. In: Suzuki H, Mayumi M, Iino S, Tsuboi S, Baba S, eds. Viral hepatitis and its related diseases. Proceedings of the Second ICMR Seminar, Kobe, Japan, 1981: 20-4.
- Arankalle VA, Tsarev SA, Chadha MS, *et al.* Age-specific seroprevalence of antibodies to hepatitis A and E viruses in Pune, India, 1982 and 1992. *J Infect Dis* 1995; 171: 447-50.
- Barzaga NG, Florese RH, Roxas JR, *et al.* Seroepidemiology of hepatitis A virus among filipinos living in selected communities in and around metro Manila. *Phil J Microbiol Infect Dis* 1996; 25: 39-47.
- Brown P, Breguet G, Smallwood L, *et al.* Serologic markers of hepatitis A and B in the population of Bali, Indonesia. *Am J Trop Med Hyg* 1985; 34: 616-9.
- Burke DS, Snitbhan R, Johnson DE *et al.* Age-specific seroprevalence of hepatitis A virus antibody in Thailand. *Am J Epidemiol* 1981; 113: 245-9.
- Communicable Disease Surveillance in Singapore, 1994. Ministry of the Environment, Singapore Government. 1994.
- Echeverria P, Burke DS, Blacklow NR, *et al.* Age-specific seroprevalence of antibody to rotavirus, *Escherichia coli* heat-labile enterotoxin, Norwalk virus, and hepatitis A virus in a rural community in Thailand. *J Clin Microbiol* 1983; 17: 923-5.
- Fock KM, Tay HH, Phya KB, *et al.* Seroprevalence of antibodies against hepatitis A (anti-HAV) in Singapore: the NFDD experience. *Singapore Med J* 1995; 36: 26-7.
- Forbes A, Williams R. Changing epidemiology and clinical aspects of hepatitis A. *Br Med Bull* 1990; 46: 303-18.
- Goh KT, Wong LYM, Oon CJ, *et al.* The seroprevalence of antibody to hepatitis A virus in Singapore. *Asia Pac J Public Health* 1987; 1: 9-11.
- Graham DY, Adam E, Reddy GT, *et al.* Seroepidemiology of *Helicobacter pylori* infection in India; comparison of developing and developed countries. *Digest Dis Sci* 1991; 36: 1084-8.
- Gust ID, Feinstone SM. Hepatitis A. In: Popper H, Schaffner F, eds. Progress in Liver Diseases. New York: Grune and Stratton, 1989; 371-8.
- Hadler SC. Global impact of hepatitis A virus infection; changing patterns. In: Hollinger FB, Lemon SM, Margolis HS, eds. Viral Hepatitis and Liver Disease. Baltimore: Williams and Wilkins, 1991; 14-20.
- Innes BL, Snitbhan R, Hoke CH, *et al.* The declining transmission of hepatitis A in Thailand. *J Infect Dis* 1991; 163: 989-95.
- Katellaris PH, Robertson G, Bradbury R, *et al.* Seroprevalence of hepatitis viruses in children in rural Vietnam. *Trans R Soc Trop Med Hyg* 1995; 89: 487.
- Lim DJ, Lingao A, Macasaet A, *et al.* Sero-epidemiological study on hepatitis A and B virus infection among dentists in the Philippines. *Int Dent J* 1986; 36: 215-8.
- Malik YA, Baharin R. Changing seroprevalence of hepatitis A in Malaysia. Fourth Western Pacific Congress of Chemotherapy and Infectious Diseases, Manila, 4-7th December, 1994.
- Mulyanto. Hepatitis A virus in some parts of West Nusa Tenggara [Abstract]. Third Scientific Meeting of the Indonesian Association for the Study of the Liver, 2nd National Congress of the Indonesian Association for Gastroenterology and Digestive Endoscopy, Palembang, Indonesia, 1985.
- Noer HMS, Sulaiman HA, Akbar N, *et al.* Seroprevalence of acute viral hepatitis in Jakarta, Indonesia. In: Suzuki H, Mayumi M, Iino S, Tsuboi S, Baba S, eds. Viral hepatitis and its related diseases. Proceedings of the Second ICMR Seminar, Kobe, Japan, 1981: 221-5.
- Poovorawan Y, Paiboonkasemsuthi S, Theamboonlers A, *et al.* Seroepidemiology of antibody to hepatitis A in the rural eastern part of Thailand. *Southeast Asian J Trop Med Public Health* 1991; 22: 35-8.
- Poovorawan Y, Theamboonlers A, Chumdermpadetsuk S. Changing seroepidemiology for hepatitis A virus infection in Thailand. *Southeast Asian J Trop Med Public Health* 1993; 24: 250-4.
- Poovorawan Y, Yodvised S, Theamboonlers A, *et al.* Hepatitis A virus antibody in mentally retarded children. *Southeast Asian J Trop Med Public Health* 1994; 25: 392-3.
- Ramia S. Antibody against hepatitis A in Saudi Arabians and in expatriates from various parts of the world working in Saudi Arabia. *J Infect* 1986; 12: 153-5.
- Sanjaya B, Mulyanto, Sumarsidi D, *et al.* HAV and HBV viral infection among kindergarten and elementary school students at Jayapura. In: Proceedings of the 4th National Congress of Indonesian Association of Gastroenterology and Digestive Endoscopy, Indonesia, 1990:223-9.
- Shapiro CN, Margolis HS. Worldwide epidemiology of hepatitis A virus infection. *J Hepatol* 1993; 18 (suppl 2): S11-4.
- Skinhoj P, Aldershvile J, Black F, *et al.* Viral hepatitis in Southeast Asian refugees. *J Med Virol* 1981; 7: 149-55.

- Sulaiman HA. Hepatitis in Indonesia. International Symposium on Viral Hepatitis and Liver Disease, Tokyo, 1993.
- Szmunn W, Dienstag JL, Purcell RH, *et al.* The seroprevalence of antibody to hepatitis A antigen in various parts of the world; a pilot study. *Am J Epidemiol* 1977; 106: 392-8.
- Tan DSK, Fang R, Collett D, *et al.* Seroepidemiologic study of hepatitis A in Malaysia. *Southeast Asian J Trop Med Public Health* 1986; 17: 201-4.
- Viranuvatti V, Hemindra P, Chainuvati T. Anti-HAV in Thai population. *J Med Assoc Thai* 1982; 65: 379-82.
- Werner GT, Frosner GG, Sareen DK. Seroprevalence of hepatitis A, B and HIV markers in Punjab. *J Indian Med Assoc* 1990; 88: 293-4.
- Yap I, Guan R. Hepatitis A sero-epidemiology in Singapore: a changing pattern. *Trans R Soc Trop Med Hyg* 1993; 87: 22-3.