
REVIEW ARTICLE

Declining hepatitis A seroprevalence: a global review and analysis

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SUMMARY

Hepatitis A virus (HAV) is spread by faecal–oral contact or ingestion of contaminated food or water. Lifelong immunity is conferred by infection or vaccination, so anti-HAV seroprevalence studies can be used to indicate which populations are susceptible to infection. Seroprevalence rates are highly correlated with socioeconomic status and access to clean water and sanitation. Increasing household income, education, water quality and quantity, sanitation, and hygiene leads to decreases in HAV prevalence. Japan, Australia, New Zealand, Canada, the United States, and most European nations have low anti-HAV rates. Although anti-HAV rates remain high in most Latin American, Asian, and Middle Eastern nations, average seroprevalence rates are declining. Surveys from Africa generally indicate no significant decline in anti-HAV rates. Because the severity of illness increases with age, populations with a high proportion of susceptible adults should consider targeted vaccination programmes.

INTRODUCTION

The proportion of persons with antibodies to hepatitis A virus (HAV) has been declining in most parts of the world in recent decades. The decline in anti-HAV seroprevalence has generally been explained by improvements in socioeconomic status, improved access to clean water and sanitation, and, in some cases, to the development and use of an effective vaccine. This paper comprehensively examines and analyses of the evidence for declining HAV rates in each of the six regions of the world – Africa, the Americas, the Middle East, Europe, South-East Asia, and the East Asia/Pacific region – and considers the factors that may be responsible for declining HAV infection rates.

Approximately 1·4 million new HAV infections are estimated to occur worldwide each year [269]. Infection is generally acquired by the faecal–oral route either through person-to-person contact or ingestion of contaminated food or water [35]. In children,

hepatitis A infection is often asymptomatic. Most infected adults, however, present with jaundice and other symptoms which may be severe. Infection generally confers lifelong immunity to all strains of HAV.

Immunity to hepatitis A can be determined from IgG anti-HAV antibodies detected in blood samples. Samples taken from a sufficient and representative number of individuals in a population can indicate prior exposure to HAV in the population. The distribution of anti-HAV seroprevalence by age group may vary significantly between countries and regions. Within countries, seroprevalence rates may vary by age, socioeconomic status, urbanization level, ethnic origin, and access to clean water and sanitation facilities. Decline in the population seroprevalence level, particularly in the seroprevalence rates of children, is an indicator of reduced HAV incidence.

REGIONAL PROFILES

The regional profiles below present the best current information on HAV seroprevalence rates and

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Table 1. *HAV seroprevalence rates among African children and young adults*

Country [ref.]	% with anti-HAV
Cameroon [20]	94 % of ages 4–6; 100 % by age 12
DR Congo (Zaire) [24]	96 % of ages 5–7; 100 % of age 10+
Djibouti [8]	99 % of young adults
Ethiopia [22]	>90 % by age 6; 100 % of age 15+
The Gambia [16]	55 % of children; >95 % of age 30+
Kenya [23]	>90 % by age 2
Liberia [14, 26]	>80 % by age 4; >90 % by age 5
Madagascar [12]	>95 % of age 5+
Namibia [9, 19]	100 % of age 7+
Senegal [4]	100 % of age 4+
Sierra Leone [7]	97 % of age 6+
Somalia [5]	>90 % of age 1+
South Africa (black) [1, 10, 15]	>90 % by age 10; 100 % of adults
Tanzania [11]	99 % of adults age 20+
Zimbabwe [6]	>95 % of age 10+

evidence, where available, for recent declines in HAV rates. This section concludes with an analysis of seroprevalence rates by age for areas with different levels of endemicity (Fig. 1).

Africa

Africa has very high rates of HAV infection. Most surveys of anti-HAV seroprevalence indicate that nearly all children have been infected by the time they reach 5 years of age (Table 1). Selected populations in some countries have slightly lower seroprevalence rates, including Cameroon [13], The Gambia [2], Mauritius [16, 17], Nigeria [3], and some South African populations [10, 15, 18]. The results of these studies may reflect the selection of unrepresentative sample populations. In South Africa, for instance, anti-HAV seroprevalence is highly correlated with race. A study of adult blood donors found anti-HAV rates of 50 % in whites, 67 % in Indians, 85 % in persons classified as Coloured, and 91 % in black donors [15]. Few surveys indicate a significant decline in anti-HAV rates in African children or adults.

The Americas

Most Latin American nations have high levels of anti-HAV seroprevalence in children and adults (Table 2), but average seroprevalence rates have decreased in most countries in the past 20 years. For example, from 1977 to 1996–1997, age-adjusted anti-HAV

Table 2. *HAV seroprevalence rates in the Americas*

Country [ref.]	% with anti-HAV
Argentina [80]	55 % of ages 6–10; 70 % of ages 21–30
Belize [38]	>95 % by age 18
Bolivia [30]	100 % by age 11
Brazil [80]	35 % of ages 1–5; >85 % by age 20
Canada [53, 65]	<20 % of children; 40–60 % in age 40+
Chile [46, 80]	31 % of ages 6–10; 79 % of ages 16–20; >95 % of age 30+
Costa Rica [84]	47 % of ages 10–14; >95 % of adults
Dominican Republic [80]	63 % of ages 1–5; >90 % by age 11
Guatemala [76]	76 % by age 3
Jamaica [34]	30 % by age 10; 73 % by age 30
Mexico [80]	40 % of ages 1–5; >90 % by age 15
Nicaragua [66]	>70 % of ages 2–4; >95 % in age 6+
Peru [49]	>95 % by age 7
United States [35, 75]	10 % in children; 70 % in age 50+
Venezuela [80]	54 % of ages 6–10; 72 % of ages 16–20

seroprevalence rates in Argentina fell from 94.2 to 55 %, in Venezuela from 96 to 55.7 %, in Chile from 98 to 58.1 %, in Brazil from 98.4 to 64.7 %, in Mexico from 98.4 to 81 %, and in the Dominican Republic from 99.8 to 89 % [61, 80].

In Santiago, Chile, age-standardized child seroprevalence fell from 54 to 41 % between 1990 and 1998 [42]. A study in rural Bolivia found a significant decrease in HAV rates between 1987 and 1997 only in the 1–5 years age group [30], indicating a recent change in the force of infection. Decreasing rates among children generally correlate with increases in socioeconomic status. In Valdivia, Chile, for example, child seroprevalence rates are highly correlated with the type of school attended [70]. Studies in Brazil indicate declining rates [85], and provide strong evidence for the importance of sociodemography in determining exposure to HAV [a].†

The United States and Canada have low levels of HAV infection. Only ~30 % of the general population in the United States has antibodies for HAV [35]. The seroprevalence in children under 5 years of age is ~10 %, and the rate rises to ~70 % in adults 50 years of age and older [75]. Anti-HAV seroprevalence rates are higher in some special populations, including some Native American communities and certain urban populations [36, 50, 79]. Less than 20 % of

† Letters within square brackets denote omitted sequences of reference citations. These citations appear in an Appendix at the end of the paper.



Fig. 1. Geographical distribution of anti-HAV seroprevalence (Reproduced with permission of the Division of Viral Hepatitis, Centers for Disease Control and Prevention).

Table 3. *HAV seroprevalence rates in the Middle East and North African regions*

Country [ref.]	% with anti-HAV
Algeria [103]	100% of age 10+
Egypt [94]	100% of all ages
Iran [96]	>90% by age 10
Jordan [111]	100% by age 5
Lebanon [108]	85% of ages 6–12; 98% of adults
Morocco [105]	>95% of young adults
Pakistan [89]	94% by age 5
Qatar [112]	100% by age 30
Saudi Arabia [91, 97]	>50% by age 10
Syria [92]	95% by age 11
Turkey [102, 110]	>50% of teenagers
United Arab Emirates [112]	60% of ages 17–20
Yemen [107]	>99% of all ages

Canadians under the age of 20 years and approximately 40–60% of Canadians over the age of 40 years have anti-HAV [39, 53, 65]. HAV seroprevalence may be higher in rural areas, in First Nations communities, and in immigrants [b].

The Middle East/North Africa

Anti-HAV seroprevalence rates in the Middle East are high. Studies show that more than 95% of adults in many nations in the region have been previously infected with HAV (Table 3). More than half of Turkish children have IgG antibodies by their late

teenage years [c]. HAV antibody prevalence in Saudi Arabia is highly dependent on socioeconomic status [91, 104]. In some populations well over half of children have anti-HAV by 10 years of age, but in higher socioeconomic populations the infection rate may be much lower [d]. In Israel rates are highly dependent on ethnic origin [98–101].

Some studies have found evidence for declining HAV rates. Overall prevalence in Turkey declined from ~90% to 72.3% during the past two decades [113]. Seroprevalence in children aged 1–12 years declined by almost 50% between 1989 and 1997 in Saudi Arabia [112]. Seroprevalence rates in young adults inducted into the Israeli military showed a consistent decrease from 64% in 1977 to 54% in 1984, 46% in 1987, and 38% in 1996 [98].

Europe

Seroprevalence rates in the regions of Europe vary from intermediate levels in Southern and Eastern Europe to low levels in Western Europe and very low levels in Northern Europe [269] (Table 4) (Fig. 2).

Southern Europe reports the highest HAV rates in Europe, although seroprevalence rates in young persons are declining. Samples collected over many years from Barcelona [185] and the greater Cataluña region [124, 172] and from Guipuzcoa in the Basque region [164] suggest a decreasing seroprevalence in Spain. Other studies in Spain over the past few decades provide further evidence for a general reduction in

Table 4. *HAV seroprevalence rates in Europe*

Country [ref.]	% with anti-HAV
Austria [167]	7% in ages 18–30; 57% in ages 41–50
Belgium [119]	>50% of age 35+
Czech Republic [117]	4% in age <20; 50% in ages 40–49; >85% in age 60+
Denmark [151]	<10% of ages 15–34; 50% of ages 50–69
Finland [184]	<10% of ages 20–29
France [133]	29% in ages 20–29; >90% by age 60
Germany [182]	14% in ages 18–29; 64% in ages 50–59
Greece [146, 152]	<10% of children; >90% by age 45
Hungary [165]	<20% in children; >50% by age 40
Iceland [122]	<5% of ages 10–50
Ireland [168, 170]	19% of ages 5–14; >90% of age 45+
Italy [160, 190]	<10% in young adults; >90% by age 50
Netherlands [181]	<10% in young adults; 50% by age 45
Norway [175]	<10% in adults ages 20–40
Poland [127, 166]	<10% in children; >75% by age 40
Portugal [116]	21% of ages 6–7; 38% of ages 18–19
Romania [161]	>50% of ages 5–9; >90% by age 30
Russia [174]	>50% by age 20
San Marino [179]	29% of ages 20–30; >90% by age 40
Spain [129]	25% of ages 13–19; 55% of ages 20–29; >90% by age 30
Sweden [121]	2% in adults ages 20–50
United Kingdom [139, 159]	9% in ages 1–9; >60% in ages 50–59

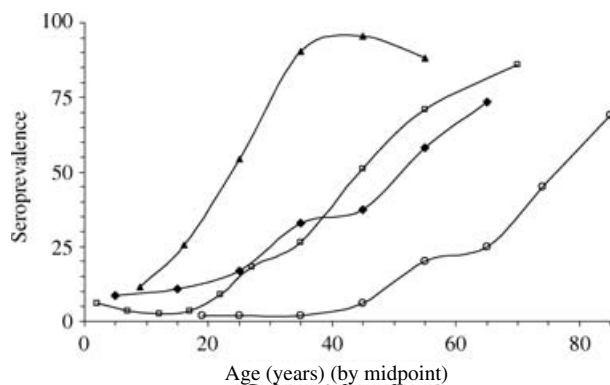


Fig. 2. Current anti-HAV seroprevalence rates in selected nations of Europe [117, 121, 129, 159]. —▲—, Spain; —□—, Czech Republic; —◆—, England; —○—, Sweden.

seroprevalence [e]. Portuguese rates are similar to those in Spain, with studies indicating comparable declines in rates [f]. Although rates in parts of Greece remain high, some regions, including Athens, report declines in rates since the 1970s [136, 146, 152]. Many studies in Italy have demonstrated decreases in anti-HAV seroprevalence in various regions, including Milan [189, 190] (Fig. 3), Padua [126, 183], Naples [132], and Palermo, Sicily [147, 178].

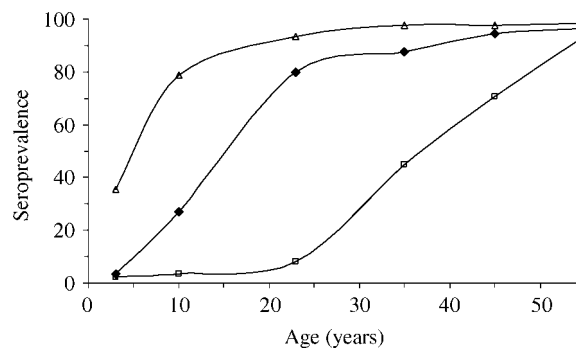


Fig. 3. Changing seroprevalence rates in Milan [189, 190]. —△—, 1958; —◆—, 1977; —□—, 1992.

Central and Eastern Europe have intermediate HAV rates [127]. In Poland, the average age of infection has shifted from early to mid-adulthood. Reports indicate possible decreases in infection rates in Warsaw [127] and other parts of Poland in the 1980s and 1990s [141, 166]. In Hungary, the proportion of seropositive blood donors dropped from 69% in 1982 to 18% in 1999 [165]. In the Czech Republic and Slovenia only about half of adults have been infected by age 40 [117, 176]. In the late 1980s in Leningrad (now St Petersburg), Russia,

approximately half of the population had anti-HAV by their 20s [174]. In Romania, Belarus and Albania, however, more than half of children have anti-HAV [g].

Western Europe has generally low rates of HAV. In Switzerland and western Austria, for instance, only about half of adults aged 40 years have anti-HAV [136, 167, 180]. Even so, some areas have reported declining rates. Belgium showed a decline between 1979 and 1989 [119, 180, 186], and rates in The Netherlands have also declined slightly from already low rates [136, 181]. In England the rate has fallen from the late 1970s [131] to the mid-1980s [139] to the mid-1990s [118, 159]. No decline was seen in Ireland [168, 170]. Rates in Germany have declined [137, 182], but significant differences are still seen between East and West Germans [182].

Scandinavia reports some of the lowest anti-HAV rates in the world. Denmark [151, 155], Finland [184], Iceland [122, 123], Norway [175], and Sweden [121, 144, 188] all have low anti-HAV seroprevalence rates. Only a few populations with higher rates have been noted, such as the Inuit of West Greenland [149].

South-East Asia

Most populations in South-East Asia have very high rates of HAV antibodies [212] (Table 5). Studies in Nepal in 1987 and 1996 found evidence of almost universal prior infection in adults [222]. In parts of Indonesia [196, 199, 200] and Bhutan [201] nearly all children are infected by age 10 years. More than half of Sri Lankan children tested in the 1970s were found to have anti-HAV [218, 227]. Many areas, however, report decreasing anti-HAV seroprevalence rates. For instance, in parts of Java, Indonesia, a 90% anti-HAV seroprevalence is only reached in adulthood [208]. In South Korea seroprevalence rates in children have declined from >50% in the 1980s to <10% in the 1990s [223]. The declining rates have been linked to improvements in water and sanitation coverage [223].

Rates in Thailand are decreasing. Longitudinal studies in both urban and rural areas have found sharp decreases in anti-HAV rates in schoolchildren [197, 207]. The age at which more than half of children have antibodies to HAV has risen in rural areas [205, 219, 220]. In Bangkok, rates in middle-income adolescents significantly decreased between 1987 and 1996 [221]. Other studies in Bangkok indicate a fall in anti-HAV seroprevalence in children and young adults [210, 226].

Table 5. *HAV seroprevalence rates in Asia and the Pacific*

Country [ref.]	% with anti-HAV
Australia [228]	50% by age 40
Bhutan [201]	90% of ages 0–12; 100% of age 12+
China [237]	>50% of ages 10–19
Hong Kong [233]	<5% in ages 1–10; 85% in ages 31–40
India [193, 198]	>95% by age 10
Indonesia [196]	95% by age 10
Japan [236]	<1% in ages 0–19; 4% in ages 20–29
Korea (South) [223]	<10% of children
Malaysia [212]	29% in ages 11–20; 88% in ages 41–60
Nepal [222]	100% of adults
New Zealand [232]	<20% of ages 36–55
Philippines [212]	42% of ages 11–15; >99% in age 40+
Singapore [234, 264]	1% in ages 10–19; >50% in ages 40–49
Sri Lanka [218]	>90% of ages 0–9
Taiwan [261]	<5% of teenagers; 66% in ages 30–39
Thailand [209, 220]	20% by age 10; >90% by age 30
Vietnam [241, 249]	>65% of ages 0–4; >95% of ages 5–9

Most regions of India have high rates of anti-HAV seroprevalence in children [h]. Some longitudinal studies have found slight declines in the average age at infection. A series of studies in Bhor Taluk, a rural area in western India, found a significant decline in the seroprevalence rate of children aged 5–10 years from 1983 to 1995 [198]. The decline was significant in children who used piped dam water, while no change was observed in children who drank well water [198], indicating a link between declining HAV rates in India and development. Nearly all persons in the study population had anti-HAV by 10 years of age [193, 198]. Studies in Pune, an urban region of southwestern India, found significant declines in anti-HAV seroprevalence among high socioeconomic status study participants between 1992 and 1998, but no similar decline in lower socioeconomic status groups [193]. The change was related to recent development, as no decline in seroprevalence was found between 1982 and 1992 [194].

East Asia and the Pacific

The East Asian region has high rates of HAV seroprevalence [212] (Table 5). Nearly all children in

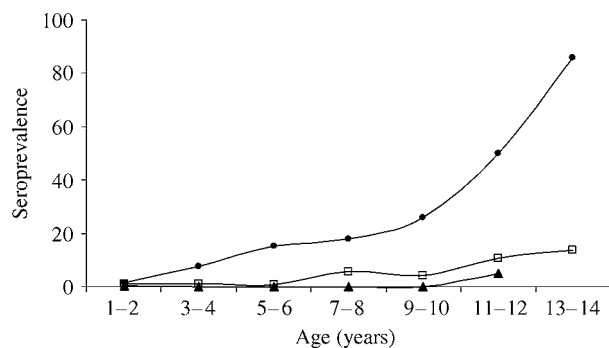


Fig. 4. Anti-HAV seroprevalence rates among children of Taipei City, Taiwan [243, 245, 259]. —●—, 1975–1976; —□—, 1984; —▲—, 1989.

Vietnam have anti-HAV by age 10 years [241, 249], and a study of eight cities across China in 1990 found that more than half of all 10- to 19-year-olds had antibodies to HAV [237]. However, infection rates in many areas are declining. In 1975, more than one-third of children under 10 years of age in Singapore had prior HAV infection [238] but by 1995 almost no Singaporean children under the age of 20 years had anti-HAV IgG [234, 264]. In Malaysia, the seroprevalence rate in children 10 years of age and younger dropped from 39% in 1985 to 15% in 1993 [212, 257]. In Tainan, Taiwan, age-specific seroprevalence rates dropped significantly from 1992 to 1998 [261], although rates remain highly dependent on socioeconomic status [263]. In China, childhood rates have dropped, particularly in urban areas [230, 244]. Significant declines have also been found in children in Taipei City, Taiwan [i] (Fig. 4), and in Hong Kong [233, 251].

In Japan, HAV infection rates are very low and seroprevalence rates have been steadily declining [235, 250, 258]. Surveys from across the country report that the age at which more than half of the population has HAV antibodies was above 30 years [246, 256] and is increasing [236, 250]. The age-adjusted population seroprevalence rate in rural Okinawa fell from 83.9% in 1970 to 69.9% in 1980, 52.3% in 1988, and 39.7% in 1996 [236] (Fig. 5). Similar declines were found in other parts of Okinawa [247, 248].

Australia and New Zealand also have low rates of HAV. A nationwide survey in Australia in 1998 found that ~40% of Australians were seropositive, including 61% of those over 40 years of age [228]. This is lower than the rates reported in the 1950s up to the end of the 1980s [231, 240, 252]. In Kawerau, New Zealand, the rate in children aged 11–13 years

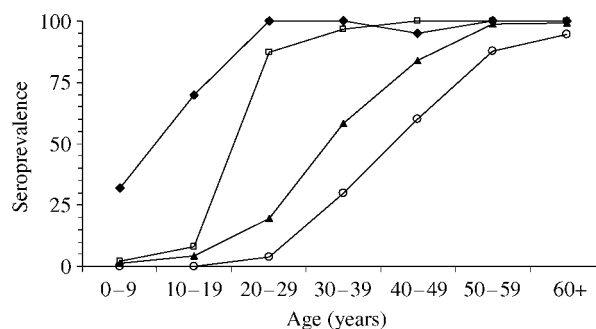


Fig. 5. Anti-HAV seroprevalence rates in Iriomote Island, Okinawa, Japan [236]. —◆—, 1970; —□—, 1980; —▲—, 1988; —○—, 1996.

dropped from nearly 30% to almost nil between 1984 and 1993 [254]. Less than 20% of persons under the age of 55 years in Christchurch, New Zealand, have anti-HAV [232]. This is lower than the rates reported in New Zealand in the 1980s [229, 254]. Most other islands in the South Pacific reported high rates in the 1970s [239, 262]. Little difference was found in anti-HAV in the Sepik district of Papua New Guinea between 1963 and 1972 [242], although rates may have dropped in the years since.

Summary of seroprevalence rates by age

Summary curves for seroprevalence rates for different endemicity zones were created by plotting seroprevalence rates by age (Fig. 6) and fitting logistic curves for each of three levels of endemicity. (Studies were selected for inclusion based on sample size.) Data from Europe and other regions with low seroprevalence rates (Australia, Canada, Singapore and Taiwan) were plotted to find a fit for low endemicity regions [j]. Data from Latin America, China, and parts of the Middle East (Saudi Arabia and Turkey) were used to fit curves for intermediate–high endemic regions [k]. Data from Africa, parts of the Middle East (Iran, Lebanon, Saudi Arabia, Syria), and parts of Asia (India, Indonesia, Nepal, Vietnam) were used to find a fit for very high endemicity regions [1]. The summary curves do not show the various age-immunity distributions that can result from cohort effects and from the population force of infection changing over time. For instance, they do not display the ripples produced by epidemic cycles, which are found in data from Europe and other low endemicity areas (Fig. 2).

The curves, however, do show clear trends for HAV infection. In areas with very high endemicity, 30–40%

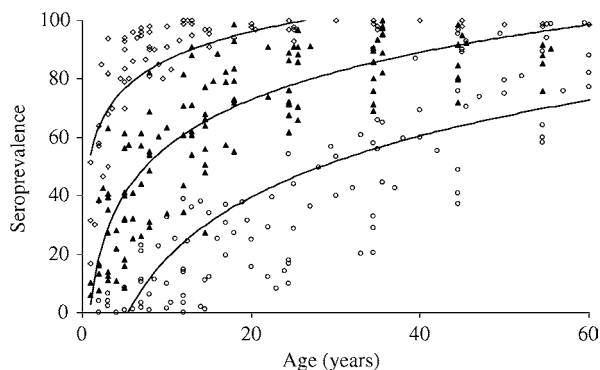


Fig. 6. Anti-HAV seroprevalence rates by endemicity level. ○, Low endemicity; ▲, high endemicity; ◇, very high endemicity.

or more of children acquire infection before 5 years of age and almost all persons have been infected by early adulthood. In areas with low endemicity, few children have anti-HAV, and many adults remain susceptible. Population immunity structure is important in predicting HAV transmission patterns. Epidemics are uncommon in highly endemic areas because most adults have acquired immunity. As areas move from high to intermediate endemicity, more adults remain susceptible to infection and hepatitis A infections may occur primarily as outbreaks [32].

WHY IS THE GLOBAL SEROPREVALENCE DECLINING?

This section will consider the evidence for the role of rising socioeconomic status, improvements in water resources, and the development of a vaccine in the decline of HAV seroprevalence rates globally.

Rising socioeconomic status

Studies from all regions of the world have consistently found an association between higher socioeconomic status and decreased HAV seroprevalence rates [m]. National age-adjusted seroprevalence rate and national median incomes [268] have a strong inverse relationship: as median income increases, population seroprevalence rates decrease.

In addition to household income and wealth, other markers of socioeconomic status are associated with HAV risk, including household educational level. Anti-HAV seroprevalence rates in children increase with lower levels of parental education [n]. Low personal levels of education are also often associated

with anti-HAV [o]. Within countries, seroprevalence rates may vary by ethnic origin [p]. As the socioeconomic status of immigrants and minority communities rises, the prevalence of HAV declines.

Rising socioeconomic status is also associated with decreased crowding. Larger family size and crowding are associated with increased risk of HAV [q].

Urban populations typically have lower rates of HAV infection than rural populations [r]. The lower rates in urban areas may be related both to improved socioeconomic status and to improved sources of drinking water. The higher levels of HAV seroprevalence in rural India have been shown to be strongly related to water supply differences [193]. In Saudi Arabia, the higher HAV rate in rural areas correlates with dependence on wells and tanker-delivered water, whereas urban Saudis have water pipes supplied by a central reservoir [91].

There is strong evidence that increasing socioeconomic levels, including improvements in household income, education, housing, and water supply, will lead to continued decreases in HAV incidence.

Improving water resources

Public health experts have long recognized the importance of the water supply in both the endemic [60, 81] and epidemic occurrence [33, 45, 134] of infectious hepatitis. Contributing risk factors for water-related HAV transmission include use of untreated water from contaminated wells and springs and inadequate or interrupted surface water-treatment processes [81].

Improved hygiene, sanitation, and drinking water quality and quantity are associated with decreased risk of HAV infection [s]. An analysis of the relationship of water and sanitation coverage [271] and age-adjusted seroprevalence rates found that seroprevalence rates decrease as access to improved water sources increases. In Taipei City, Taiwan, for example, municipal water coverage increased from 92% in 1976 to 99% in 1990. Rates of anti-HAV decreased over this time period, remaining at ~10% since 1985 [260]. In Korea, the waterworks supply rate increased from 33.2% in 1970 to 42% in 1974 and 82.9% in 1996. This improvement correlated with an increase in GNP from \$594 in 1975 to \$1647 in 1979 to \$10543 in 1996 and was associated with a significant decrease in anti-HAV levels [223].

Low-income households may have limited access to clean water sources, which increases risk of HAV. National water and sanitation coverage rates are

correlated with median incomes: low-income nations have poor water coverage [268, 271]. Water sources have unequal risk of contamination. In general, faecal coliform levels are significantly higher in unprotected water sources like rivers and streams than in protected water sources like protected springs and boreholes [25, 215]. Use of river water, spring water, or well water is associated with increased risk of HAV infection [156, 193, 198]. Furthermore, use of multiple water sources may increase the likelihood of exposure to contaminated water.

Access to a water tap inside the home or to clean bottled water is critical for reducing HAV infection risk [t]. In areas where water for drinking and domestic use is carried from the source to the home for storage until use, water quality can be affected by contamination at the source, contamination during collection, and contamination during storage [266]. Contamination during storage is associated with the type of water storage container, the location of the container (inside or outside), the use of a lid or other cover, the length of storage time, and boiling of drinking water [213, 215]. Water in containers may have significantly higher rates of HAV contamination than running water [213]. A study in Rio de Janeiro found that the absence of piped water in the home was the best predictor of HAV seroprevalence [85].

HAV contamination is a particular problem in areas with poor sanitary facilities. Contamination of basic water sources like wells and boreholes may result from only a few infectious persons washing or disposing of excreta in or near water sources. Use of a pit latrine or having no sanitary facilities is associated with higher anti-HAV compared to having a water toilet [u]. The measured levels of HAV in unprotected water sources vary with seasonal rain changes as waste is washed into water sources [v]. The presence of an open sewage channel near the house has also been associated with increased risk of HAV [27, 56].

Use of water for hygiene purposes, such as hand-washing, may reduce the spread of infectious agents via the faecal–oral route and other direct routes of transmission. A study in China found an increased risk of HAV with no hand-washing before food preparation and cooking, before eating, and after defecation [255]. A dirty kitchen (characterized by food particles on the floor, unwashed utensils, and/or the presence of flies, animals, or poultry) was also associated with increased risk [255]. In Uruguay, seroprevalence is associated with poor sanitary conditions [59]. A higher number of water taps in the home,

which could promote use of water for washing, is associated with decreased HAV risk [27].

Contamination of municipal water sources is usually due to a flaw in the water treatment system. An analysis of outbreaks of waterborne disease in the United States over a 35-year time-period classified the causes of waterborne outbreaks into five major categories: use of contaminated untreated surface water, use of contaminated untreated groundwater, inadequate or interrupted treatment, distribution network problems, or other. More than 80% of the outbreaks were associated with deficiencies in the treatment and distribution of water [54]. Outbreaks of hepatitis A attributable to water supply characteristics have been estimated to be less than 8% of the annual reported cases of hepatitis A in the United States [31], but in other parts of the world the rate may be much higher. In some Indian cities, seroprevalence rates have been found to be higher among users of municipal water supplies compared to those using a common tap or well [214]. This is probably due to a failure in the water treatment system. Exposure to contaminated water via these mechanisms is unequal based on socioeconomic status, geography, and other characteristics.

Studies of risk factors for HAV infection consistently find that improved water sources reduce HAV infection.

Availability of vaccine for risk groups

A number of risk groups have been associated with direct transmission of HAV from infected individuals to susceptible persons [267]. Children who are not toilet-trained or are in day-care, institutionalized persons, drug users, homosexual men, travellers to areas of high endemicity from areas with low HAV infection rates, and workers in certain occupations, including students and teachers, day-care workers, food industry and sanitation workers, and medical workers, are likely to have an increased number of the types of contacts that transmit HAV.

HAV incidence in populations with increased risk may be able to be reduced through vaccination, particularly in communities with generally low rates of hepatitis A. Recommendations for immunization programmes vary based on the population considered to be at risk [w]. Cost–benefit analysis shows that targeted vaccination is more economical than mass vaccination, particularly in areas with high anti-HAV prevalence [x].

Although cost barriers may limit access to immunization, an effective hepatitis A vaccine is available and may be useful in reducing infection among populations at increased risk.

CONCLUSION

Analysis of current and historical information about hepatitis A infection patterns and risk factors shows a strong association between socioeconomic improvements, increased water coverage, and decreasing HAV infection rates. However, the mechanisms behind the decrease in HAV incidence are not clear. A

key effect of the declining rate of HAV transmission in many parts of the world is that adults remain vulnerable in the event of an outbreak. Poor sanitation and contaminated water supplies usually produce infection in early childhood, which results in mild illness. In areas that have made a transition from endemic to epidemic HAV transmission patterns, susceptible adults who become infected may experience severe disease. Analysing water treatment and seroprevalence data using models of HAV transmission dynamics might clarify the role of water in the transmission of HAV and improve our ability to make decisions about preventive interventions.

APPENDIX. Single-letter text citations

Text	References
[a]	[28, 37, 44, 56, 64, 67, 74, 78]
[b]	[48, 53, 58, 62]
[c]	[93, 102, 110, 113, 114]
[d]	[90, 95, 97, 106, 109]
[e]	[115, 120, 128, 129, 138, 140, 157, 169]
[f]	[116, 150, 153, 154]
[g]	[130, 142, 161, 173]
[h]	[191, 192, 195, 202, 203, 214, 216, 217, 224]
[i]	[243, 245, 259, 260]
[j]	[65, 116, 119, 124, 125, 129, 139, 140, 157, 159, 169, 178, 179, 181, 182, 190, 231, 238, 261]
[k]	[27, 37, 42, 74, 80, 93, 102, 106, 112, 237]
[l]	[5, 20, 22, 24, 92, 95, 96, 103, 108, 191, 194, 200, 204, 206, 217, 222, 241]
[m]	[15, 20, 22, 28, 29, 36, 37, 42–44, 46, 50, 51, 55–57, 59, 64, 67, 68, 70, 73, 75, 79, 80, 83, 87, 88, 91, 99, 102, 104, 112, 114, 120, 124, 131, 143, 146, 148, 158, 168, 172, 193, 202, 203, 211, 223, 263]
[n]	[27, 28, 42, 52, 56, 69, 91, 114, 116, 146, 177, 178, 204, 211]
[o]	[41, 46, 55, 73, 79, 101, 120, 124, 162, 172, 179, 181, 255]
[p]	[10, 15, 18, 36, 38, 48, 77, 79, 99–101, 118, 231, 232, 254]
[q]	[27, 48, 56, 58, 69, 84, 85, 100–102, 116, 120, 140, 148, 158, 160, 162, 177, 178, 193]
[r]	[47, 53, 91, 104, 112, 136, 138, 146, 162, 209, 230, 244, 252, 253, 257, 261]
[s]	[22, 27, 34, 42, 47, 48, 55, 56, 59, 66, 68, 69, 78, 85, 91, 115, 145, 156, 193, 198, 213, 214, 255]
[t]	[34, 52, 55, 66, 148]
[u]	[22, 42, 47, 66, 255]
[v]	[17, 21, 82, 86]
[w]	[32, 35, 135, 187, 265, 270]
[x]	[40, 63, 71, 72, 163, 171, 225]

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