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Hepatitis A virus seroprevalence by age and world region, 1990 and 2005

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ABSTRACT

Objective: To estimate current age-specific rates of immunity to hepatitis A virus (HAV) in world regions by conducting a systematic review and meta-analysis of published data. The estimation of the global burden of hepatitis A and policies for public health control are dependent on an understanding of the changing epidemiology of this viral infection.
Methods: Age-specific IgG anti-HAV seroprevalence data from more than 500 published articles were pooled and used to fit estimated age-seroprevalence curves in 1990 and 2005 for each of 21 world regions (as defined by the Global Burden of Disease 2010 Study).
Findings: High-income regions (Western Europe, Australia, New Zealand, Canada, the United States, Japan, the Republic of Korea, and Singapore) have very low HAV endemicity levels and a high proportion of susceptible adults, low-income regions (sub-Saharan Africa and parts of South Asia) have high endemicity levels and almost no susceptible adolescents and adults, and most middle-income regions have a mix of intermediate and low endemicity levels.
Conclusion: Anti-HAV prevalence estimates in this analysis suggest that middle-income regions in Asia, Latin America, Eastern Europe, and the Middle East currently have an intermediate or low level of endemicity. The countries in these regions may have an increasing burden of disease from hepatitis A, and may benefit from new or expanded vaccination programs.

1. Introduction

Tens of millions of individuals worldwide are estimated to become infected with hepatitis A virus (HAV) each year [1]. HAV is transmitted primarily via ingestion of contaminated food or water or through direct contact with an infectious person. The incidence rate is strongly correlated with socioeconomic indicators and with access to safe drinking water: as incomes rise and access to clean water increases, the incidence of HAV decreases [2,3]. The HAV endemicity level for a population is defined by the results of age-seroprevalence surveys that measure the proportion of each age group that has acquired immunity to HAV, either through infection or immunization, as demonstrated by the presence of IgG anti-HAV antibodies in serum [4]. Immunization has been available since the early 1990s but is not yet widely used [5,6], so most individuals with anti-HAV antibodies acquired immunity through infection.

The severity of HAV infection in infected individuals is strongly related to age. While young children often have asymptomatic HAV infection, older children and adults often experience symptomatic disease. A typical symptomatic presentation includes a week of gastrointestinal and flulike symptoms, followed by several weeks of jaundice, and then a convalescent period that lasts for several weeks [7]. Although rare, infection can also cause acute liver failure and death, and this risk increases with age [8].

The burden of HAV infection on communities and nations is highly linked to the average age at infection. In high endemicity countries, nearly all children become infected at an early age, when asymptomatic infection is likely. As the incidence decreases, the average age at infection gradually increases. In low endemicity countries, the incidence rate is very low and few individuals become infected in childhood, so most children and many adults remain susceptible to infection. Because the risk of developing symptomatic HAV infection increases with age, as a country or subpopulation experiences an epidemiological transition to a lower endemicity, those who are infected are at an increased risk of symptomatic HAV infection, including acute liver failure and death. Thus, a decrease in population incidence often creates an increase in costs per case of HAV infection, and at times an increase in total public health costs related to hepatitis A. For example, each case during an outbreak in a low endemicity country will lead to total costs of several thousand U.S. dollars for treatment and for containment activities such as prophylactic vaccination [9]. The direct costs of medical care and the indirect costs of lost productivity due to several weeks of hospitalization and several months of missed

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Table 1
Regional prevalence estimates, 2005.

	Region (GBD region)	Concordant WHO region(s)	Largest countries by 2005 population[a]	Estimated level of endemicity[b]	Evidentiary support[c]
1	High-income Asia Pacific	Western Pacific	Japan, Republic of Korea, Singapore	Very low	Extensive
2	Central Asia	Europe	Uzbekistan, Kazakhstan, Azerbaijan	Intermediate	Very limited
3	East Asia	Western Pacific	China	Low	Extensive
4	South Asia	Southeast Asia/Eastern Mediterranean	India, Pakistan, Bangladesh	High	Extensive
5	Southeast Asia	Southeast Asia/Western Pacific	Indonesia, Philippines, Vietnam	Low	Somewhat limited
6	Australasia	Western Pacific	Australia, New Zealand	Very low	Moderate
7	Caribbean	Americas	Cuba, Dominican Republic, Haiti	Low	Very limited
8	Central Europe	Europe	Poland, Romania	Low	Somewhat limited
9	Eastern Europe	Europe	Russia, Ukraine, Belarus	Low	Somewhat limited
10	Western Europe	Europe	Germany, France, United Kingdom	Very low	Extensive
11	Andean Latin America	Americas	Peru, Ecuador, Bolivia	Intermediate	Somewhat limited
12	Central Latin America	Americas	Mexico, Colombia, Venezuela	Intermediate	Limited
13	Southern Latin America	Americas	Argentina, Chile, Uruguay	Intermediate	Moderate
14	Tropical Latin America	Americas	Brazil, Paraguay	Intermediate	Extensive
15	North Africa/Middle East	Eastern Mediterranean	Egypt, Iran, Turkey	Intermediate	Moderate
16	High-income North America	Americas	United States, Canada	Very low	Extensive
17	Oceania	Western Pacific	Papua New Guinea, Fiji, Solomon Islands	Intermediate	Very limited
18	Central sub-Saharan Africa	Africa	Democratic Republic of the Congo, Angola	High	Very limited
19	East sub-Saharan Africa	Africa	Ethiopia, Tanzania, Sudan	High	Very limited
20	South sub-Saharan Africa	Africa	South Africa, Zimbabwe, Namibia	High	Limited
21	West sub-Saharan Africa	Africa	Nigeria, Ghana, Côte d'Ivoire	High	Very limited

[a] Population data from UNFPA's State of World Population 2005.
[b] High: ≥90% have immunity by age 10; intermediate: ≥50% have immunity by age 15; low: ≥50% have immunity by age 30; very low: <50% have immunity by age 30.
[c] Extensive: ≥5 articles per country in the region published in or after 1980; moderate: ≥3 but <5 articles per country in the region; somewhat limited: ≥2 but <3 articles per country in the region; limited: ≥1 but <2 articles per country in the region; very limited: <1 article per country in the region.

work or school can make HAV infection costly for affected individuals and their families. At the societal level, hepatitis A outbreaks can have significant economic impacts through disrupted trade and tourism.

Knowledge of current age-specific anti-HAV seroprevalence rates in each country and world region is important in order to establish public health priorities and to adopt appropriate vaccination policies. In high endemicity countries, vaccination is not recommended because nearly every young child will acquire immunity very early in life following asymptomatic infection [10]. In intermediate endemicity countries, universal childhood vaccination may be appropriate in order to protect the health of adolescents and young adults, although cost can be a significant barrier when allocating limited public health resources [10]. In low endemicity countries, targeted vaccination of high-risk population groups is usually recommended rather than universal vaccination [10].

This systematic review followed the guidelines set forth in the operations manual of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD Study), which divides the world into 21 regions based on geography and epidemiological profiles [11]. The objective of this study was to estimate the age-specific anti-HAV seroprevalence rate in each of 21 world regions in 1990 and in 2005 by conducting a meta-analysis of the data from more than 500 published articles. These data will be useful for modeling the estimated burden of disease due to HAV infections. The results are also helpful for identifying the world regions that now have an intermediate endemicity profile and may be candidates for childhood hepatitis A vaccine programs.

2. Methods

2.1. Systematic review

A systematic review was used to identify all original research articles on anti-HAV seroprevalence published in or after 1980 that were reasonably representative of the general population rather than a special high-risk group or patients with acute or chronic liver disease. Review articles, outbreak investigations, animal studies, environmental studies, and genetic and other laboratory-based studies were excluded. In total, 637 eligible articles in 17 languages from more than 125 countries and territories were determined to meet the eligibility criteria. A full report on the studies identified by the systematic review, which includes a summary of each article, has been published elsewhere [12]. Information about age-specific seroprevalence in the study population was extracted from each of these eligible studies. For this paper, the extracted age-seroprevalence data were grouped by study year and world region, and the pooled data were used to fit estimated age-seroprevalence-curves for each world region in 1990 and 2005.

2.2. Data for the 1990 and 2005 models

Data collected between 1995 and 2008 (or, if the study year was not listed in the article, published between 1996 and 2009) were used to fit the estimated age-seroprevalence curves for 2005. Data collected between 1985 and 1994 (or, if the study year was not provided, published between 1986 and 1995) were used to fit the estimated age-seroprevalence curves for 1990. In a few instances, there were fewer than eight age-seroprevalence data points from studies published during the stipulated time frame, so additional information was required for curve fitting. Consequently, articles published between 1980 and 1985 were used to fit the 1990 estimates for Central Asia, Australasia, and Oceania. One additional article from outside the set time frame for the systematic review was used to fit the 2005 estimates for Oceania [13]. There were no articles published after 1995 for Central, Southern, and West sub-Saharan Africa, so these three regions were assumed to have experienced no change in seroprevalence since 1990. Table 1 summarizes the evidentiary support available for each region. Reference information and study details for all of the articles used for fitting models can be obtained from the report on the systematic review [12].

2.3. Curve fitting

All eligible studies that reported seroprevalence rates for two or more age groups were included in the analysis. The median of each age group, or the mid-point if a median was not reported, was plot-