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Incidence of Hepatitis A in Argentina after vaccination

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SUMMARY. In Argentina, the annual incidence rate of reported hepatitis A disease ranged from 70.5 to 173.8 per 100 000 during 1995–2004. A single dose universal hepatitis A immunization program aimed at children aged 12 months was started in June 2005. The aim was to observe the impact of universal vaccination against hepatitis A in Argentina. A longitudinal analysis of hepatitis A rates reported in Argentina since 1995 to the National Notifiable Diseases Surveillance System (SINAVE). Incidence rates in 2007 were compared with those for the prevaccination baseline period (1998–2002), overall and by age group and geographical regions. Overall vaccine coverage in Argentina was 95% in 2006 for the single dose. After initiating the program, a sharp decrease in disease rates was observed. The annual incidence of 10.2 per 100 000 during 2007 represents 88.0% reduction with respect to the average incidence rate for the period 1998–2002 ($P < 0.001$). For children aged 1 year, an 83.1% reduction in disease was observed in 2007, compared with the baseline period ($P < 0.001$). Furthermore, a sharp decline was also observed in all other age groups 87.1% [2–4 years], 88.7% [5–9 years], 83.6% [10–14 years], 78.8% [15–49 years], 20.7% [>50 years]. Also important reductions were observed in all Argentinian regions. Following the implementation of universal hepatitis vaccination with a single dose to children at 12 months of age, hepatitis A rates have declined substantially in Argentina. Monitoring is needed to verify that vaccination continues to proceed and that low rates are sustained.

Keywords: Argentina, hepatitis A, incidence rates, single dose, vaccination.

INTRODUCTION

Hepatitis A is one of the most common viral infections worldwide. Hepatitis A is typically transmitted via the faecal-oral route, generally through close personal contact or through contaminated food or water. Low income, low educational level, crowding and lack of access to safe drinking water and sanitary facilities are associated with increased hepatitis A virus (HAV) infection.

As socio-economic status and access to safe drinking water are increasing, the HAV infection rate is declining in most parts of the world [1–3]. However, because HAV infection in children is often asymptomatic but most infected adults present with jaundice and other potentially severe symptoms, this decrease in the infection rate has a paradoxical effect. As socio-economic conditions improve, individuals become infected at a later age when disease is more severe. Thus, hepatitis A morbidity may increase as the incidence rate of infection decreases [3,4].

Abbreviations: ALF, acute liver failure; HAV, hepatitis A virus; SINAVE, National Notifiable Diseases Surveillance System.

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Argentina is considered a country with intermediate HAV endemicity [2,5,6] and the disease is an important public health problem, being a leading cause of acute liver failure (ALF) and liver transplants in children [7–9]. A universal single-dose hepatitis A immunization program aimed at children aged 12 months was started in June 2005. This study aimed to assess the impact of the current vaccination strategy by evaluating changes in reported cases of hepatitis A since its implementation.

MATERIAL AND METHODS

The cases and incidence rates per 100 000 population of hepatitis A by age, province and year were obtained from the National Surveillance System (SINAVE), Ministry of Health. SINAVE is a passive national surveillance system through which provinces voluntarily report nationally notifiable diseases. Hepatitis A is reportable by law to the relevant public health authority in all provinces. Case reports are submitted weekly to SINAVE by province health departments. Hepatitis A has been a nationally notifiable disease since 1960 but surveillance system has been reinforced since 1993. Since then, hepatitis has been reported in the categories: 'A', 'B', others and unspecified. A reportable case is defined as an acute illness with discrete onset of symptoms and jaundice and/or elevated serum aminotransferase levels

in a person who tests positive for IgM antibody to HAV or who is a contact of a laboratory-confirmed case.

Data were arrayed by age group and by five geographical regions. The categories were defined as follows:

1 Groups of age: <1, 1, 2–4, 5–9, 10–14, 15–49, >50 years.
2 Regions: Northeast (NEA), including Chaco, Corrientes, Formosa and Misiones provinces; Central (Centro), including Buenos Aires City, Buenos Aires Province, Córdoba, Entre Ríos and Santa Fe provinces; South (SUR), including Chubut, La Pampa, Neuquén, Río Negro, Santa Cruz and Tierra del Fuego provinces; Cuyo, including La Rioja, Mendoza, San Juan and San Luis provinces and Northwest (NOA), including Catamarca, Jujuy, Salta, Santiago del Estero and Tucumán provinces.

Unspecified hepatitis cases were assumed to have hepatitis A rather than another form of hepatitis. In the analysis by age groups, cases with unspecified age were excluded. Overall incidence hepatitis A rates in 2007 were compared with mean incidences rates during the prevaccination pre-outbreak baseline period (1998–2002). Similar comparisons were made by age groups and geographical regions.

Incidence rates in 2007 were compared with appropriate baseline incidence rates by calculating a normal z statistic using Epidat v3 (Xunta de Galicia, Spain and PAHO/WHO). A P-value <0.001 was chosen for assessing the statistical significance of these changes, because as a result of large denominators in these comparisons, even small differences in rates were statistically different at the most typically used cutoff of $P = 0.01$. We chose to use a more conservative definition of statistical significance to better highlight differences of potential public health importance.

RESULTS

Argentinean government has used different hepatitis A vaccines since vaccination program began. The average country vaccine coverage was 95.0% in 2006, eight provinces presented coverage 95% and more, seven provinces 90–94% and eight provinces 60–89%. In Argentina, approximately 95% of all the routine immunizations in children are given gratuitously in public health centres.

In the 10 years preceding the immunization program (1995–2004), the yearly reported incidence of unspecified and hepatitis A rates in Argentina ranged from 70.5 to 173.8 per 100 000 inhabitants (Fig. 1). The most affected age group was 5 to 9 years old. During 2003–2004, an important outbreak of hepatitis A occurred, with an average incidence rate of 155.5 per 100 000. From 1998 through 2002 (the pre-outbreak, pre-immunization baseline period), the mean incidence of reported hepatitis A disease was 85.5 per 100 000 (95% CI: 66.7–104.3).

Relative to the average rate during the baseline period (1998–2002), the rate in 2007 represented an 88.0% decline overall, with significant declines in all age groups (Table 1). By 2007, rates among children aged less than 1 year has declined by 81.2%, 1 year by 83.1%, 2–4 years by 87.1%, 5–9 years by 88.7%, and those among children aged 10–14 years by 83.6%. Although rates among persons 15 to 49 years of age also declined significantly by 78.8%, the percent reduction among children was greater than for adults. There was no significant difference in the group >50 years old (20.7% reduction). In the five vaccinating regions, incidence rates in 2007 were 5.9 (NEA), 7.8 (Centro), 9.7 (SUR), 18.9 (Cuyo) and 22.0 (NEA) per 100 000 inhabitants. Baseline rates were 6 to 14 times higher than in 2007, all the reductions were statistically significant. (Table 1).

DISCUSSION AND CONCLUSIONS

Universal hepatitis vaccination with a single dose at 12 months of age was implemented in Argentina in 2005 [10]. Argentina's Ministry of Health decided to monitor the impact and follow up the strategy to decide or recommend a second dose. This report describes the important decline observed in hepatitis A incidence rates in 2007. The 2007 rate was the lowest recorded rate in 12 years of surveillance. This decrease coincided with the implementation of recommendations for routine hepatitis A vaccination, but the

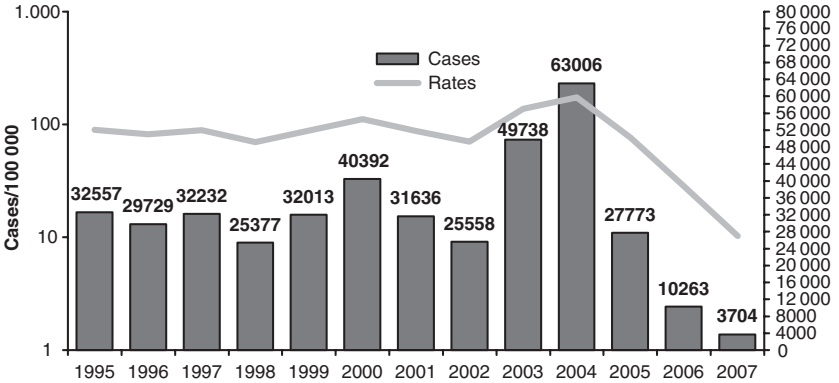

Fig. 1 Reported rates and cases of Hepatitis A, Argentina, 1995–2007.

Table 1 Hepatitis A incidence overall and by age groups and by geographical regions, 1998–2002 and 2007*

	Baseline (1998–2002)	2007	% Decline	*P*-value
Overall	85.5	10.2	88.0	<0.0001
Age (years)				
<1	32.2	6.1	81.2	0.0001
1	67.9	11.5	83.1	<0.0001
2–4	201.3	26.1	87.1	<0.0001
5–9	248.8	28.2	88.7	<0.0001
10–14	108.6	17.9	83.6	<0.0001
15–49	20.6	4.4	78.8	0.009
50 +	5.9	4.7	20.7	>0.05
Regions				
Centro	69.4	7.8	88.8	<0.0001
Cuyo	137.0	18.9	86.2	<0.0001
NEA (Northeast)	69.3	5.9	91.5	<0.0001
NOA (Northwest)	132.0	22.0	83.4	<0.0001
SUR (South)	132.4	9.7	92.7	<0.0001

*Incidence rates for baseline period and 2007 are per 100 000 inhabitants.

causation cannot be guaranteed because the observed decline could be partially attributable to the immunization caused by 2003–2004 outbreak.

While available data do not allow for quantifying the relative contribution of vaccination and temporal trends to the observed declines in incidence, it is important to consider that these declines since 2005 have been unprecedented in magnitude and have been observed in all age groups and regions, showing marked herd immunity effect. More importantly substantial diminutions in ALF due to hepatitis A have been observed since 2005. Comparing 2007 to 2005, there was a 95% reduction in ALF related to hepatitis A and since July 2006 only a few cases were observed [11].

Several mass vaccination programs in different countries such as the United States, Israel, Puglia region in Italy, Catalonia in Spain and North Queensland in Australia have resulted in rapid reduction in disease incidence, and low incidence levels have been maintained among vaccine recipients as well as across other age groups [12–16].

In Israel, since the introduction of vaccination program, the mean incidence rate of Hepatitis A disease decreased from 50.4 per 100 000 (1993–1998) to 2.2 to 2.5 per 100 000 inhabitants (2002–2004) representing more than 95% reduction [13]. Important changes in hepatitis A incidences have been observed in the United States, specially in states where hepatitis A vaccination has been recommended (88% reduction from 1999 to 2003), even with modest levels of vaccination coverage [12]. Reductions observed in Argentina are similar to reductions observed in these countries. Monitoring is needed to verify that vaccination continues to proceed and that low rates are sustained.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

REFERENCES

1 Jacobsen KH, Koopman JS. Changing hepatitis A seroprevalence: a global review and analysis. *Epidemiol Infect* 2004; 133: 1005–1022.
2 Tanaka Jorge. Hepatitis A shifting epidemiology in Latin America. *Vaccine*. 2000; 18: S27–S60.
3 Jacobsen KH, Koopman JS. The effects of socioeconomic development on worldwide hepatitis A virus seroprevalence patterns. *Int J Epidemiol* 2005; 34(3): 600–609.
4 Van Damme P, Van Herck K. Effect of Hepatitis A vaccination programs. *JAMA* 2005; 294: 246–248.
5 González J, Fay O, Cañero-Velasco MC *et al.* Infección por virus de hepatitis A en niños en Argentina. *Acta Gastroent Latinoam* 1997; 27: 331–334.
6 Tapia-Conyer R, Santos IJ, Cavalcanti AM *et al.* Hepatitis A in Latin America: a changing epidemiologic pattern. *Am J Trop Med Hyg* 1999; 61: 825–829.
7 Ciocca M, Ramonet M, Cuarterolo M, López S, Cernadas C, Alvarez F. Prognostic factors in pediatric acute liver failure. *Arch Dis Child* 2008; 93: 48–51.
8 Ciocca M, Moreira-Silva SF, Alegría S *et al.* Hepatitis A as an etiologic agent of acute liver failure in Latin America. *Pediatr Infect Dis J* 2007; 26(8): 711–715.
9 Centeno MA, Bes DF, Sasbon JS. Mortality risk factors of a pediatric population with fulminant hepatic failure undergoing orthotopic liver transplantation in a pediatric intensive care unit. *Pediatr Crit Care Med* 2002; 3(3): 227–233.
10 Ministerio de Salud y Ambiente, Argentina. Resolución 653/05, 113(30677). Buenos Aires, Argentina: Boletín Oficial de la República Argentina, 2005. p.3.
11 Cervio G, Trentadue J, Dagostino D, Luque C, Armoni J, Debbag R. Impact of Hepatitis A as universal vaccination on the incidence of fulminant hepatic failure in four Liver Transplant Centers in Argentina. Global Hepatitis A Meeting, Miami, December 2007. Abstract Book, p. 153. Available at http://www.havmeeting.info/index.php?S-prog (Last accessed 8 July 2008).
12 Wasley A, Samandari T, Bell BP. Incidence of hepatitis A in the United States in the era of vaccination. *JAMA* 2005; 294: 194–201.

13 Dagan R, Leventhal A, Anis E, Slater P, Ashur Y, Shouval D. Incidence of hepatitis A in Israel following universal immunization of toddlers. *JAMA* 2005; 294: 202–210.
14 Lopalco PL, Salleras L, Barbuti S *et al.* Hepatitis A and B in children and adolescents: what can we learn from Puglia (Italy) and Catalonia (Spain)? *Vaccine* 2001; 19: 470–474.
15 Dominguez A, Salleras L, Carmona G, Batalla J. Effectiveness of a mass hepatitis A vaccination program in pre-adolescents. *Vaccine* 2003; 21: 698–701.
16 MacIntyre CR, Burgess MA, Hull B, McIntyre P. Hepatitis A vaccination options for Australia: review article. *J Paediatr Child Health* 2003; 39: 83–87.

