

# SINGLE-DOSE UNIVERSAL HEPATITIS A IMMUNIZATION IN ONE YEAR OLD INFANTS IN ARGENTINA: HIGH PREVALENCE OF PROTECTIVE ANTIBODIES UP TO 11 YEARS FOLLOWING VACCINATION

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## Abstract

## Objective

To estimate the persistence of antibodies response following at least 9 years after single dose HAV vaccination

## Methods

- **Study design:** cross sectional study. May 2015-April 2016 period.
- **Setting:** Hospital de Niños de San Justo, Buenos Aires; Hospital de Niños Orlando Alassia, Santa Fe, Hospital del Niño Jesús and Clinics from the public subsystem in Tucumán city (Central and Northwest region of Argentina).
- **Inclusion Criteria:** immunocompetent children that have received a single dose HAV vaccine at 12 ± 1 months at least 9 years before.
- **Exclusion Criteria:** Past history of Hepatitis A; 2 doses of vaccine; <9 years from vaccination, primary or secondary immunodeficiency.
- **Blood samples:** Seropositivity defined as antibody titers ≥ 10mIU/mL (ELISA) Dia.Pro AVAB.CE (Italy).
- **Demographic and social data assessed through a questionnaire.**
- **Statistical analysis:** Logistic regression analysis used to evaluate association between demographic and social variables and seropositivity. EpiInfo 7 program used (CDC, Atlanta, GA, USA).

## Results

Population characteristics	N=1119	
Province of residence; n (%)		
Buenos Aires	355	31,7%
Tucumán	380	34,0%
Santa Fe	384	34,3%
Gender female; n (%)	541	48,3%
Age (years); Mean (95%CI)	10,76	(10.73-10.78)
<b>Median time after vaccination (Years) (range)</b>	<b>9.7</b>	<b>(9.0-11.3)</b>
Mean people per room (95%CI)	2.37	(2.31-2.43)
Overcrowding; n (%)	163	14,6%
Access to tap water; n (%)	1037	92,7%
Sewers; n (%)	646	57,8%
Urban residence; n (%)	1057	97,0%
School attending; n (%)	1116	99,7%
Mother's educational level; n (%)		
Primary/Incomplete secondary	694	62,1%
Complete secondary	299	26,8%
Tertiary/University	124	11,1%

Table 1. Demographic and general characteristics of studied population

Of 1119 samples, 980 (87.6%) had anti-HAV IgG ≥ 10 mIU/mL (Figure 3). Anti-HAV GMC was 28.0 mIU/mL (95% CI: 26.8-29.3 mIU/mL). Reverse cumulative distribution of anti-HAV antibody levels (mIU/mL) is shown in Figure 4.

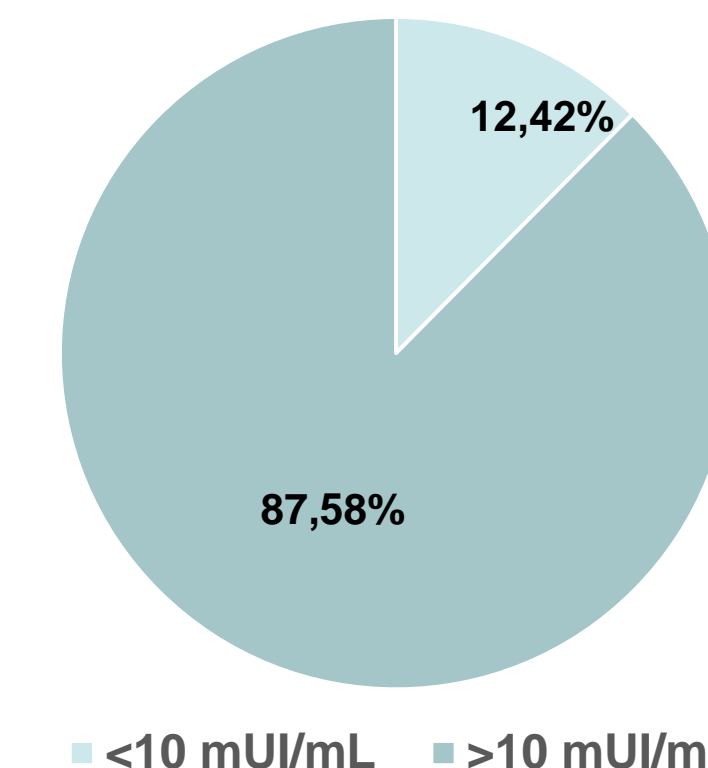


Figure 3. Prevalence of protective anti-HAV Ab

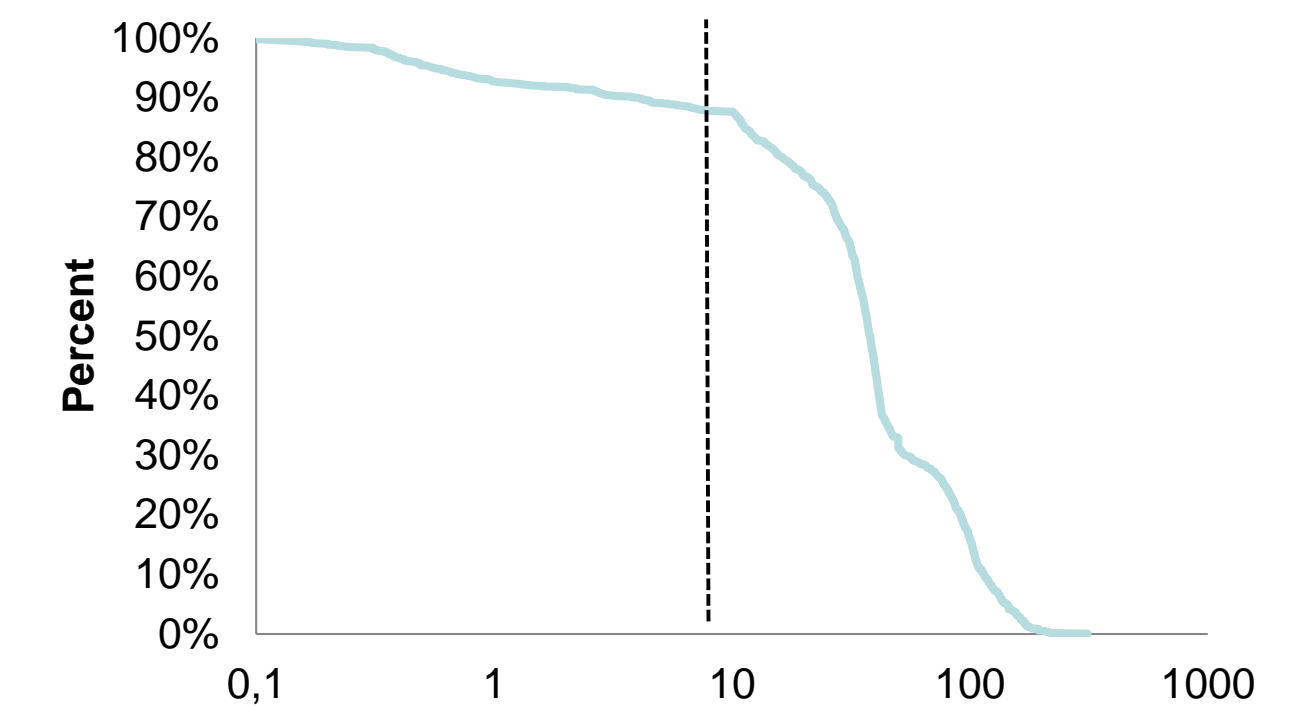


Figure 4. Anti-HAV antibody levels (mIU/mL) in base 10 log scale

Variable	Positive samples n/N=981/1119		Negative samples n/N= 138/1119		OR	CI 95%	p
	n/N	%	n/N	%			
Santa Fe	353/384	91.9%	31/384	8.1%	1.94	1.27-2.95	0.002
Tucumán	339/380	89.2%	41/380	10.8%	1.25	0.85-1.84	0.3
Buenos Aires	289/355	81.4%	66/355	18.6%	0.45	0.32-0.65	<0.0001
Male gender	509	51.9%	69	50.0%	0.93	0.65-1.32	0.74
Access to tap water	911	92.9%	126	91.3%	1.24	0.65-2.35	0.51
Sewers	565	57.6%	81	59.1%	0.94	0.65-1.35	0.8

Variable	Positive samples		Negative samples		p
	Mean	IC95%	Mean	IC95%	
Age (years)	10.74	10.71-10.77	10.85	10.75-10.94	<0.05
Time post-vaccination (y)	9.70	9.68-9.73	9.82	9.72-9.90	<0.05
People per room	2.38	2.31-2.45	2.32	2.14-2.50	NS

Table 2. Univariate analysis. Demographic and social variables correlation with seroprotection

In the univariate analysis, lack of seroprotection was associated to a longer post-vaccination time. Also, higher seroprotection rates were observed in Santa Fe and lower rates resulted in San Justo, Buenos Aires compared to the global rate (91.9% vs 87.6% OR 1.94 (95%CI 1.27-2.95); p=0.002 and 81.4% vs 87.6% OR 0.45 (95%CI 0.32-0.65); p <0.001, respectively) (Table 2). These differences couldn't be explained by socio-economic or other demographic reasons in logistic regression analysis.

## Conclusions

A decrease in protective HAV-Ab is expected over time. However, this long term seroprevalence assessment resulted in good immunologic protection up to 11 years post-vaccination in Argentina. These findings, are aligned with the low current disease burden and confirm the success of the intervention. Studies aiming to assess cellular immune memory response in vaccinated individuals who lost Ab protection would be of importance to determine the need of a booster dose in the future.

**Background:** Single-dose Hepatitis A Virus (HAV) vaccination was implemented for all Argentinean children aged 12 months in 2005, instead of the standard two-dose schedule. Previous studies demonstrated a dramatic decline in HAV infection rates, fulminant hepatitis, and liver transplantation along with low viral circulation and high prevalence of protective antibody response 6 years following the intervention. This study assessed long term seroprotection against HAV after vaccination with this novel scheme.

**Methods:** Children who received one dose of HAV vaccine at 1 year of age, at least nine years before enrollment, were included at three centers in Argentina between May-2015 and April-2016. Demographic and socio-economic characteristics of the child, mother and house were collected through a questionnaire after informed consent signature. Blood samples were tested for anti-HAV antibodies. Antibody titers ≥10 mIU/mL were considered seroprotective. Logistic regression analysis was done to evaluate associations between different variables and seroprotection.

**Results:** Of 1119 children included, 97.0% lived in urban areas, 92.7% had safe water access and 57.8% had sewers at home. Mean age was 10.7 years, and the mean post-vaccination interval was 9.7 years (Range 9.0-11.3 y). Of the total, 87.6% had protective antibodies against HAV. Higher seroprotection rates were observed in Santa Fe compared to the global rate (91.9% vs 87.6% OR 1.94 (95%CI 1.27-2.95); p=0.002). In contrast, lowest rates resulted in San Justo, Buenos Aires (81.4% vs 87.6% OR 0.45 (95%CI 0.32-0.65); p <0.001). No association between socio-economic variables and seroprotection was found. Geometric mean concentration (GMC) of HAV Ab titers was 28.0 mIU/mL (95% CI: 26.8-29.3 mIU/mL)

**Conclusion:** Single-dose universal hepatitis A immunization in infants resulted in sustained immunologic protection up to 11 years in Argentina. Lower seroprevalence rates in San Justo have no clear reason and are not associated with an increase in HAV cases in that area. These findings, along with the low current disease burden confirm the success of the intervention.

## Background

Single dose hepatitis A vaccination was implemented in 2005 for all children at 12 months in Argentina. Afterwards, there was a sharp decrease in hepatitis A cases and rates, acute liver failure and liver transplantation that persists currently (Figure 1 and 2).

In 2012 SAGE endorsed this strategy to which several countries of the region adhered.

Previous immunogenicity assessments in different cohorts showed a 93% and 97% prevalence of protective antibodies (Ab), 4 and 6 years following vaccination, respectively. This study assessed long term seroprotection against HAV after vaccination with this novel scheme.

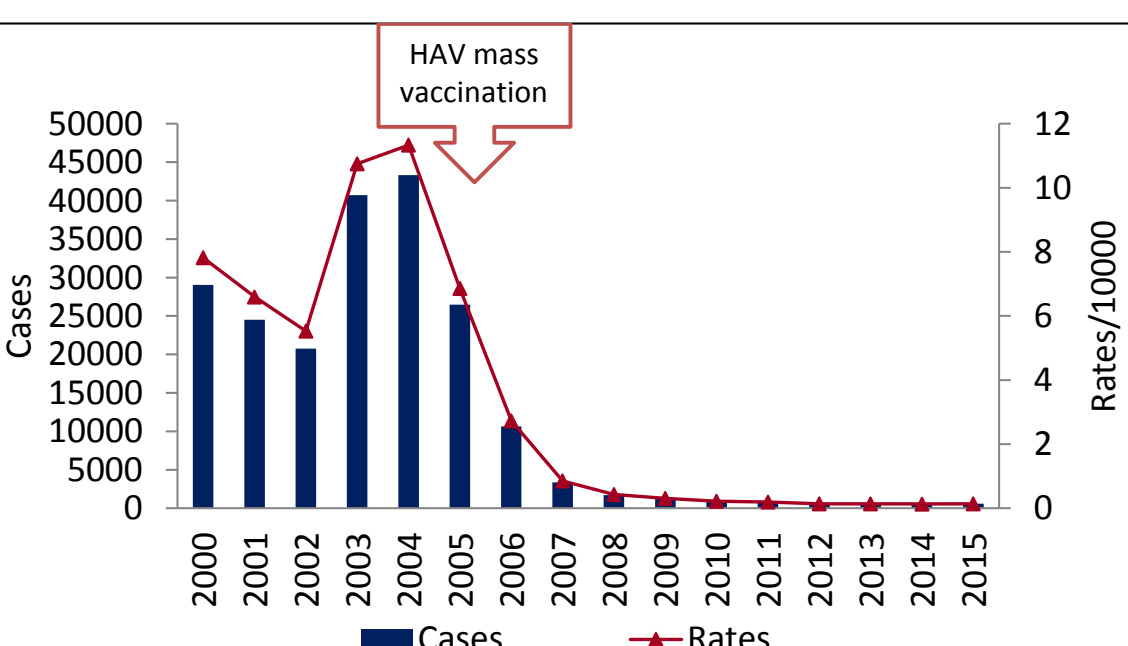


Figure 1. Hepatitis A cases and rates.

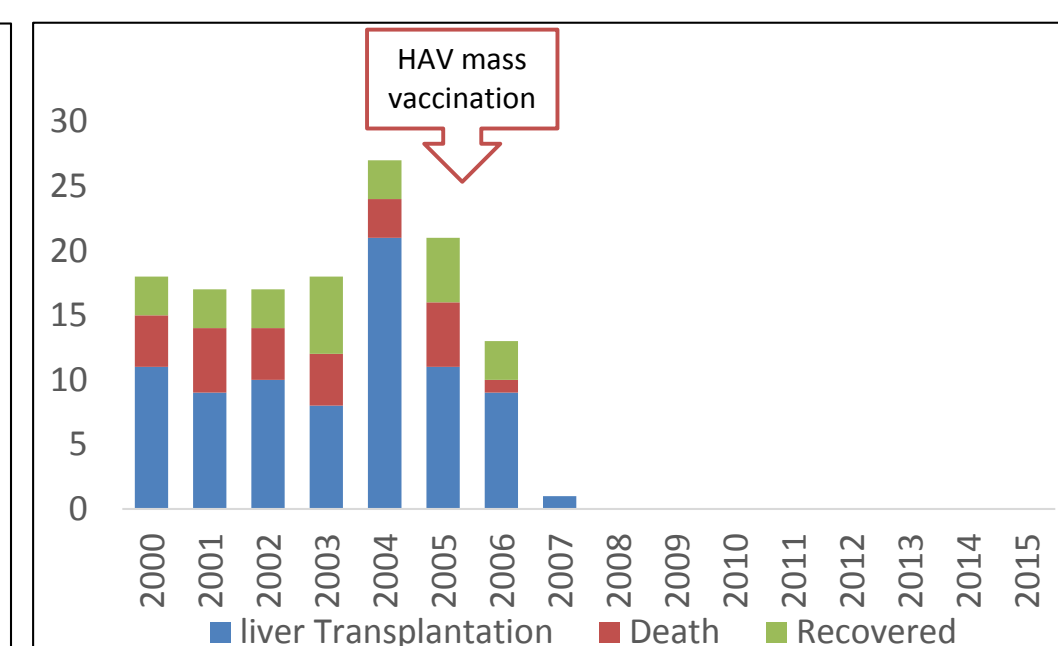


Figure 2. HAV associated Fulminant Hepatic Failure Cases