Impact of a Single Dose Immunization Strategy against Hepatitis A in Argentina.

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Geographical distribution of Hepatitis A Virus Infection

Anti-HAV Prevalence
- High
- High/Intermediate
- Intermediate
- Low
- Very Low
Access to drinking water (% of population) 2001

Población (% por partido/departamento):
- 0% a < de 10%
- 10% a < de 20%
- 20% a < de 30%
- 30% a < de 40%
- 40% a < de 50%
- 50% a < de 60%
- 60% a < de 70%
- 70% a < de 80%
- 80% a < de 90%
- 90% a < de 100%

Access to Sanitation (% of population) 2001

Safe water 77 %   Area: 2,736,690 sq km   Sewage 42.5 %
Population: 39,000,000 (mostly urban)
Birth cohort: 700,000
Urban population: 89.4 %
National Health Surveillance System

Modular System (since 2001)

Medical consultations + Cards

Early Alert

Sentinel

Sentinel Units
- Hepatitis
- Diarrheas
- Febrile Illness
- Nosocomial Infections

Immunizables

Vaccines

TBC

Lab Surveillance System

Specific Networks
Provinces Networks

Laboratories

Specialized

Programs

Meningoencephalitis

STD

HUS

Pneumonies

Injuries

Meningoencephalitis

Immunizables

Vaccines

TBC

P & C of VH in LA & B
Brasilia 19-21 March 2014
SENTINEL UNITS (SU)
for VIRAL HEPATITIS
& population density
(27 SU in 18/24 Provinces)

1 dot = 100 inhab / km²

*Common working protocol
  - Guidelines consensus
  - Web resident specific software

*External Quality Control for Serology
  - Biannual Panel for HBV & HCV

*Fluent communication
  - Monthly newsletter (electronic)
    “El Mangrullo”
  - Annual meetings (n:22)(since 1992)
HAV infection in Argentina

anti-HAV prevalence in children from Argentina (under 10 years old) \( n = 3167 \)

*Acta Gastr Latin 27 (1997)*

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Prevalence of hepatitis viruses in an anti-human immunodeficiency virus-positive population from Argentina. A multicentre study


\( n = 484 \)

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**Survival rates**

1. HTAL POSADAS: 27.1%
2. HTAL MUÑIZ: 41.7%
3. HTAL FERNANDEZ: 31.2%

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**Survival rates**

1. HAV: 84%
2. HBV: 58.5%
3. HCV: 68.5%
4. HIV: 1.9%
5. HHV: 6.6%

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**Survival rates**

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antiHAV prevalence in children from Argentina
(under 10 years old) n = 3167

Acta Gastr Latin 27 (1997)
Hepatitis notification in Argentina 1995-2004

Due to: HAV Unspecified HBV HCV Other

Source: Epidemiological Surveillance National System SINAVE

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<table>
<thead>
<tr>
<th>Region</th>
<th>2003</th>
<th>2004</th>
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<tbody>
<tr>
<td>NorthEast</td>
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<tr>
<td>Center</td>
<td>173.8</td>
<td>192</td>
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<tr>
<td>South</td>
<td>246</td>
<td></td>
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<tr>
<td>Total Country</td>
<td>173.8</td>
<td>192</td>
</tr>
</tbody>
</table>

Notification Rates/100,000
Hepatitis A & unspecified: age groups 2003 - 2004

Source: Epidemiological Surveillance National System SINAVE
Etiology of Fulminant Hepatic Failure in Argentina


<table>
<thead>
<tr>
<th>Etiology</th>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indeterminate</td>
<td>29.1%</td>
<td>30.1%</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>19.4%</td>
<td>5%</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>14.6%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Drug Induced</td>
<td>12.1%</td>
<td>0.5%</td>
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<tr>
<td>Hepatitis A</td>
<td>11.2%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>3.4%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Toxic</td>
<td>2.4%</td>
<td></td>
</tr>
<tr>
<td>Wilson disease</td>
<td>2.4%</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>5.4%</td>
<td></td>
</tr>
</tbody>
</table>

206 Adults, 219 children

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CAUSES of LIVER TRASPLANT in CHILDREN at NATIONAL PEDIATRIC HOSPITAL (Hospital Garrahan)

- Fulminant hepatic failure: 9%
- Biliary atresia: 3%
- Cirrhosis: 26%
- Chronic Cholestasis: 27%
- Others: 3%
- HAV infection: 35%
- Autoimmune Hep: 2%
- Toxic Hep: 2%
- No data: 28%

n = 143  X year: 5.4 y  Rank: 0.6 - 22 y  53% fem  Period: 11/92 - 11/01

Background summary

- Intermediate / High incidence HAV infection country
- Main cause of Fulminant Hepatic Failure and Liver Transplantation in children
Single dose Hepatitis A Vaccination Strategy

✓ > 95% immunologic response at 30 days with single dose.

✓ Wide experience with single dose for outbreaks control.

✓ To change the age of immunization to 12 months. Decision based on previous epidemiological studies.

✓ Environment Viral Circulation would act as natural booster and favor a prolonged protection

✓ To perform studies to validate the intervention and analyze the need for a second dose.

✓ Affordable costs.

Epidemiology Dir & Advisory Group for VH & Argentinian Pediatric Society
## Hepatitis A vaccine incorporation: 30/6/2005

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</thead>
<tbody>
<tr>
<td>2 meses</td>
<td></td>
<td>2ª dosis</td>
<td>1ª dosis</td>
<td>1ª dosis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4 meses</td>
<td></td>
<td>2ª dosis</td>
<td>2ª dosis</td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>12 meses</td>
<td></td>
<td>3ª dosis</td>
<td>3ª dosis</td>
<td>3ª dosis</td>
<td></td>
<td>1ª dosis</td>
<td>1ª dosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 meses</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 años</td>
<td></td>
<td>Iniciar o completar esquema [3]</td>
<td>Refuerzo</td>
<td>2ª dosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 años</td>
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<td></td>
<td></td>
<td>Refuerzo [4]</td>
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<td></td>
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</tr>
<tr>
<td>16 años</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Refuerzo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cada 10 años</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Refuerzo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Puerperio o post-aborto inmediato</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 dosis [4]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- [1]: Inicia vacunación
- [2]: Segunda dosis
- [3]: Completar esquema
- [4]: Puede repetirse
Hepatitis A Vaccine Coverage. Argentina 2005-2012

Data Source: ProNaCEI
Monitoring the impact of the intervention

1. Passive & active Surveillance of cases; Notification rates

2. Fulminant Hepatic Failure and Liver transplantation

3. Laboratory Survey with Demographic & Socioeconomic data
   3.1 Seroprotective antibodies prevalence immediately before vaccination
   3.2 Seroprotective antibodies prevalence 4 - 5 years post vaccination
Monitoring the impact of the intervention

- Cases and Rates reported to the National Epidemiological Surveillance System from 2000 to 2013.

- Fulminant Hepatic Failure (FHF) cases obtained from main children hospitals.

- Liver Transplantation (LT) cases reported by the National Central Unique Institute for Coordination of Ablation and Implant.
Cases y Rates. Hepatitis A 2000 - 2011

Rate 65/100.000

Rate 7.8/100.000  (p<0.001)

Source: Health National Surveillance System SNVS
Hepatitis A and unspecified Hepatitis.
Cases and rates – Argentina 2000-2013

Data Source: SNVS- C2, MSAL

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P & C of VH in LA & B
Brasilia 19-21 March 2014
Hepatitis A and unspecified Hepatitis. Rates per region – Argentina 2000-2013

Data Source: SNVS- C2, MSAL
Hepatitis A and Unspecified notified cases

Data Source: SNVS- SIVILA

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P & C of VH in LA & B
Brasilia 19-21 March 2014
HAV associated Fulminant Hepatic Failure cases Argentina, 1993 -2013

Hospital Nac “Prof. Dr. J.P. Garrahan”. Fundación Favaloro, Hospital Italiano, Hospital Univ Austral

Access to drinking water (% of population)

National Survey 2001

National Survey 2010
Access to Sanitation (% of population)

Mapa 3.4.2
Porcentaje de población en hogares con acceso a saneamiento por partido/departamento
Año 2001

Población (% por partido/departamento)
- 0% a < de 10%
- 10% a < de 20%
- 20% a < de 30%
- 30% a < de 40%
- 40% a < de 50%
- 50% a < de 60%
- 60% a < de 70%
- 70% a < de 80%
- 80% a < de 90%
- 90% a = 100%

Paises del Cono Sur de Sudamérica

Fuente de Datos
- Censo Nacional de Población, Hogares y Viviendas
- Sistema de Indicadores de Desarrollo Sostenible (SADYS)
- Sistema de Información Ambiental Nacional (SIAEN)

National Survey 2001

Mapa 3.4.2
Porcentaje de población en hogares con acceso a saneamiento por partido/departamento
Año 2010

Hogares, en %
- Limite provincial
- Limite departamental
- 0.0
- 0.5 - 30.0
- 30.1 - 60.0
- 60.1 - 90.0
- 90.1 - 100.0

SECTOR ANTÁRTICO ARGENTINO

National Survey 2010
Conclusions

✓ This strategy has been highly effective for controlling HAV disease in all age groups –till now– in our country.

✓ Argentina will maintain this strategy and commits to monitoring as well as strengthening surveillance on hepatitis A epidemiology.

✓ Long term surveillance will be critical for defining the sustained success of this unique intervention.
* HAV Protocols
Cities included:
* San Miguel de Tucumán
* Sta Fe de la Veracruz
* El Palomar
* San Justo
* Cdad Autónoma BsAs

#1.- **Circulation Protocol**
500 (5x100) children 12 month of age (pre vaccination single-dose)

#2.- **Prevalence Protocol**
1250 (5x250) children 60 month of age (at four years receiving single-dose)
Monitoring the impact of the intervention

3.1. Sero protective Ab prevalence immediately before vaccination

- 12 months to 12 months and 29 days healthy unvaccinated children from low, intermediate and high Hepatitis A prevalence areas from the country (5 cities).

- March-November 2011.

- Past history of Hepatitis A infection excluded

- Sero protective antibodies titers: antiHAV IgG > 10 mIU/ml

- Those with antiHAV IgG > 10 mIU/ml were tested with IgM to discard recent HAV infection
3.1 Results

*433 children studied

- 29.5% antiHAV IgG > 10mUI/ml
  All of them antiHAV IgM neg

- No association between socio-economical variables and seroprotective antibodies
Monitoring the impact of the intervention

3.2 Seroprotective Ab prevalence 4 - 5 years post vaccination

- 60 to 72 months healthy children from low, intermediate and high Hepatitis A prevalence areas of the country (same hospitals as previous) and vaccinated at 12 months with a single dose.

- March-November 2011.

- Past history of HAV infection or > 1 dose vaccine excluded.

- Sero protective antibodies titers: antiHAV IgG > 10 mIU/ml
3.2 Results

*1139 children studied

- 93% (95%CI: 91.7-94.6) antiHAV IgG > 10 mIU/ml

- Assistance to kindergarten and mothers instruction level associated with sero protective antibodies in multivariate analysis:
  - OR 2  (CI95%: 1.26 -3.3) and
  - OR 0.26 (CI95%: 0.09-0.8) respectively.
Conclusions

✓ This strategy was effective to control the disease since its implementation up to date.

✓ The low percentage of pre vaccinated sero protected children confirms the right decision of introducing the vaccine at 12 months.

✓ Single dose vaccination achieve high middle term immunologic response.

✓ Argentina will maintain this strategy and commits to continue monitoring as well as strengthening surveillance on hepatitis A epidemiology.

*2013 monitoring almost finished.
WHO recommends Argentina’s strategy

COLOMBIA and PARAGUAY have incorporated during 2013 a single dose of HAV vaccine at one year of age in their national immunization schedules.

In 2005, public health authorities in Argentina began a universal immunization programme in 12-month-old children based on a single dose schedule of inactivated HAV vaccine. In 2007, with vaccination coverage of 95%, the incidence of symptomatic viral hepatitis A had dropped by >80% in all age groups. Six years after implementation of this country-wide single-dose programme, no hepatitis A cases have been detected among vaccinated individuals, whereas among the unvaccinated a number of cases have occurred, confirming continued circulation of hepatitis A virus in the Argentinian population.
### Immediate Individual Notification of Suspect Case

#### Gastroenteric Conditions
- Botulism
- Botulism of the infant
- Cholera
- Diarrhea acute sanguinolent
- Typhoid fever and paratyphoid fever
- Intoxication by molluscs
- Urine syndrome hemorrhagic hemolytic
- Trikinisis
- Toxin-infections alimentary

#### Immunopreventable Conditions
- Whooping cough
- Diphtheria
- Poliomyelitis: flaccid paralysis under 15 years
- Rubella
- Congenital rubella
- Sarampion
- Tetanus neonatal
- Tetanus other ages

#### Meningoencephalitis
- Meningoencephalitis bacterial
- Meningoencephalitis mycotic, parasitic
- Meningoencephalitis viral
- Meningoencephalitis tuberculosis in children under 5 years
- Meningoencephalitis not specified

#### Vectorial Conditions
- Dengue
- Dengue grave
- Encephalitis by arbovirus
- Yellow fever
- Yellow fever of the Western Nile
- Yellow fever recurrent
- Leishmaniasis visceral
- Malaria
- Peste
- Tifo epidemic

#### Zoonotic Conditions
- Cutaneous anthrax
- Cutaneous anthrax extra cutaneous (Anthrax)
- Hemorrhagic fever in Argentina
- Hantavirus
- Leptospirosis
- Psittacosis
- Rabies animal
- Rabies human

#### Respiratory Conditions
- Human grippe by a new subtype of virus
- Acute respiratory syndrome SARS

#### Envenenamiento por animal por ponzoños
- Arachnoiditis
- Escorpionism
- Poisoning

#### Other Events
- Outbreak of any etiology
- Encephalopathy espongiform
- Other events with risk to public health
- Viral encephalitis

**Hepatitis Virales**
- Hepatitis A
HAV VIRUS CIRCULATION IN ARGENTINA 1998-2011

AY644670 SLF88 Genotype IIB
M14707 HM175 Genotype IB

47.16 Buenos Aires, 2008
44.5 CABA, 2009

Arg4.7 San Juan, 2002
Arg1.9 Buenos Aires, 1998
Arg10.5 Bahía Blanca, 2002
Arg26.16 CABA, 2004
Arg9.5 Bahía Blanca, 2002
Arg29.12 Tucumán, 2004
Arg2.19 CABA, 1999
Arg2.22 Buenos Aires, 2002

X75215 GBM/WT

47.21 CABA, 2009

Arg5.4 Buenos Aires, 1997
Arg8.11 Santa Fe, 2001
Arg26.4 Sgo del Estero, 2004
Arg26.8 Chaco, 2004
Arg31.8 CABA, 2005
Arg22.4 Buenos Aires, 2003

47.20 CABA, 2009
44.7 CABA, 2009
47.17 Buenos Aires, 2008
42.4, 42.7, 42.9, 42.10 Mendoza, 2009
47.18 CABA, 2008
47.15 Buenos Aires, 2008
44.9 CABA, 2011
HM769724 Santa Fe, 2006

Previously HAV vaccine

Genotype IA
SERVICIO HEPATITIS Y GASTROENTERITIS
DEPARTAMENTO VIROLOGIA

LABORATORIO NACIONAL DE REFERENCIA
INSTITUTO NACIONAL DE ENFERMEDADES INFECCIOSAS (INEI)
ADMINISTRACION NACIONAL DE LABORATORIOS E INSTITUTOS DE SALUD (ANLIS)

“Dr. Carlos Gregorio Malbrán”

www.anlis.gov.ar/INEI/virolog/hepatitis
Our best n° 12 player!!

BRAZIL: see you at the final match ... !!!! 😊😊