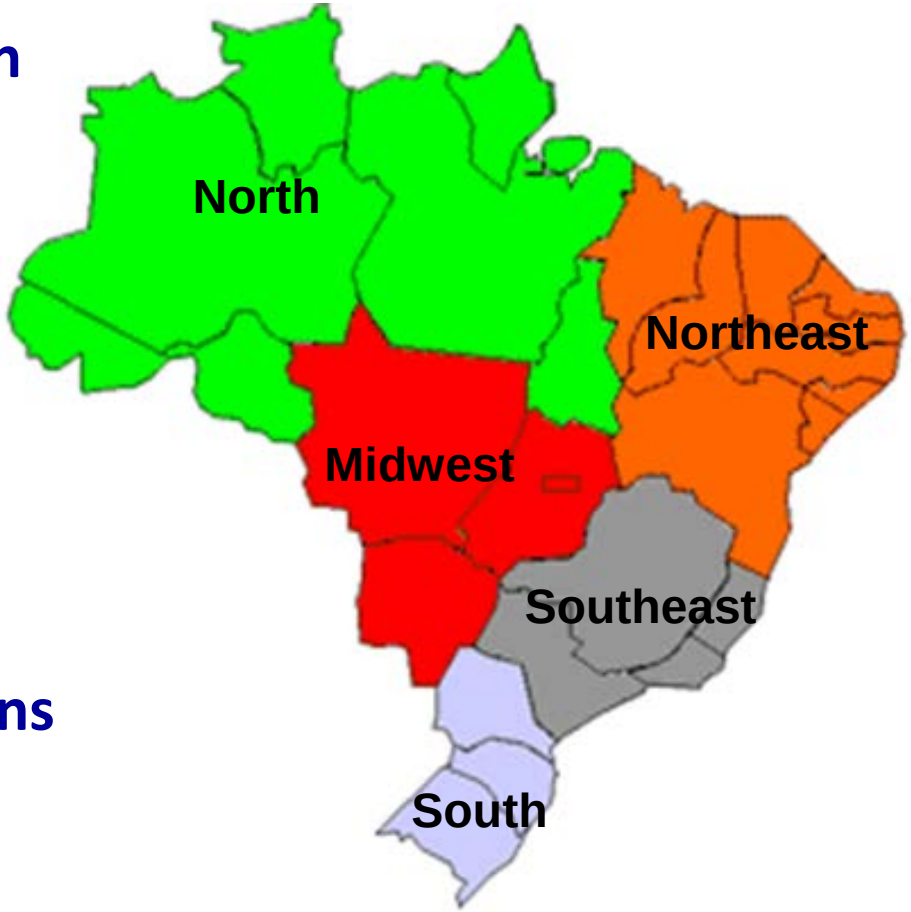
Epidemiology of Hepatitis A and Hepatitis E in Brazil

Themis Reverbel da Silveira

Brasilia, 19-21 March 2014

BRAZIL

- Inhabitants ~200.000.000 million
- Extension: 85,142,153 km2
- Heterogenous population
- Ethnic miscigenation
- A developing country
- Significant economic growth
- Problems with sanitary conditions
- Striking regional differences



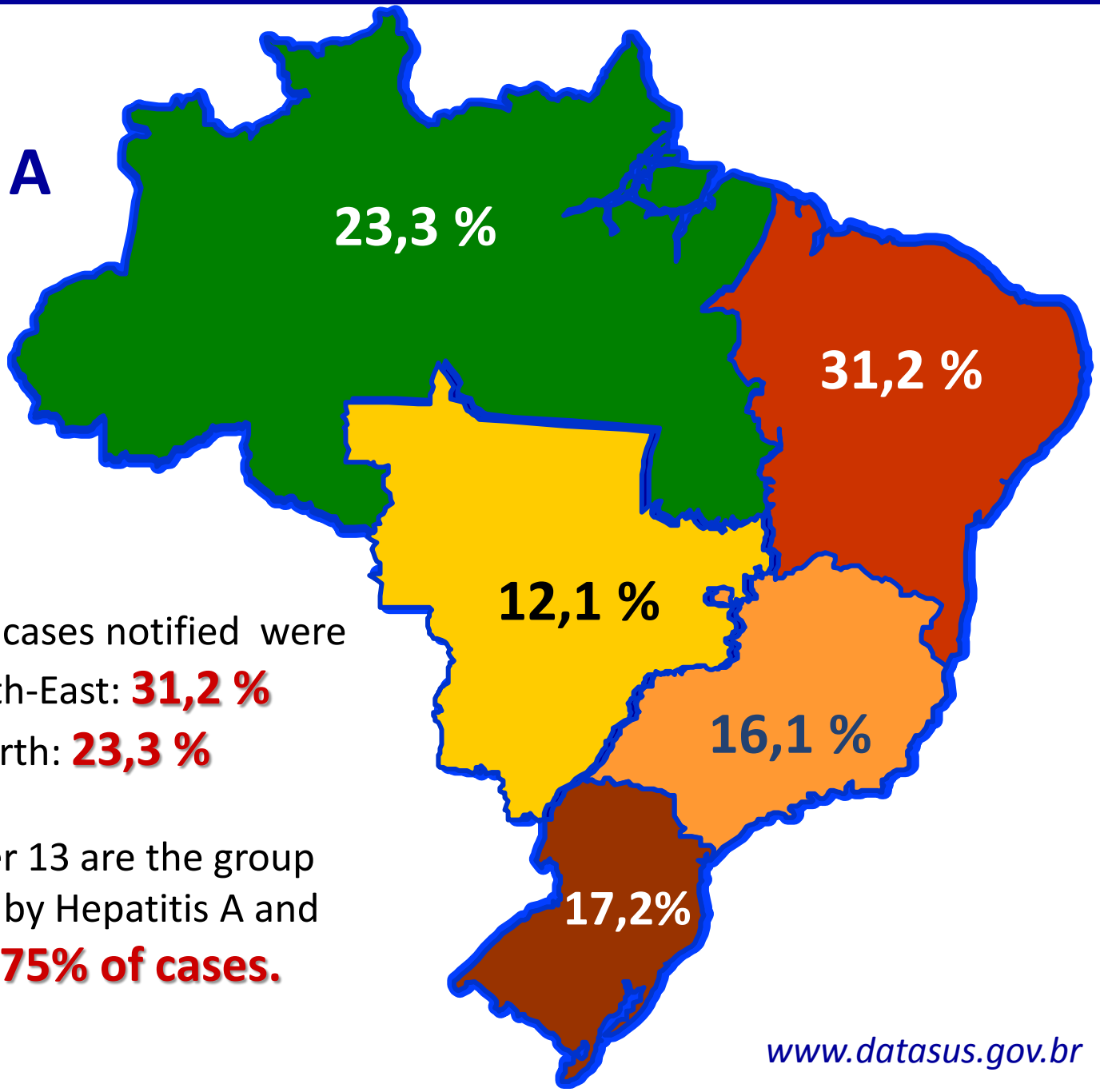
http://www.censo2010.ibge.gov.br

Cases of Viral Hepatitis notified between 1999 and 2011 in Brazil

Hepatitis	n	%
A	138,305	40.2 %
B	120,343	34.9 %
C	82,041	23.8 %
D	2,197	0.64 %
E	967	0.28 %
Total	343, 853	

SINAN/SUS/MS IBGE
25/07/2012

Hepatitis A



The majority of cases notified were in the North-East: **31,2 %** and North: **23,3 %**

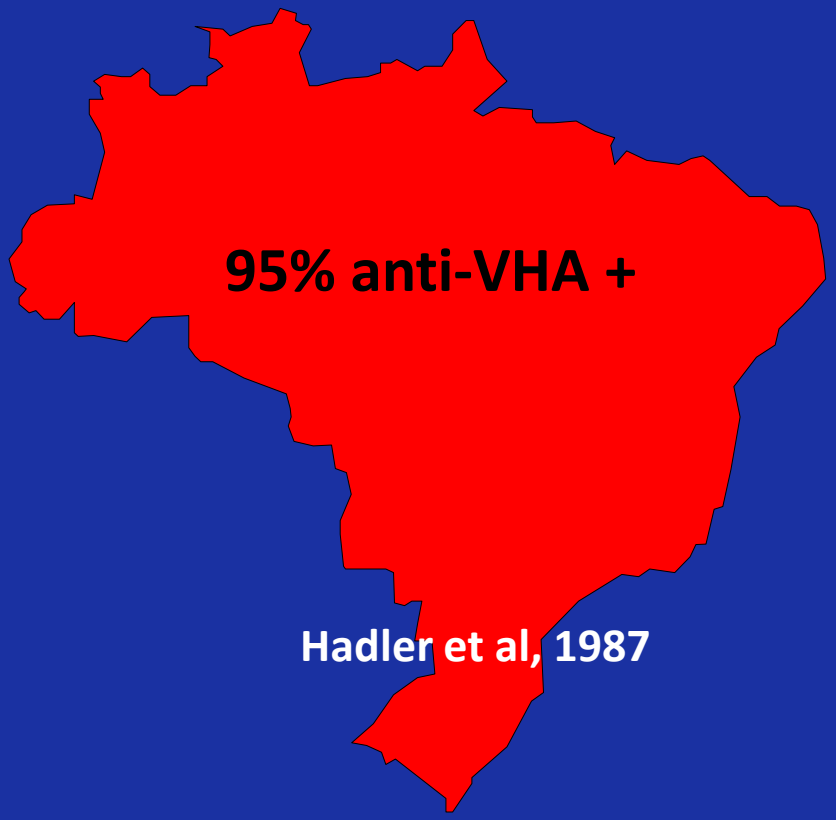
Children under 13 are the group most affected by Hepatitis A and account for **75% of cases.**

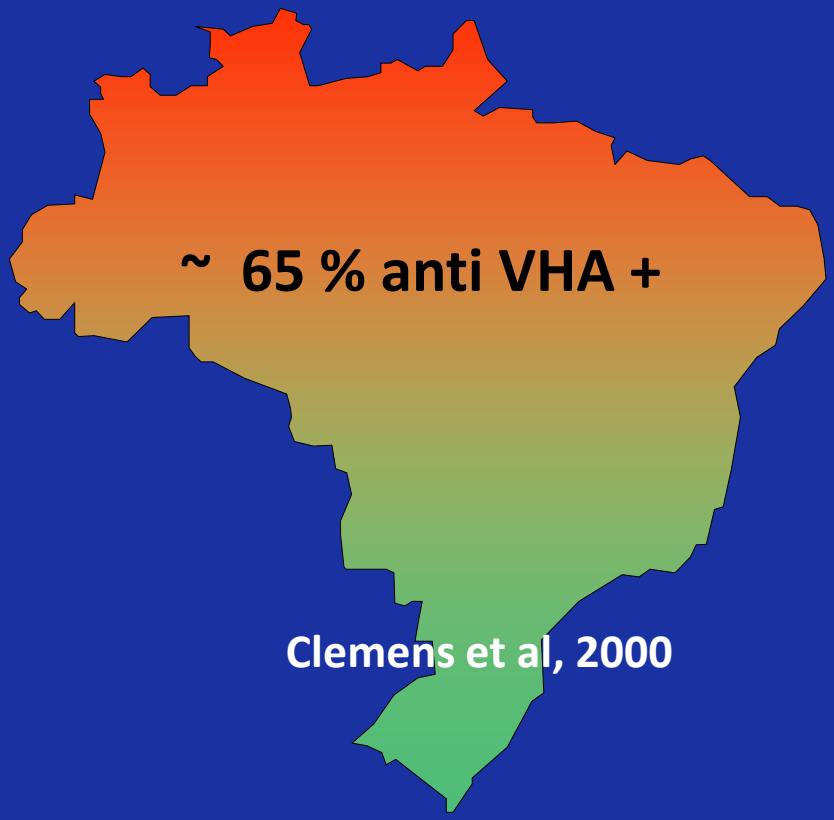
www.datasus.gov.br

Hepatite A

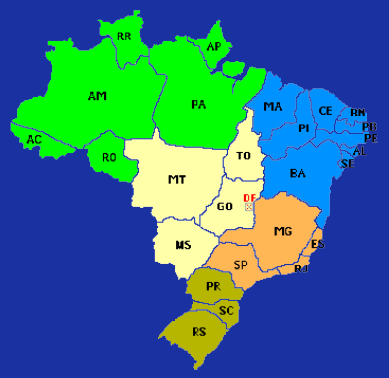
Shfting susceptibility

Prevalence





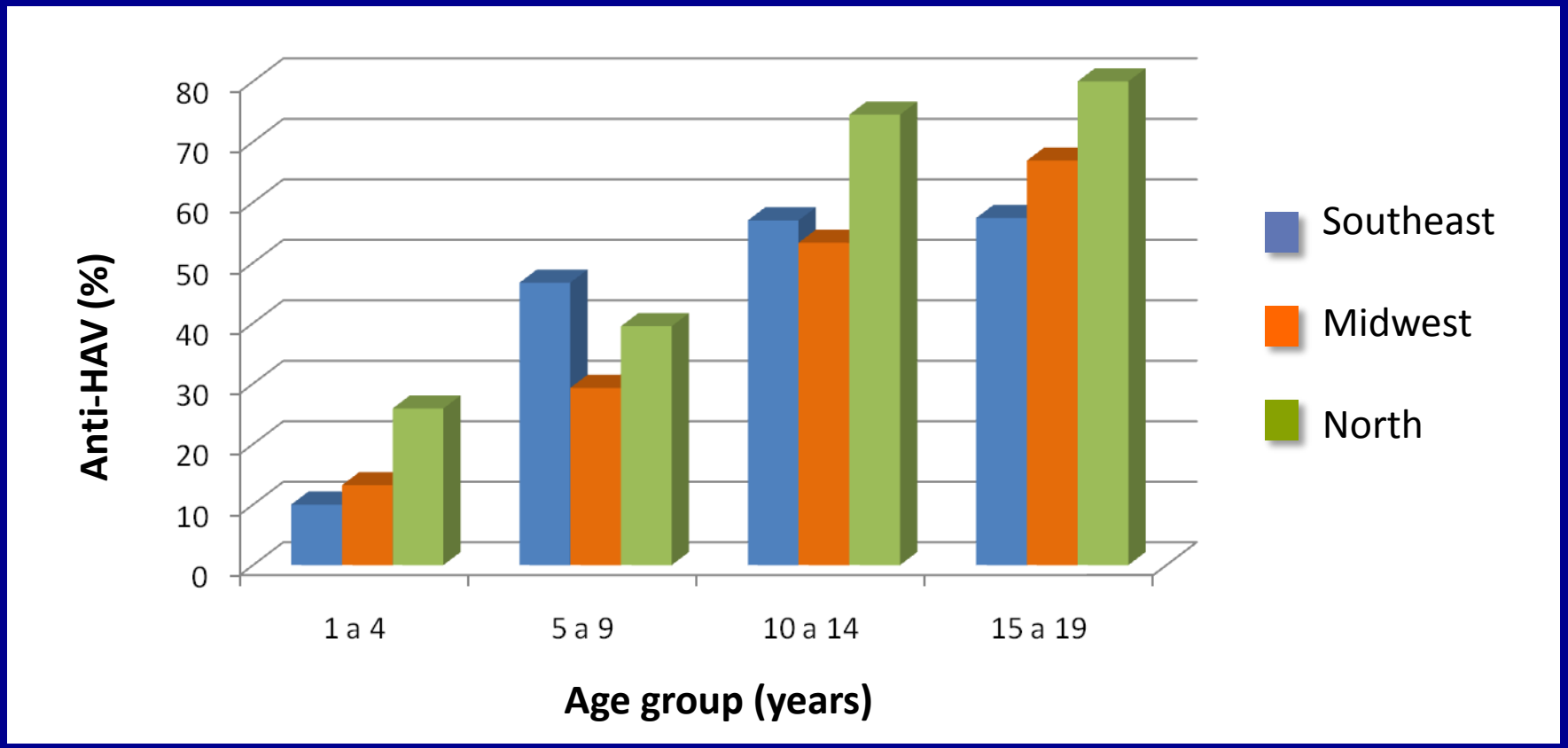
The prevalence of hepatitis A varies greatly In different Brazilian regions.



It is well known that HAV infection is strongly correlated with poverty and inadequate sanitation.

Despite the improvements in sanitary conditions, <u>hepatitis A is still endemic and outbreaks may occur.</u>

Analysis of age distribution of anti-hepatitis A virus seropositivity according to Brazilian Regions



A large number of children from one-four years of age (74.1-90%) were susceptible to a HAV infection The overall prevalence of anti-HAV antibodies was 12.1% (10-25.9%). Among those participants from one-18 years of age, the prevalence was 41.9% (39.8-49%)

Vitral et al, 2012

Transition from a high to a medium endemicity of hepatitis A virus

A significant decrease in HAV seroprevalence among children aged one-18 years old, indicates that the rates decreased from 70-40.4% in the span of 9 years ($p < 0.0001$).

The data suggest that a decrease in the infection rate of HAV may be occurring even among the lower socioeconomic groups in Brazil who live on the periphery of capital cities.

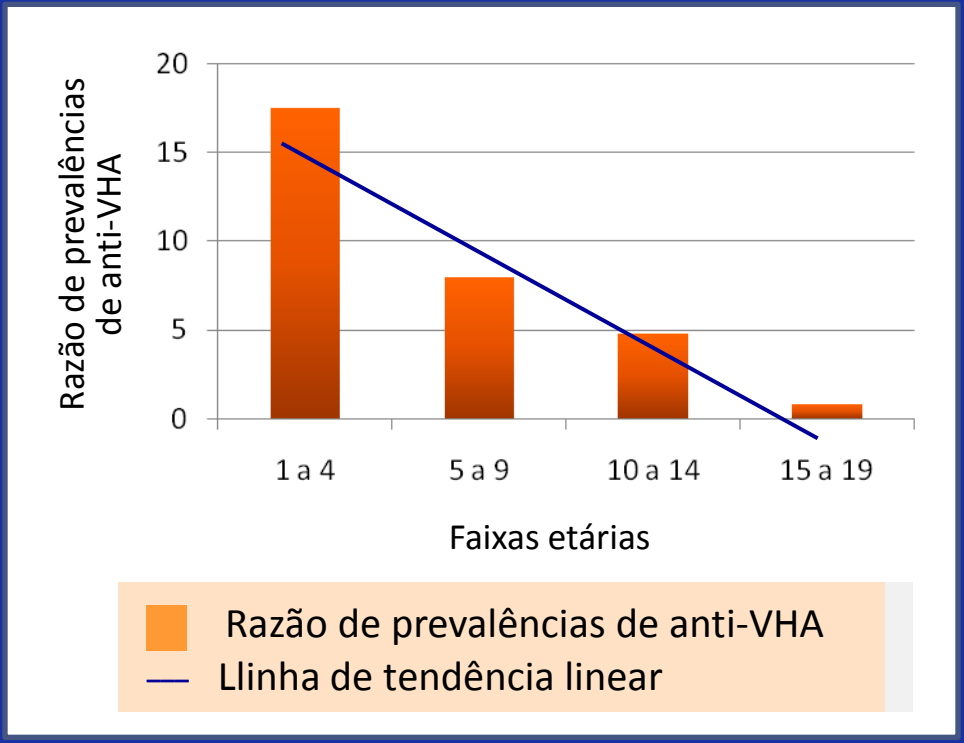
Claudia Lamarca Vitral et al

" Declining prevalence of H A virus antibodies among children from low socioeconomic groups reinforces <u>the need for the implementation of hepatitis A vaccination in Brazil"</u>

Mem Inst Oswaldo Cruz, 107(5): 652-658, August 2012

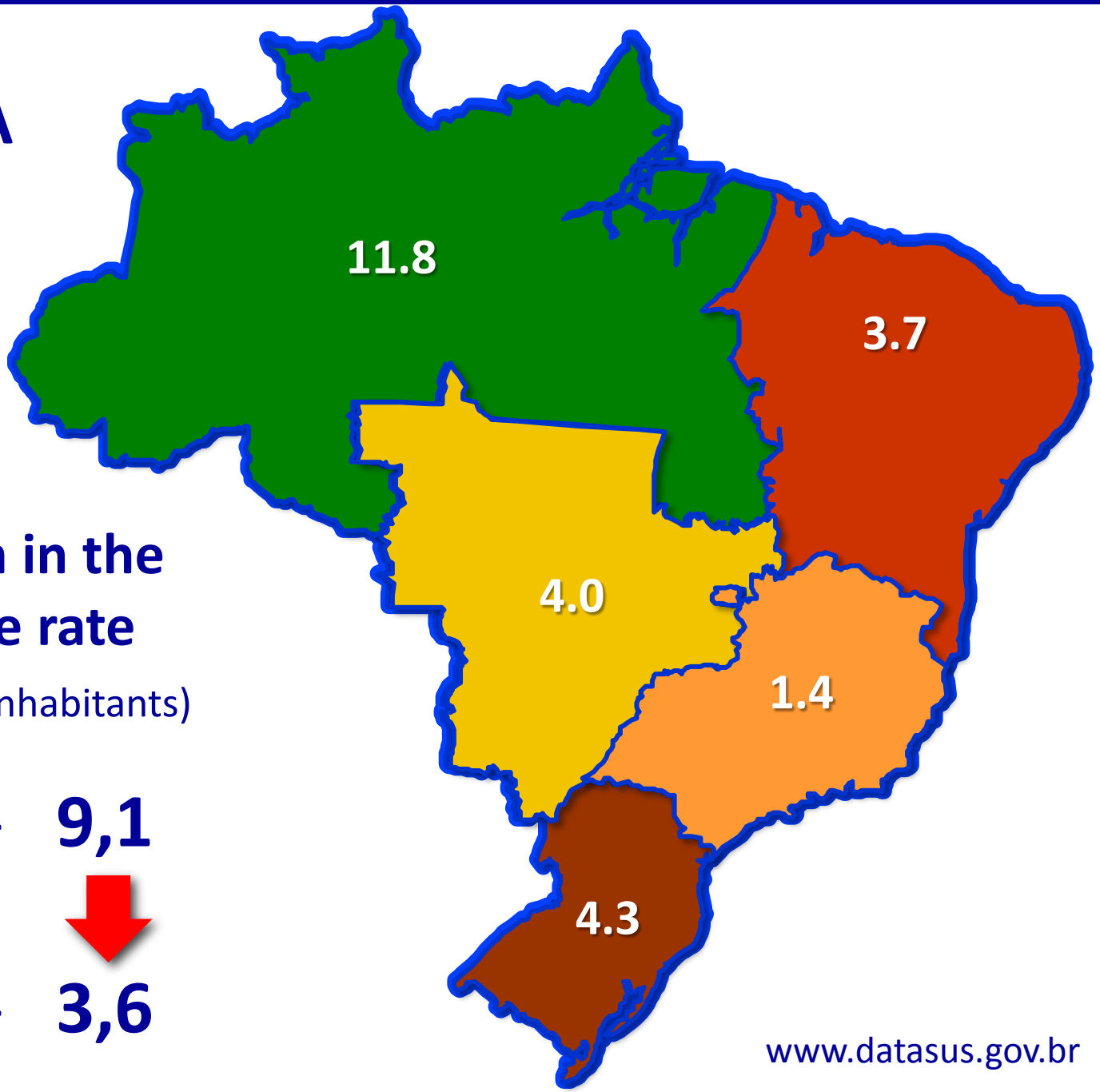
Shifting susceptibility to hepatitis A among children and adolescents over the past decade

The results suggest that the endemicity of hepatitis A in Porto Alegre has been declining over the past decade, and that children and adolescents, particularly those in the lowest socioeconomic strata, are more susceptible to the disease.



Lenita S. Krebs, Tani M. S. Ranieri, Carlos O. Kieling, Cristina T. Ferreira, Themis R. da Silveira, J Pediatr 2011

Hepatitis A



Reduction in the Incidence rate

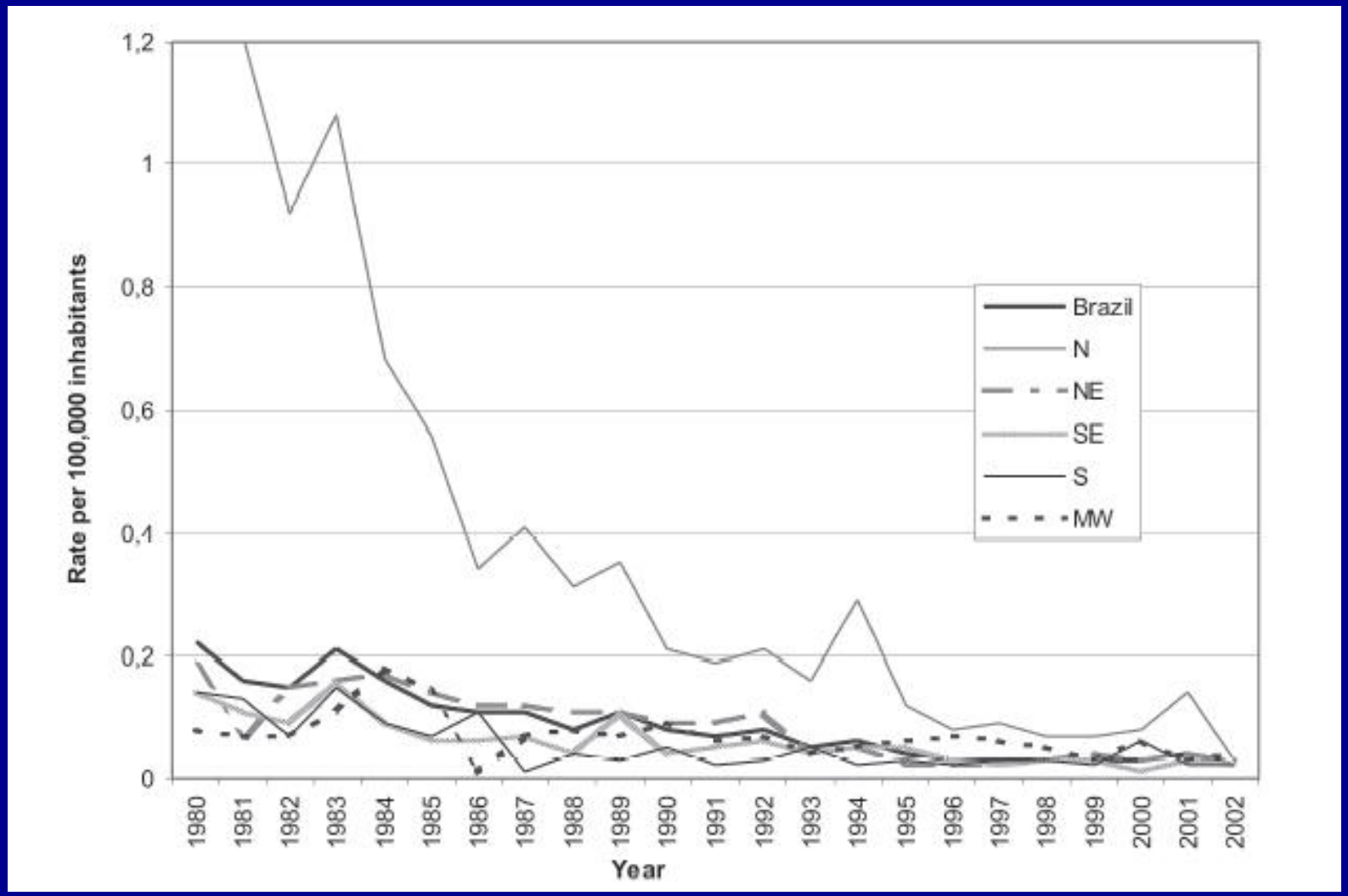
(per 100,000 inhabitants)

2006 - **9,1**

2010 - **3,6**

www.datasus.gov.br

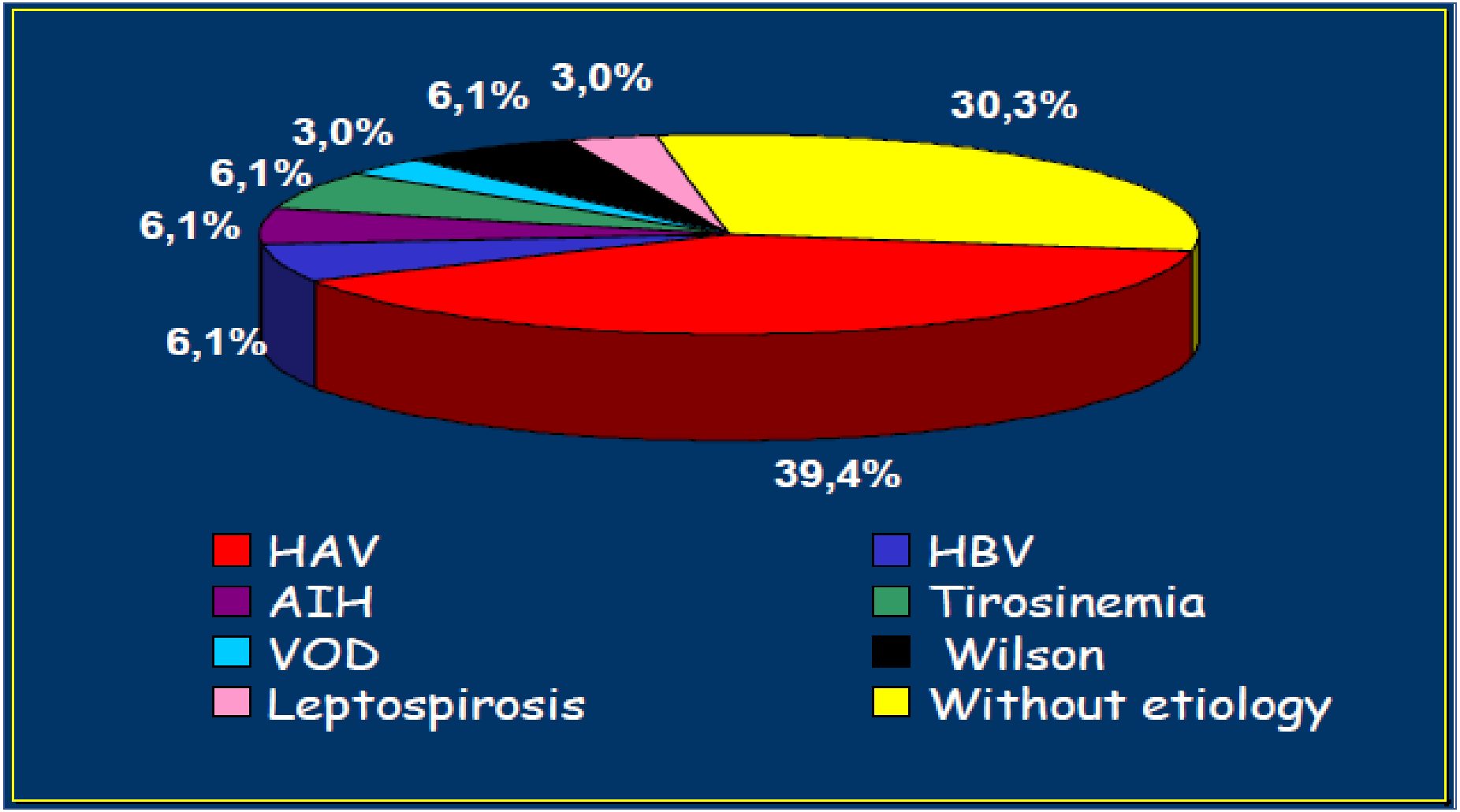
The drop of mortality in hepatitis A results from increases in the quality of health care and greater availability of liver transplantation in specialized centers in major urban cities



Vitral CL, Gaspar AMC, Souto FJ. Mem Inst Oswaldo Cruz 2006; 101:119-127

Acute hepatic failure in 33 children.

Porto Alegre (1998-2007)



Journal of Viral Hepatitis. 2008,;15 (Suppl. 2):66–68

Latin America

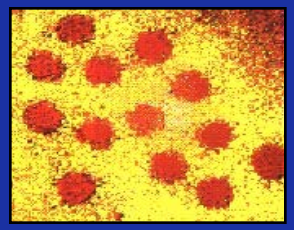
HAV vaccination has been incorporated in the immunization programs of three countries.

In Argentina, the introduction of a single dose of HAV vaccine reduced cases by > 80% in a 2 year period

Hepatitis A vaccine

It is still not included in the Brazilian National Program for Immunization.

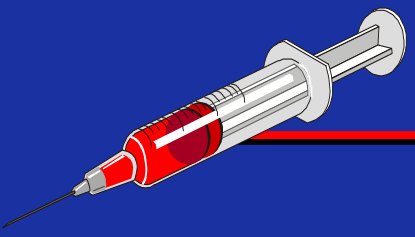
It is offered at Reference Centres for Special Immunobiologicals for groups that are at high risk for HAV infection or at private immunization clinics.



Improvements in sanitary facilities represent a powerful method to reduce the transmission and the control of HAV

but

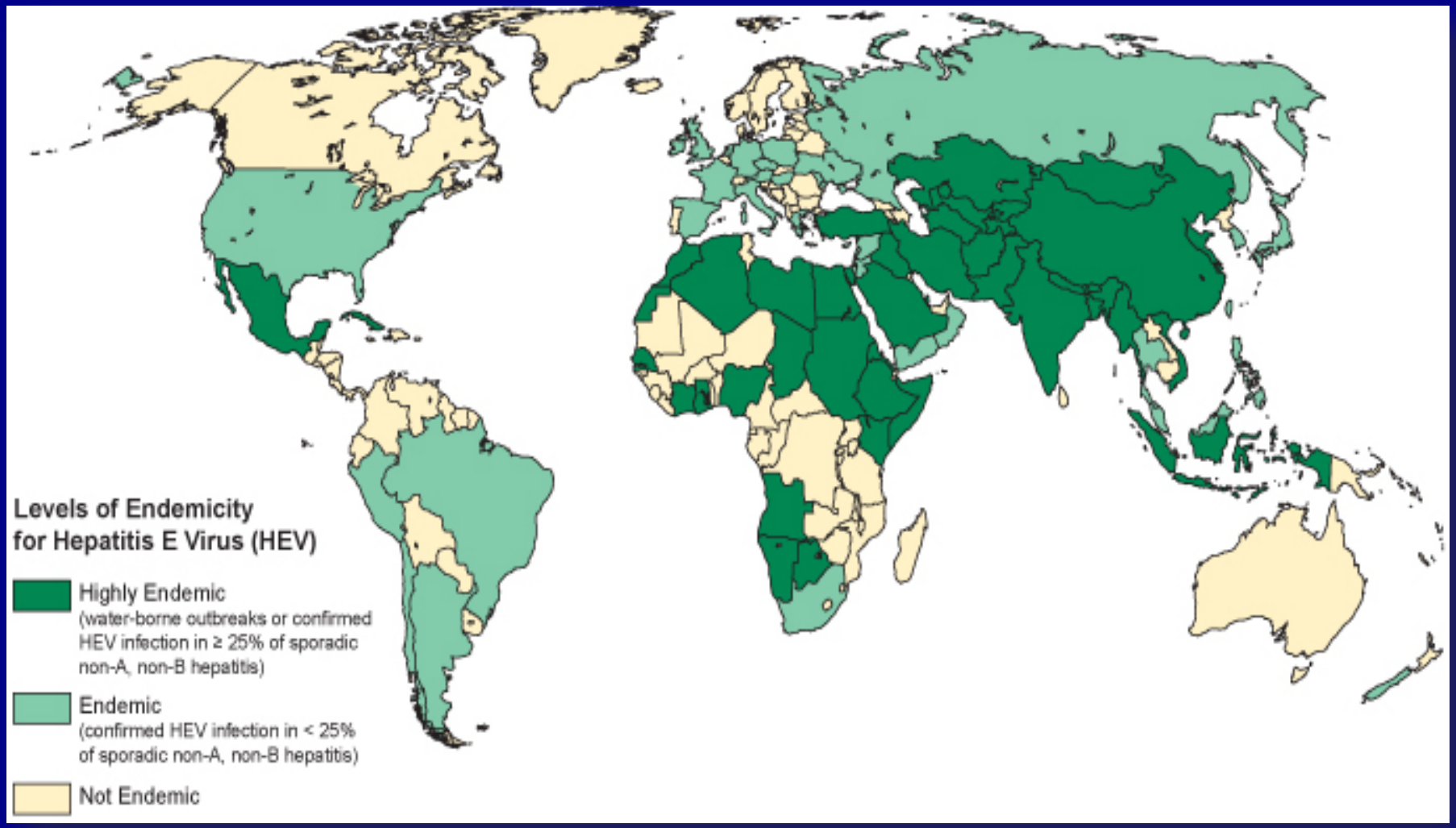
<u>we cannot wait</u> until the conclusion of the Brazilian Program of Basic Sanitation.



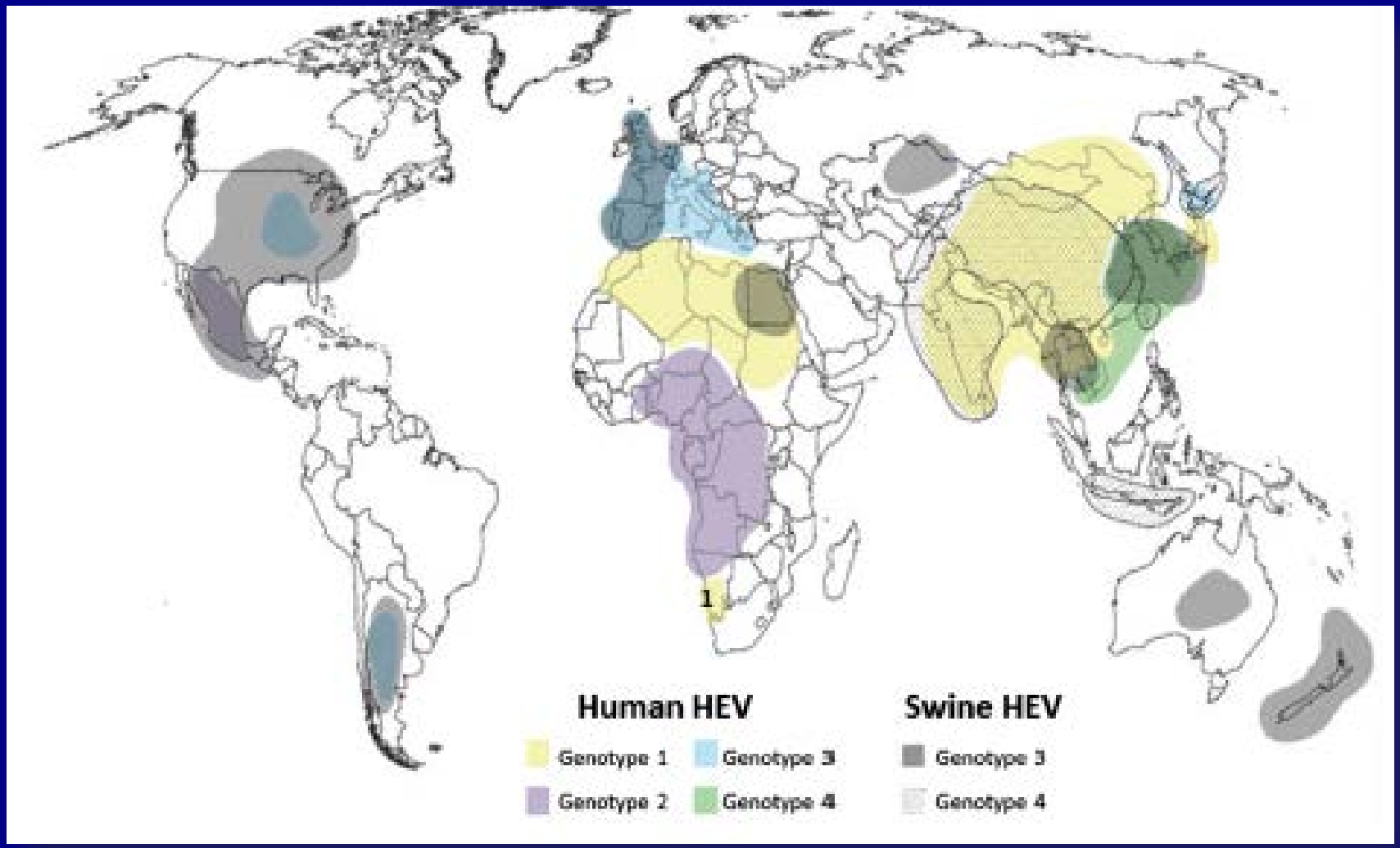
In countries that have experienced a reduction from high to medium HAV endemicity global immunization is likely to be cost-effective.

Therefore, as per WHO recommendations, HAV vaccination in children ≥ 1 year old is encouraged.

Endemicity for Hepatitis E Virus



Geographic distribution of the HEV genotypes in swine and humans

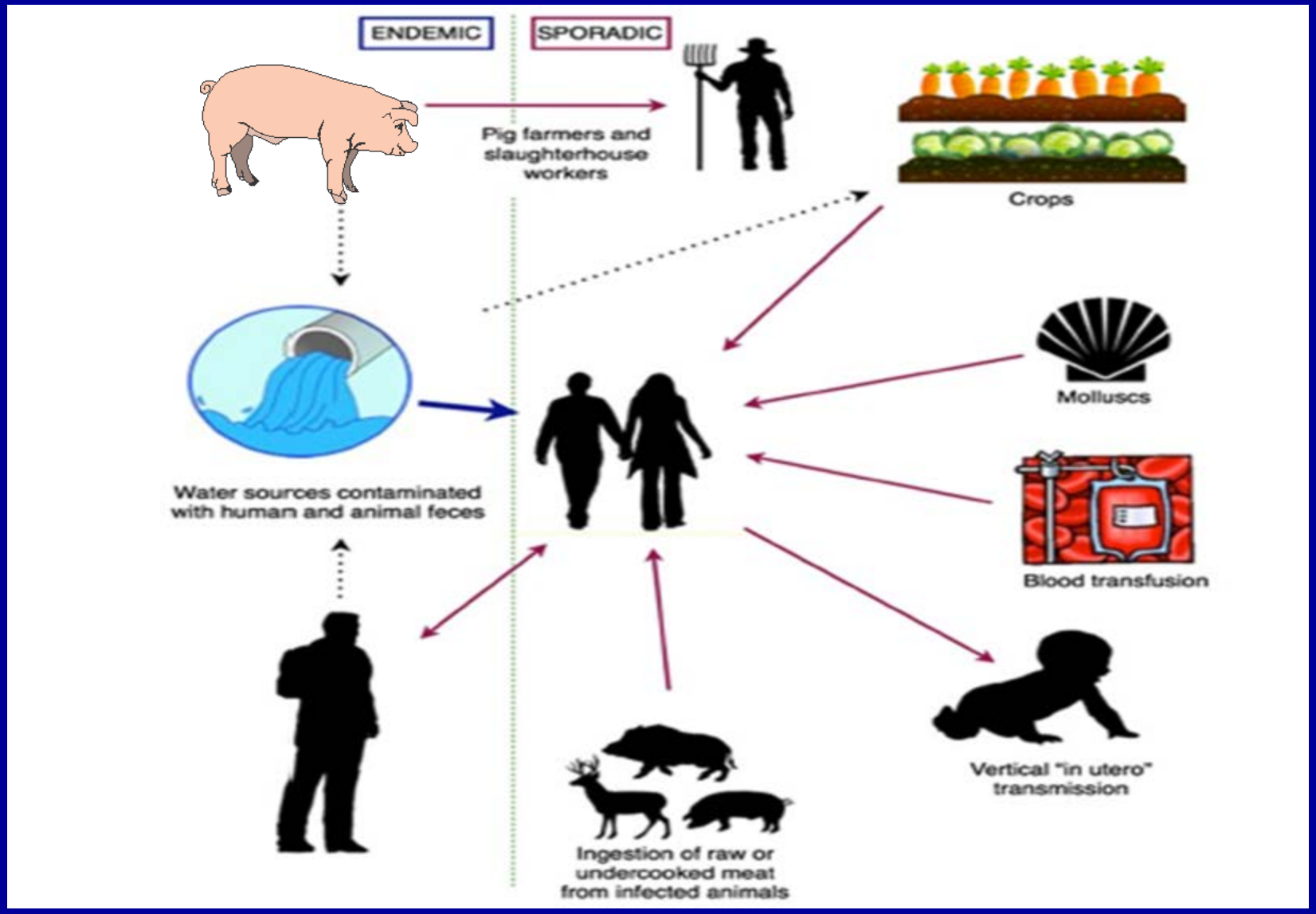


Péres-Gracia MT, Suay B. et al., Infect Genet Evol.22,40–59 2014

- **Evidence of historical outbreaks as early as 1794** (Teo, 2012)
- **Currently, the infection with HE virus represents <u>the most frequent cause for acute hepatitis and jaundice in the world</u>**
- **According to WHO around 2 billion people live in endemic areas!**

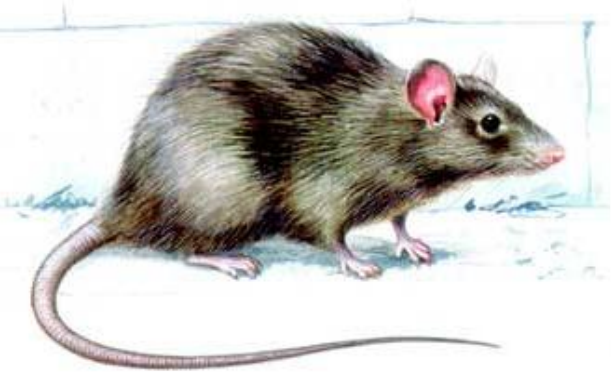
Data on HEV infections in Brazil are scarce

Transmission routes of HEV



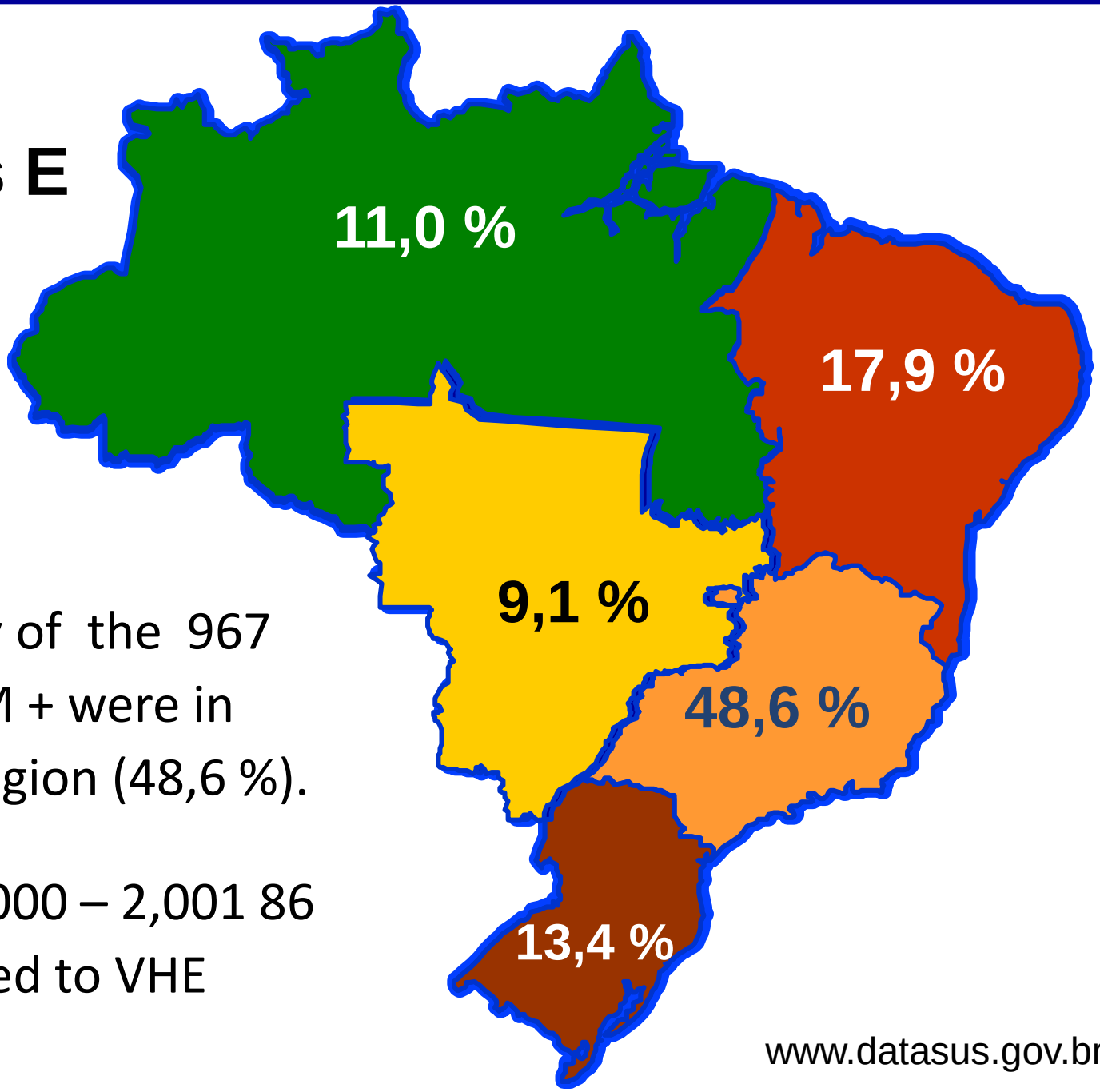
Péres-Gracia MT, Suay B. et al., Infect Genet Evol.22,40–59 2014






Hepatitis E



The majority of the 967 anti-HEV IgM + were in Southeast region (48,6 %).

Between 2,000 – 2,001 86 deaths related to VHE

www.datasus.gov.br

Prevalence of serum IgG anti-hepatitis E antibody + in normal populations in different Brazilian regions

Population/study	Region	N of cases	IgG anti-HEV (+)
Gold miners / Pang et al	Amazon basin	97	6.1
General population/Souto et al	Amazon basin	299	3.3
Blood donors /Parana et al	Northeast-Salvador	200	2.0
Pregnant women/Trinta et al	Southeast –Rio	304	1.0
Blood donors/Gonçales (ALT>2UNL)	Southeast – Campinas	40	7.5
Individuals from rural areas from urban areas/ Trinta et al	Southeast –R.de Janeiro	145	2.1
Blood donors/Gonçales (ALT>2UNL)	Southeast- R. de Janeiro	260	0
Low socioecon.community/Santos	Southeast – R.de Janeiro	699	2.4
Low socioecon.community/Silveira	South – Porto Alegre	830	5.9
Children (2 – 9 years old) Assis et al	Amazon basin (MT)	487	4.5
			(0 – 7,5 %)

Carrilho, Clemente da Silva Gastroenterol Hepatol 2005; 28: 118-
Silveira et al - unpublished data

Epidemiology of hepatitis A and E virus infection in Brazil

Prevalence of serum IgG anti-hepatitis E vírus (HEV) in São Paulo city, Southeastern Brazil, by age

Age interval (years)	Positive serum total anti-HEV	
	No. of cases	% (95% CI)
2-4	61	0.0
5-9	108	0.0
10-14	104	1.05 (0,0-3.04)
15-17	58	1.63 (0.0-4.98)
18-29	250	1.63 (0.07-326)
30-39	184	2.19 (0.05-4.32)
40-49	123	243 (0.0-5.19)
50-59	81	2.25 (0.0-5.56)
>60	90	3.09 (0.0-6.74)
Total	1059	1.68 (0.91-2.46)

FJ Carrilho , C Mendes Clemente · LC da Silva

Prevalence of serum IgG anti-hepatitis E antibody + in some risk groups in different Brazilian regions

Population/study	Region	N of cases	IgG anti-HEV (+)
Acute NANBNC Hepatitis/Souto	Amazon basin	16	12,5
Paraná et al	Northeast-Salvador	17	29
Lyra et al	Northeast –Salvador	12	17
Acute hepatitis A/ Paraná et al.	Northeast – Salvador	24	25
Lyra et al.	Northeast – Salvador	50	38
Acute hepatitis C/ Paraná et al	Northeast – Salvador	1	0
Acute hepatitis B/ Paraná et al	Northeast – Salvador	26	11
Lyra et al	Northeast – Salvador	42	10
Cleaning service workers/Gonçales et al	Southeast-Campinas	5	13
Health care workers	Southeast-Campinas	117	2,6
Women at risk for HIV	Southeast-Campinas	193	18
Prostitutes	Southeast-Campinas	21	14

Hepatitis E antibodies IgG in farm workers of Mato Grosso, Brazil

A transversal study in 54 farms in Mid-West, Brazil to estimate the prevalence of anti-HEV IgG +

- 310 exposed to pigs and 101 blood donors
  Test MP Diagnostics Biomedicals Asia Pacific, Singapura - Kit commercial ELISA (genotypes 1 and 2)

- The associations with age, history of blood transfusion and contact with other farm animals, access to potable water and sanitary conditions were analysed.

Silva S & Souto F, 2012

Hepatitis E antibodies IgG in farm workers of Mato Grosso, Brazil

A logistic regression model was constructed

- 310 exposed to pigs - **8,4 %** anti-HEV+
- 101 blood donors from urban area - **4 %** anti HEV+

No association was observed between positivity and contact with pigs.

In this rural region the exposition to swines was not a risk factor for HEV infectio

Silva S & Souto F, 2012

Chronic hepatitis, cirrhosis, acute-on-chronic liver failure have been described in immunocompromised individuals

Davern, 2013

A single acute case has been confirmed

Lopes dos Santos et al., 2010

HEV genotype 3 infections are common in Brazilian swine livestock

Vitral et al., 2005; dos Santos et al., 2009, 2011;de Souza et al., 2012

Seroprevalence of hepatitis E antibodies in a population of recyclable waste pickers in Brazil

Martins et al .Journal of Clinical Virology 2014, 59: 188

April 2010 — May 2011

A cross-sectional study was conducted among recyclable waste pickers from all 15 recycling cooperatives in Goiânia City. (Midwest).

The participants were tested for serological markers indicative of HEV infection. (Recomwell HEV IgG and IgM, Mikrogen GmbH, Neuried, Germany). Positive ELISA results were confirmed by immunoblot analysis.

Seroprevalence of hepatitis E antibodies in a population of recyclable waste pickers in Brazil

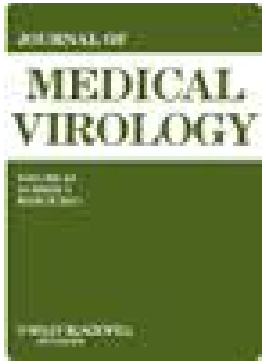
R.M.B. Martins[a,*], N.R. Freitas[b], A. Kozlowski[a], N.R.S. Reis[a], C.L.R. Lopes[b], S.A. Teles[b], N.R. Gardinali[c], M.A. Pinto[c]

Markers	Positive		95% CI
	No.	(%)	
IgG anti-HEV			
ELISA	24	(5.6)	3.7–8.3
Immunoblot	22	(5.1)	3.4–7.6
IgM anti-HEV			
ELISA	4	(0.9)	0.3–2.5
Immunoblot	3	(0.7)	0.4–2.4

CI: confidence interval.

Conclusions: These findings demonstrated that the prevalence of HEV antibodies among recyclable waste pickers in Central Brazil is relatively low and increased with age.

A retrospective study was performed with 96 serum samples from renal transplant recipients with unexplained liver enzymes ↑



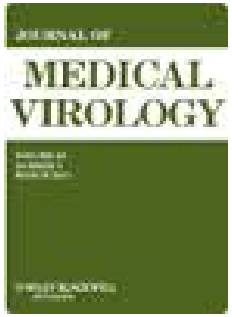
Three confirmed cases of HEV infection identified that lacked seroconversion to HEV IgG antibodies using a sequence analysis the strains were classified as genotype 3 with a low percent identity to previously characterized strains.

Prevalence 3,1 % and a novel genotype 3 subvariant may be circulating !

Passos et al. First report and molecular characterization of Hepatitis E virus infection in Renal Transplant Recipients in Brazil. J Med Virology 85:615, 2013

Gomes-Gouvêa et al. #1754 Liver Meeting AASLD 2013

Evidence of Hepatitis E Virus Infection in Liver Transplant recipients from Brazil



284 liver transplant patients

Serum samples collected between January and May 2013

Tested fot the presence IgG and IgM (ELISA – Mikrogen, Neuried, Germany)

Anti-HEV IgG positive in 23 / 284 - 8,1 %

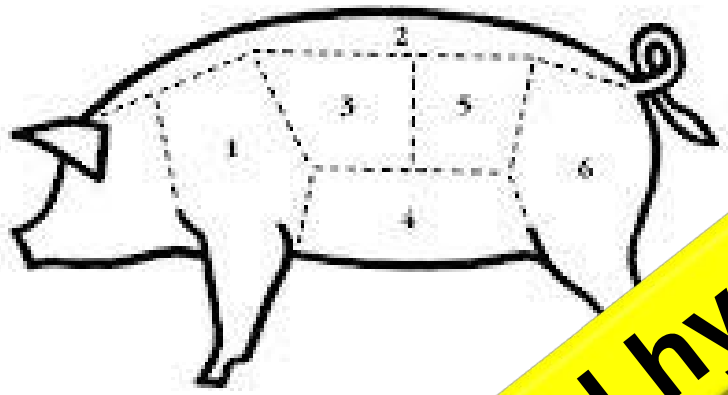
Anti-HEV IgM positive in 6/ 230 - 2,6 %

1 pt. was IgM and IgG positive with normal ALT/AST

The prevalence of anti-HEV antibodies is higher in liver tansplant recipients than that previously observed in immunocompetent populations in Brazil

- Epidemiology complex and still incompletely understood
- In developing countries the infection occurs both as sporadic and an epidemic disease.
- Anti-HEV antibody rates increases with age
- Persons who handle swine had a higher risk for hepatitis E (farmers, veterinarians).
- Approximately **11 %** of commercial pig livers sold in US contain infectious HEV *(Davern, 2013)*

Prevention on HEV Infecti



king Pork

t higher than 56°Celsius
for at least 20 minutes!
(Barnaud, 2012)

Co EV screening when transferring blood to susceptible patients

Sanitary and hygienic measures

The morbidity and mortality assocated with HEV may be preventable.

A vaccine has been deleloped and tested in a trial of 1,794 Nepalese and showed good efficacy (95%) in preventing genotype 1.

Recombinant genotype in China (over 100,000 volunteers). Efficagy 100 %, both genotype 1 and 4 infections prevented.

Hecolin-Park,2012

“We must plan for the future, because people who stay in the present will remain in the past”. *Abrahm Lincoln*