

Cuban Medical Literature

Vaccination Strategies Against Hepatitis B and Their Results: Cuba and the United States, 2003

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BACKGROUND

The first plasma-derived vaccine against Hepatitis B was licensed in the United States in 1981, while the recombinant vaccine was licensed in 1986 1.

In 1987, The Hepatitis Technical Advisory Group of the WHO recommended the integration of the Hepatitis B vaccine into PAI vaccines. In 1992, the World Health Assembly recommended that this vaccine be introduced in 1995 in those countries where the prevalence was higher than 8%, and in 1997, in all countries regardless of their endemic situation 2.

The vaccine had been imported and used in Cuba before 1990 on high risk groups such as patients and staff in dialysis services. The vaccine had not been used systematically because of its high cost .

VACCINATION STRATEGIES

The first clinical trials of the Cuban recombinant vaccine against Hepatitis B were concluded in 1990. This vaccine, called Heberbiovac, is produced in the Genetic Engineering and Biotechnology Center with minimum reactogenicity, and high immunogenicity and efficacy 3,4.

A vaccination strategy was designed and included in the National Immunization Program in 1992. The essential groups in the strategy are:

1. Vaccination of all newborn children, applying the first dose in maternity hospitals.
2. Vaccination of previously identified risk groups, emphasizing prevention before exposure.
3. Complete immunization of the population under twenty years of age in 2000.

Cuba and the United States started universal vaccination of newborn children in the same year, though it had been recommended in the USA in 1991 5.

Cuba has achieved important results in the reduction of this disease 6. Observe the results attained in each country and the differences in the strategies applied.

Chronology of Immunization Practices Against Hepatitis B in the USA (1982-2002) 7

1982 Publication of the first official recommendation on the use of the Hepatitis B vaccine. Vaccination is recommended for the high-risk groups identified.

1984 Recommendation to test pregnant women at a high risk for contracting the infection, and immunize children of mothers infected with the Hepatitis B virus associated with Hyper-immune Gamma Globulin B.

1985 Vaccination is recommended for people who have been in hyper-endemic zones for more than 6 months, and for heterosexuals with multiple sex partners.

1988 Recommendation to test for AgHBs in all pregnant women.

1990 Vaccination is recommended for workers exposed to blood and other body fluids, and families living in highly endemic areas.

1991 Vaccination recommended for all newborns.

1995 Vaccination recommended for eleven and twelve-year-old children.

1999 Vaccination recommended for those under 18 years who have not been vaccinated.

2002 A priority is established to administer the first dose of Hepatitis B vaccine at birth.

Chronology of Immunization Practices Against Hepatitis B in Cuba (1987-2002)

1987 Instructions given to test all pregnant women for AgHBs. Prevention and control program for viral hepatitis begins.

1989-1990 Clinical trial of the Cuban recombinant Hepatitis B vaccine.

1992 Initiation of a vaccination strategy that includes immunization of all newborns part of the National Immunization Program, vaccination of high risk groups, immunization of everyone under 20 years old by the year 2000.

- Vaccination for students in juvenile reform centers.
- Initiation of vaccination drives for third and ninth-graders, 8- and 14-year-olds, respectively.
- Vaccination campaign for allied health sciences students exposed to risk, as well as dentistry and nursing students.
- Vaccination campaign for medical students.

1996-97 Vaccination drive for all school children under 15 in Pinar del Río Province.

- Vaccination of people in contact with infected cases.
- Vaccination campaign for all school children in the country under 15, and for primary care doctors and nurses.
- Instructions to vaccinate all individuals with sexually transmitted infections and their partners.
- Vaccination campaign for insulin-dependent diabetic patients and those with chronic renal insufficiency treated in primary care. Vaccination of people in confinement.

2001 Vaccination drive for all diabetic patients.

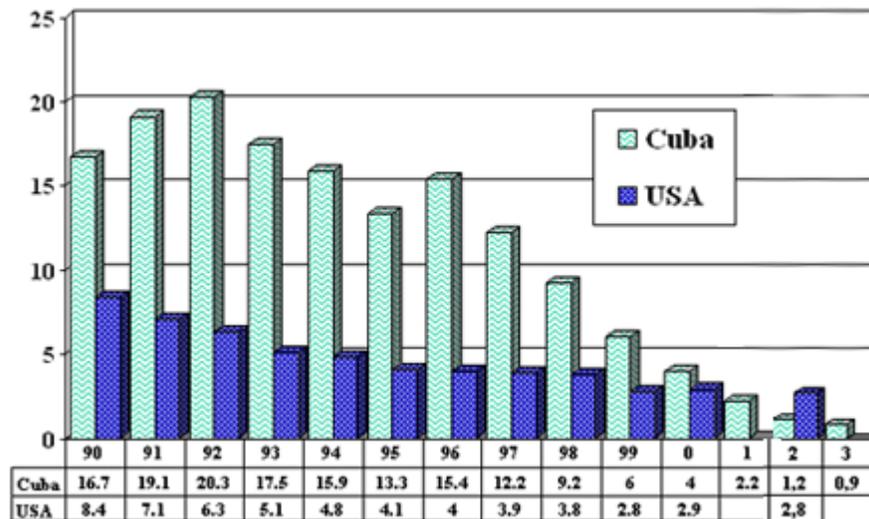
Vaccination Coverage against Hepatitis B in Children Age One and Under Cuba-USA(*) 1995-2002

Year	USA * %	CUBA** %
1995	68	99.2
1996	81.8	99.7
1997	83,7	98.3
1998	87	100
1999	88.1	100
2000	90.3	100

2001	88.9	100
2002	89.9	98

* USA, children age 19-35 months

Incidence of Acute Hepatitis B. Cuba-USA 1990-2003



**Source: National Statistics Division, Ministry of Public Health, Havana.

Main Differences Between the Vaccination Strategies Against Hepatitis B in Cuba and the United States:

United States	Cuba
<ul style="list-style-type: none"> • Surveillance using surveillance sites. • Increasing vaccination coverage, but still under 95%. • Use of Hyper-immune Gamma Globulin; vaccination scheme at 0, one and six months. Serologic follow-up 9-15 months for children of positive mothers. • Vaccination "campaigns" were not carried out in the selected groups. • Vaccination of seventh-grade adolescents in 1995. • Vaccination of children under 18 since 1999. 	<ul style="list-style-type: none"> • General individualized surveillance. • Vaccination coverage higher than 95%. • No use of Hyper-immune Gamma Globulin; vaccination scheme at 0, one, 2 and 12 months. Serologic follow-up 7 and 18 months in children of positive mothers. • Use of vaccination campaigns in the selected groups. • Vaccination of cohorts of 8 and 14 year-olds since 1994. Vaccination of the population under 20 since 2000.

PREVENTION OF PERINATAL TRANSMISSION

Several studies have been conducted in Cuba on the presence of Hepatitis B in pregnant women, and their results show figures ranging between 1.7% and 0.4 % in different hospitals in Havana.

A program of Hepatitis B perinatal prevention has been implemented since 1992, whereas detection of

AgHBs in all pregnant women started in 1987. Samples are taken during the 19 th or 20 th week of pregnancy. A second blood sample is taken from those women who tested positive. Those that test positive again are then considered positive.

Infected mothers are referred to Gastroenterology after puerperium, for diagnosis and definitive treatment.

All newborn children receive their first dose of Hepatitis B vaccine within the first 24 hours after birth. The clinical assay with newborn children of positive mothers with Hyperimmune Gamma Globulin B obtained in the Hemoderivates Plant, without reactogenicity and with levels of protective AchBs in 81.1% of them, was completed in February 2004. At the beginning of 2005, the clinical assay with the newborn babies of positive mothers will be extended throughout the country for their ulterior introduction in the program of perinatal prevention.

Hyper-immune Gamma Globulin is not administered because importation of blood derivatives is prohibited in Cuba, to avoid possible HIV transmission. Clinical trials are now being carried out on newborn children with Hyper-immune Gamma Globulin obtained from the Blood Derivatives Plant, so that it can be introduced in the perinatal prevention program.

Infants born to negative-testing mothers receive 0.5 mcgs by intramuscular injection at 0, 1 and 6 months. Those of positive-testing mothers receive the same doses at 0, 1, 2, and 12 months.

In addition, all children of positive mothers are under continuous assessment and risk evaluation by their primary care doctor. This follow-up includes tests for AntiHBs at 7 and 18 months of age. Children not reaching 10UI/1 are reactivated with a dose , with a new determination of antibodies one month later. In the United States, serologic follow-up is done between 9 and 15 months of age 9.

Efficacy of Hepatitis B Vaccination for Children of Infected Mothers (7 months of age, Cuba 1992 -2001)

Results	AgHBs	%
Negative	395	94.5
Positive	23	5.5
Total	418	100

Effectiveness from 96% to 99%

Impact of Vaccination on Acute Hepatitis B Cuba 1992 -2003

Age group	1992	2003	Reduction %
-1 Year	4	0	100
1-4	62	0	100
5-9	135	0	100
10-14	148	1	99.3
Subtotal	349	1	99.7
15-24 Years	652	9	98.6
25-59	1,100	78	92.9
60-64	39	2	95.0
65 y +	51	7	86.3
Total	2,194	97	95.6

Source: National Registry of Notifiable Diseases, Ministry of Public Health Statistics Division, Havana. USA's Goals for 2010: Comparison to Cuba's Results by 2003

Source: Epidemiology and Statistics Divisions, Ministry of Public Health, Havana

CONCLUSIONS:

1. The United States and Cuba are the two producers of recombinant vaccines against Hepatitis B recognized by the WHO in the Americas.
2. Both countries started the application of a universal vaccination strategy against Hepatitis B on newborns in 1992.
3. The main programmatic differences are found in perinatal prevention, with different vaccination dosages for children of positive mothers, and in the use of Hyper-Immune Gamma Globulin.
4. In the vaccination of risk groups, Cuba has given priority to protection before exposure. Several campaigns have been carried out to achieve high coverage levels in a short period, especially among these groups.
5. Vaccination by cohorts of 8- and 14 year-old children initiated in 1994 ensured the protection of the Cuban population under 20 by 2000.
6. Cuba's coverage of one-year-old children is much higher than that in the United States.
7. The reduction of incidence of this acute disease for all ages reaches 95.6 % in Cuba and 67 % in the United States (years 2003 and 2002 respectively).
8. In 2001, Cuba reached the goals the United States has set for 2010.

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INTRODUCTION

In 1992 the WHO advised all countries with a hepatitis B prevalence higher than 5 % to start universal vaccination of infants in 1995 and all countries with a lower prevalence to start universal vaccination in 1997. Because the estimates from the United Kingdom are based on a sample size of 18 876 respondents we expect those estimates to be much more certain [9]. Therefore, we chose parameter values based on the estimates given in [2] for the United Kingdom (see Table 1 c) and the estimates for the heterosexual populations as follows. Transmission of hepatitis B virus results from exposure to infectious blood or body fluids containing blood. It is 50 to 100 times more infectious than human immunodeficiency virus (HIV).[26] Possible forms of transmission include sexual contact,[27] blood transfusions and transfusion with other human blood products,[28] re-use of contaminated needles and syringes,[29] and vertical transmission from mother to child (MTCT) during childbirth. As of 2018, there are eight medications licensed for the treatment of hepatitis B infection in the United States. These include antiviral medications lamivudine, adefovir, tenofovir disoproxil, tenofovir alafenamide, telbivudine, and entecavir, and the two immune system modulators interferon alpha-2a and PEGylated interferon alpha-2a.