Viral hepatitis prevention board meeting
Prevention and control of viral hepatitis in the Russian Federation: lessons learnt and the way forward. Moscow, 25-26 October 2018

Achievements and new prospects of the hepatitis B massive preventive vaccination programme in the Russian Federation

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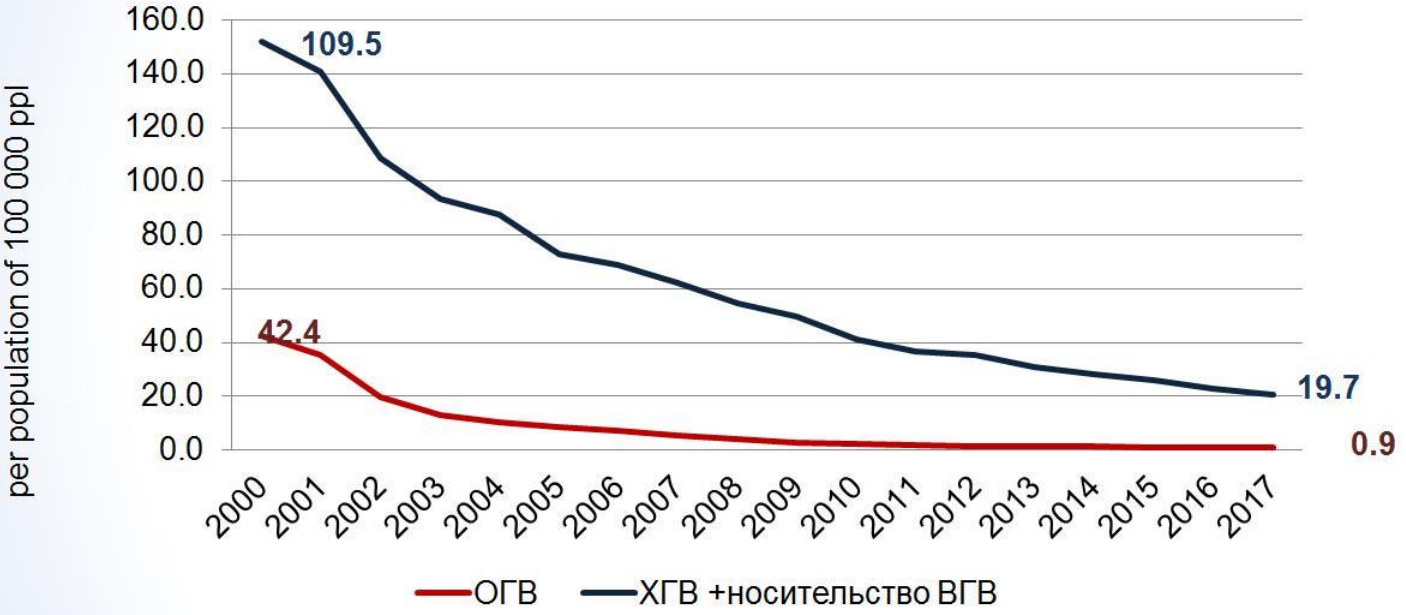
Improvement in the monitoring of viral hepatitis B in the Russian Federation

- **Reduction in the morbidity rate of acute viral hepatitis B and in the detection frequency of chronic viral hepatitis B**



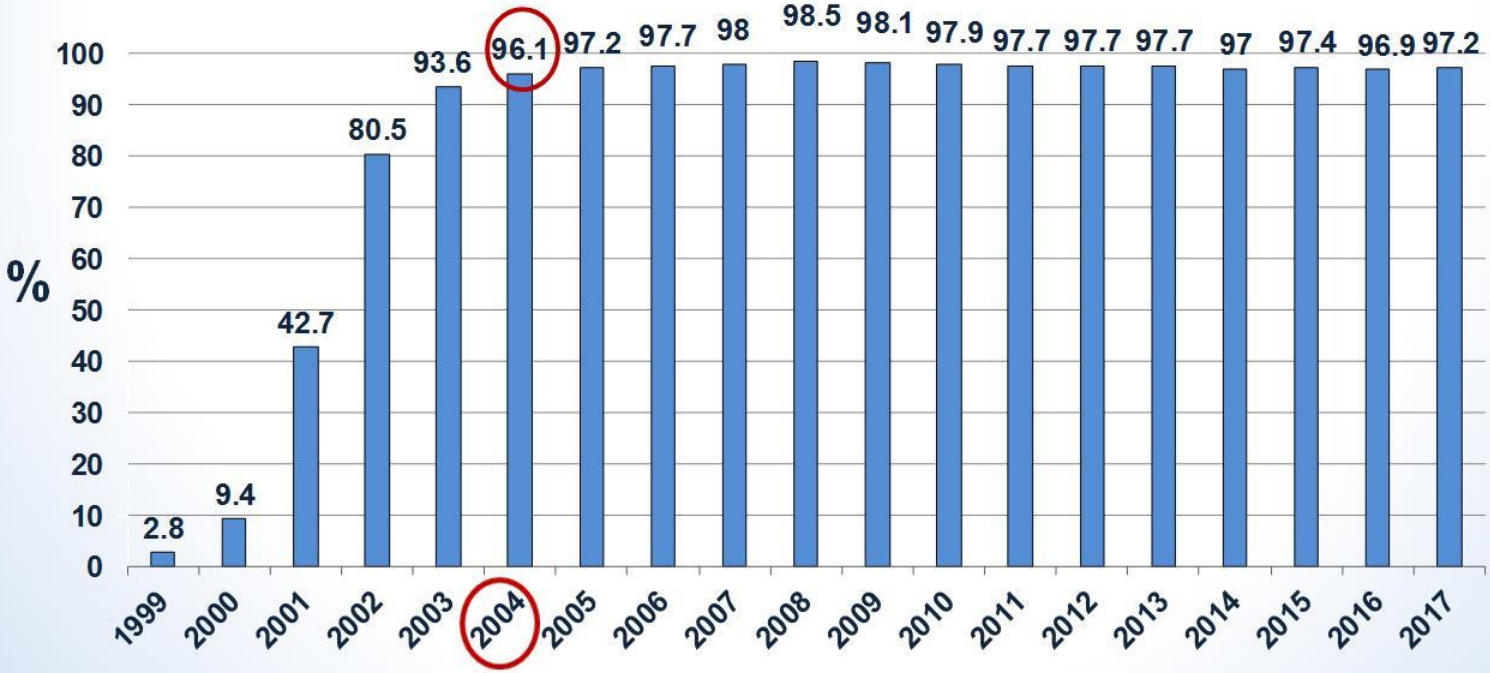
In the Russian Federation in 2017:

- **in 9 subjects (10,6%) of the RF there were registered no cases of acute viral hepatitis B disease** (in 2016 – in 11 subjects, in 2015 – in 12 subjects)
- **among children up to 17 years old there were registered 12 cases of acute viral hepatitis B** (in 2015 and 2016 each, there were registered 22 cases of acute viral hepatitis B)

Progress in HBV Control in Russia

- Wide coverage of infants by triple vaccine doses, i.e. over 95% since 2004

Coverage of 1 year-olds by triple HBV vaccine doses in RF in 1999-2017 гг.

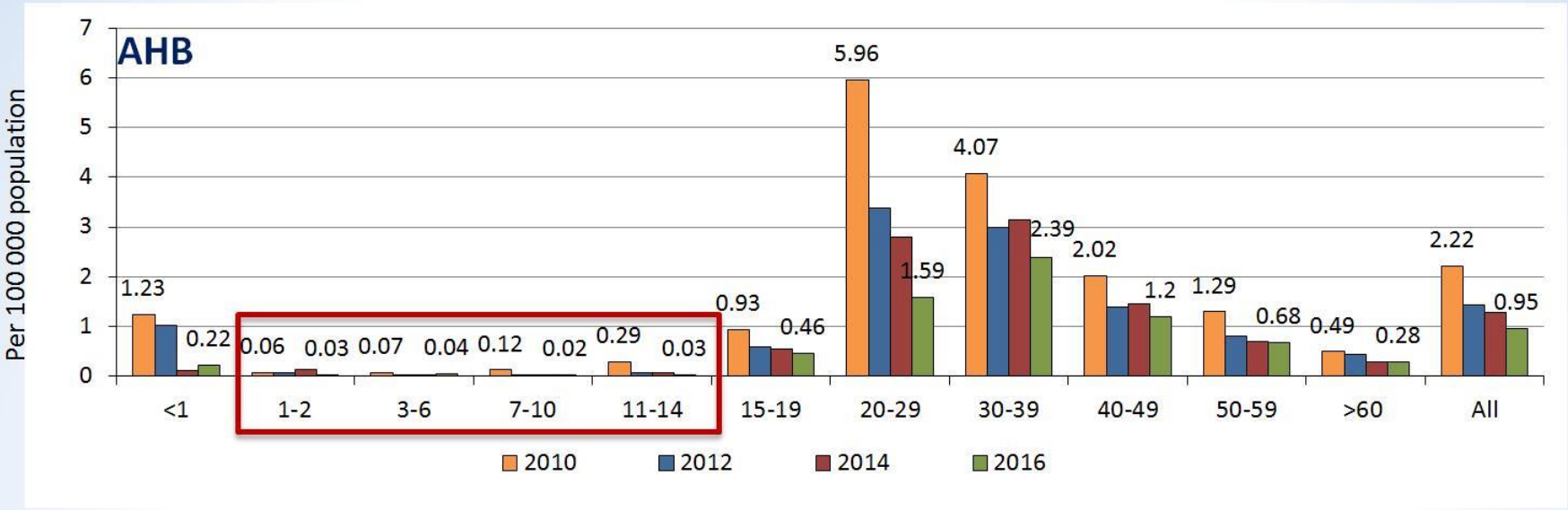


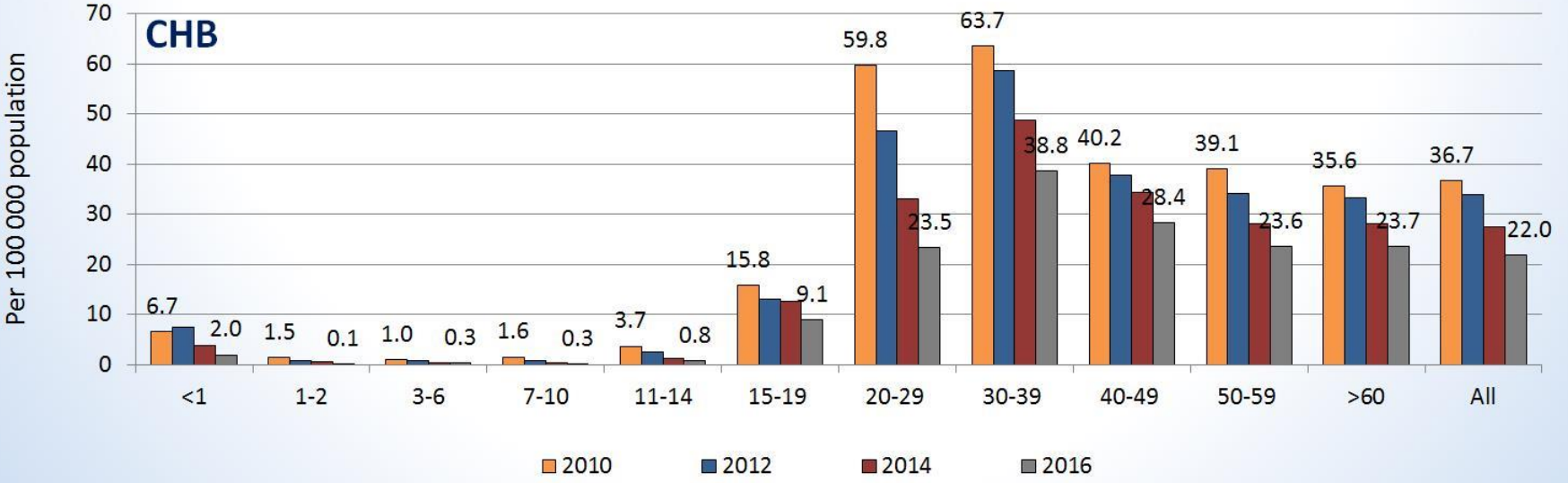
HBV immunized (accrual) and acute (ОГВ) and chronic (ХГВ) HBV cases, registered in 2000-2017

- In 2015-2017, Russia immunized against HBV annually over 3 000 000, including over 1 500 000 children.
- Total immunized since campaign start is about 100 MM.

RF population coverage of triple vaccine doses against hepatitis B in 2012 and 2016

Incidence of acute and chronic Hepatitis B in different age groups, Russia, 2010-2016





Hepatitis B Vaccination Program in Russia

1996

- vaccination of newborns and children at high risk of infection (born to HBsAg-positive mothers, household contacts, children in orphanage, frequently transfused, hemodialysis);
- vaccination of adults from high risk groups (health care workers, medical students, frequently transfused and hemodialysis patients, household contacts, PWID);

1997

- **universal vaccination of newborns;**

2001

- universal vaccination of all children 13 years of age;

2006

- catch-up vaccination of children from 1 to 17 years of age and adults from 18 to 35 years of age;

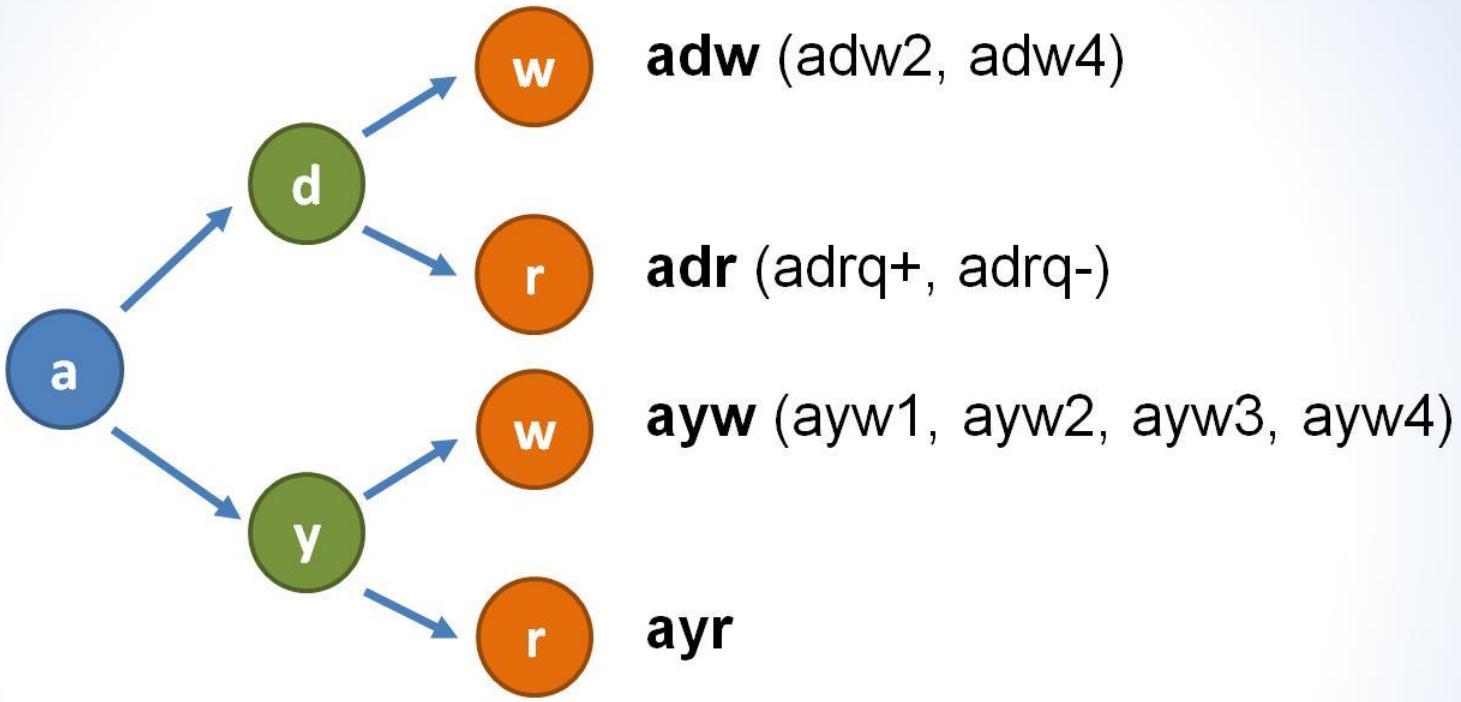
2007

- catch-up vaccination of adults from 18 to 55 years of age.

HBV monovaccines used in RF, included in the Public Formulary

Medication/ vaccine	Producer
HBV, recombinant, yeast	Kombiotech, Russia
Regevac B	Binnopharm, Russia
HBV, recombinant	Microgen, Russia
Biovac B	Vokhard Ltd., India
HBV, recombinant (rDNA)	Serum Institute of India Ltd.
Shanvac B	Shanta Biotechnix Ltd., India
Eberbiovac	Ebere Biotech C.A., Cuba
Endgerics B	GSK Biologicals, Belgium
Euvax B	El G Джи Life Sciences Ltd., South Corea

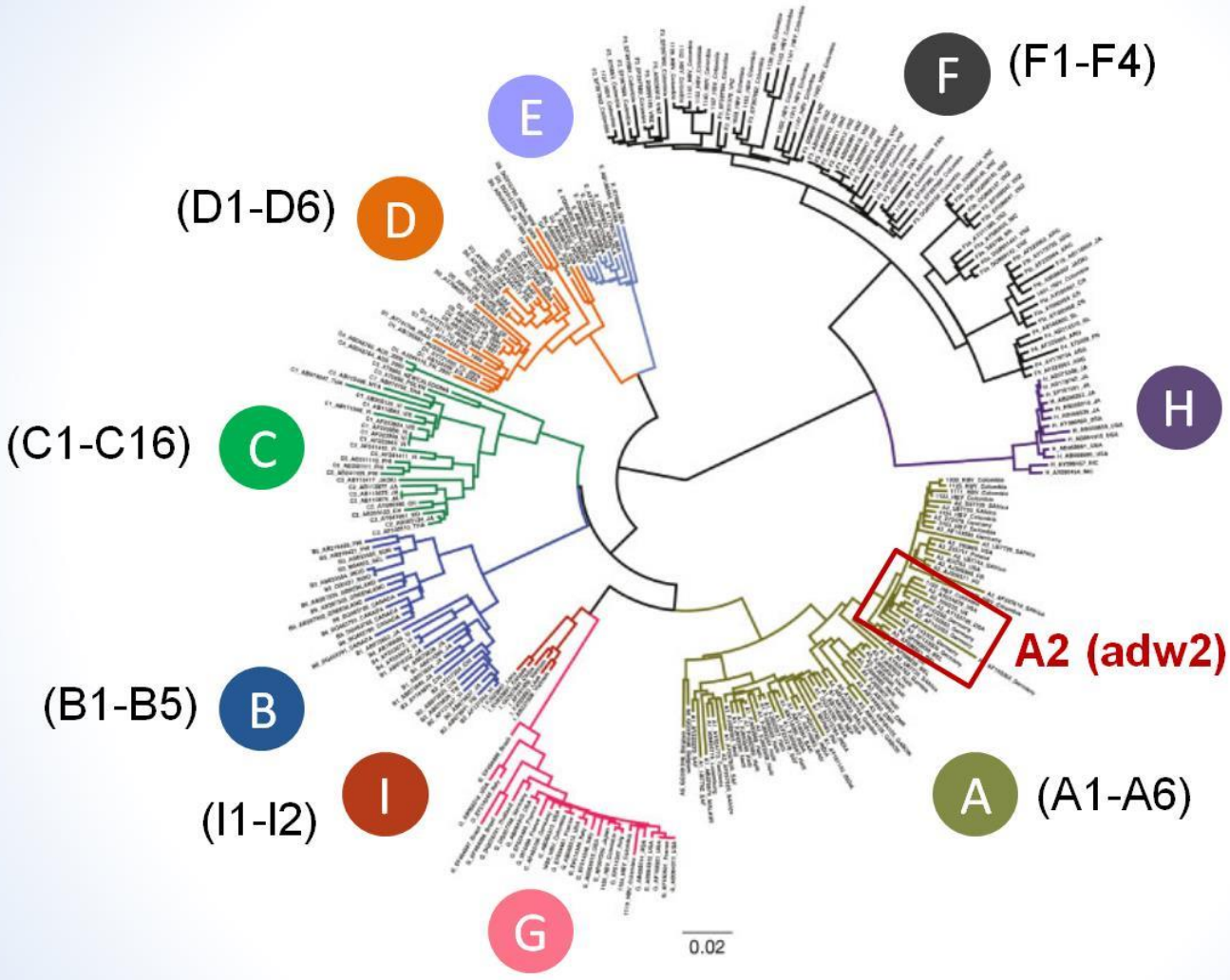
HBV sero- sub-types



"a" HBsAg determinant is present in all serotypes and located within 124-147 amino acid positions of the main solvent-exposed region.
122 and 160 amino acids determine affiliation to d/y and w/r subtypes respectively.

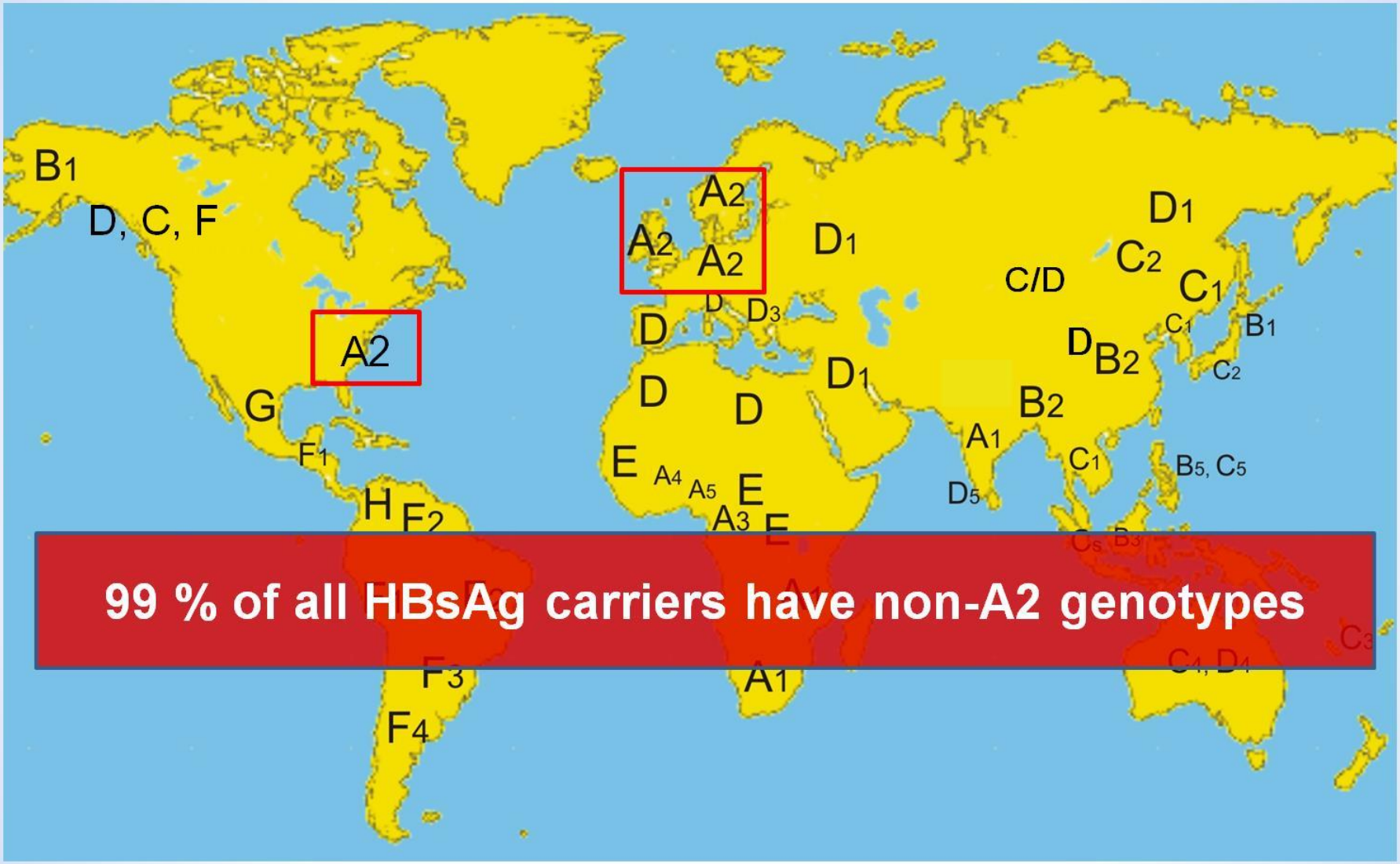
Le Bouvier GL et al. J Infect Dis. 1971; 123:671-675; Courouce AM et al. Bibl Haematol. 1976; 42:89-127; Okamoto H et al. J Virol. 1987; 61:3030-3034; Okamoto H et al. J Gen Virol. 1988; 69:2575-2583.

Hepatitis B virus genotypes



Kramvis A. Intervirology; 2014; 57:141-150; Alvarado-Mora MV. et al. Antiviral Therapy 2013; 18:459-465

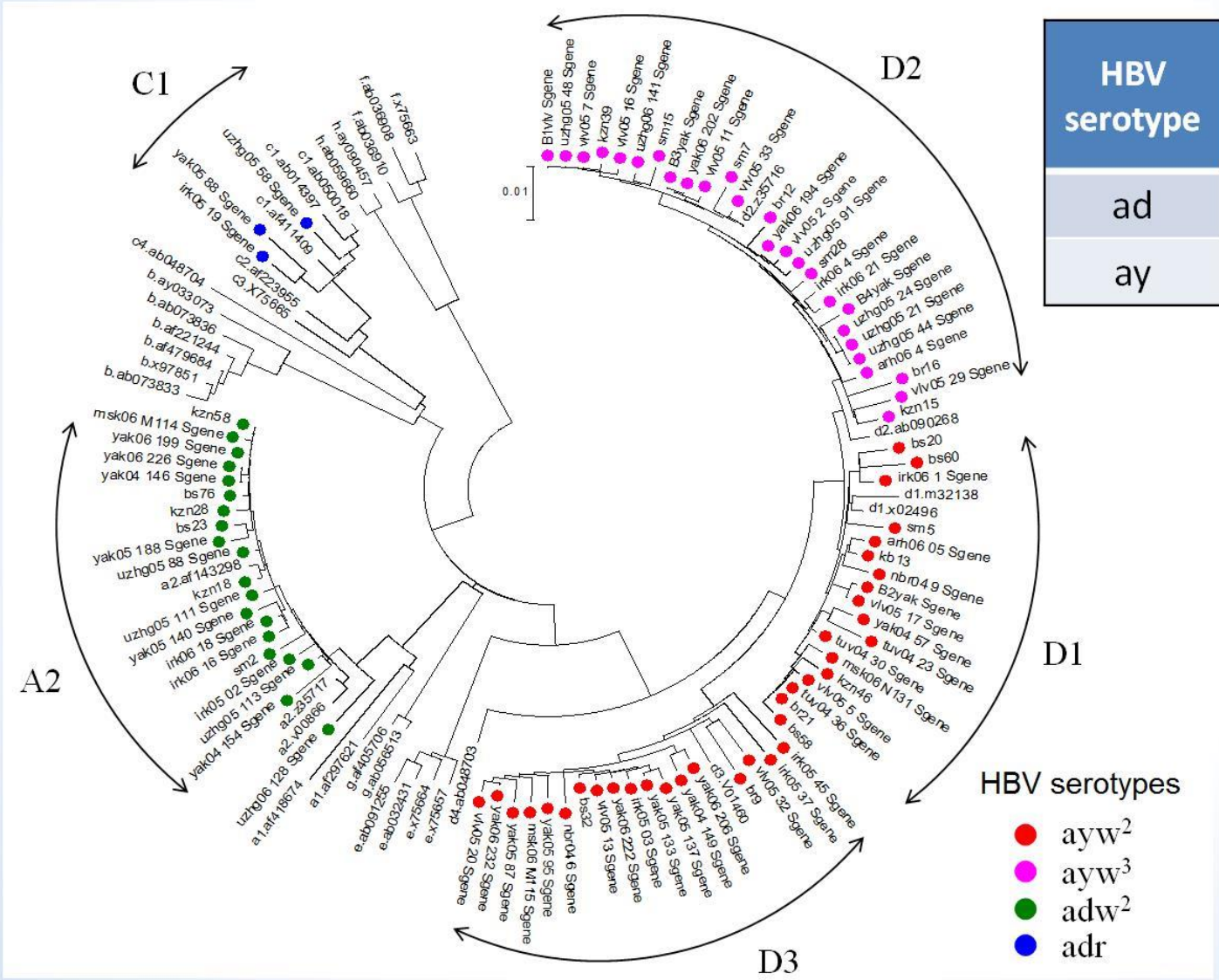
Worldwide distribution of HBV Genosubtypes



99 % of all HBsAg carriers have non-A2 genotypes

Schaefer S., Gerlich W. Textbook of Hepatology, 2007, p. 825; Kramvis A. Intervirology; 2014; 57:141-150

Prevalence rate of HVB subgenotypes and serotypes, circulating in the RF



HBV serotype	Detection frequency in the RF
ad	15%
ay	85%

Is the current prophylactic hepatitis B vaccination satisfactory?

International decision makers:

Yes, > 90 % protection rate

Problems: Nonresponders, mother to child transmission

But: Asymptomatic break-throughs are frequent

Gerlich WH. Indian J Med Res. 2017 Apr;145(4):414-419.

Evidence of protection against clinical and chronic hepatitis B infection 20 years after infant vaccination in a high endemicity region. (Thailand)

Poovorawan et al. (2011) J Viral Hepat 18:369–375

During the 20-year follow-up, no subject acquired new chronic HBV infection or clinical hepatitis B disease." (N=222)

12.8 % asymptomatic HBV infections in the 2nd decade

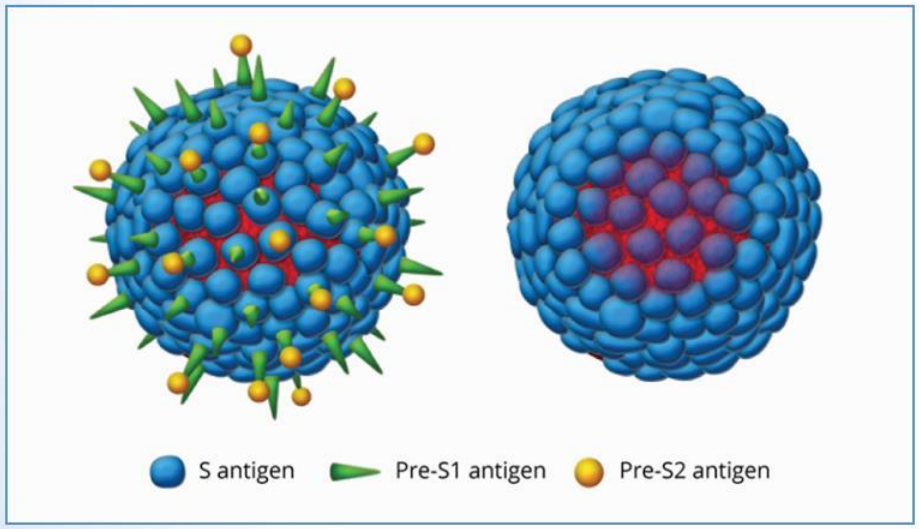
As many as in the unvaccinated control group

Gerlich WH. Indian J Med Res. 2017 Apr;145(4):414-419

HBV monovaccines used in RF, included in the Public Formulary

Medication/ vaccine	Producer	Antigenic composition as per instruction
HBV, recombinant, yeast	Kombiotech, Russia	ay and/or ad
Regevac B	Binnopharm, Russia	ayw
HBV, recombinant	Microgen, Russia	ad
Biovac B	Vokhard Ltd., India	
HBV, recombinant (rDNA)	Serum Institute of India Ltd.	
Shanvac B	Shanta Biotechnix Ltd., India	
Eberbiovac	Ebere Biotech C.A., Cuba	
Endgerics B	GSK Biologicals, Belgium	
Euvax B	El G Джи Life Sciences Ltd., South Corea	

G3 HBV vaccines



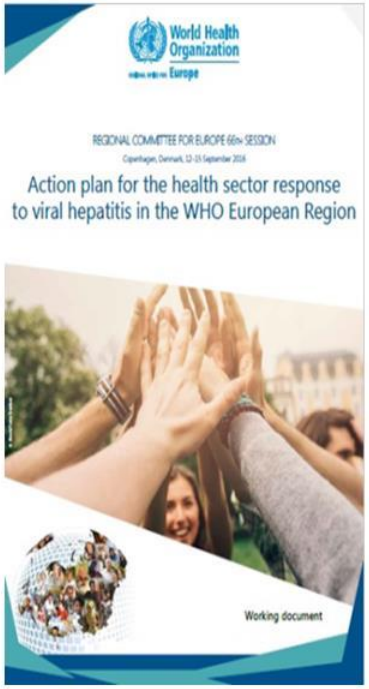
1. **G1 vaccines were blood plasma -** received from donor plasma, taken from patients with chronic viral liver lesion and were of a danger to health. So there use was stopped.

2. **G2 recombinant vaccines -** use HBV envelope S protein, synthesized in yeast fungi cells.

3. **G3 vaccines –** contain one (Pre-S2) or two (Pre-S1 и Pre-S2) extra envelope proteins and were developed in mammals' transfectant cells.

Hepatitis B control in the WHO European region

Objective 3:
Hepatitis B control through immunization



Target indicators for hepatitis B control:

- Children coverage with triple doses of vaccines against hepatitis B – 95%
- Coverage of interventions, focused on prevention of inter-generational transmission of hepatitis B from mother to child – 90%
- Prevalence of HBsAg ≤0,5% in vaccinated cohorts

More data required to confirm regional goals achieved

- **The reports do not inform about newborns' coverage by 1st HBV vaccine dose (not later than 24 h on delivery).**
  - This value is important to evaluate timely newborns' coverage, and decision is required to change or improve the reporting.

- **Data is required on chronic HBV prevalence among the immunized.**
  - The more than a decade-old studies were not representative due to inadequate n tested, or "comfortable" sampling used.

Objectives of the survey

Primary objective:

- To estimate the seroprevalence of hepatitis B surface antigen (HBsAg) in school children attending 5th grade in the Russian Federation on the national and federal district level.

Secondary objectives:

- To estimate the distribution of different marker combinations (anti-HBs, anti-HBc, HBsAg)
- To describe vaccination coverage based on patient files

Sampled population:

- Children attending 5th school grade in the Russian Federation

Sample Size

Estimates:

- 1 national estimate
- 8 federal districts estimates

	Expected prevalence	Upper precision bound	Sample size
Per federal district	0.30%	0.94%	1,474
Total (8 federal districts)	0.30%	0.50%	11,788

Following values were used for the sample size calculations:

$\alpha = 0.05$

Power = 80%

Design effect = 1.7

Summary

1. **The fairly wide coverage by HBV immunization:**
   - infants (under 1 year of age): over 95%.,
   - children from 0 to 17 years old – over 95%,
   - adults - approximately 70%

   to lower acute HBV incidence below 1,0/ 100 000

2. **It is required:**

- **Ensure federal registration and record-keeping of 1st injection to newborns during first 24 h after birth.**
- **Improve HBV vaccines.**

- Develop and use G2 vaccines, containing RF-relevance ay and ad antigen determinants, which is preferred versus HBsAg ay vaccine.
- Develop and implement in health care the G3 HBV, containing max. set of antigen determinants being are relevant to circulating virus genotypes.

- **Improve HBV immunization programme effectiveness evaluation.**

- Conduct serosurveys to determine HBsAg prevalence among the immunized in RF.

Thank you for your attention!