Hepatitis B Infection
Iranian programs for Control

Who should Screen for HBV in Iran?
Who should vaccinate against HBV in Iran

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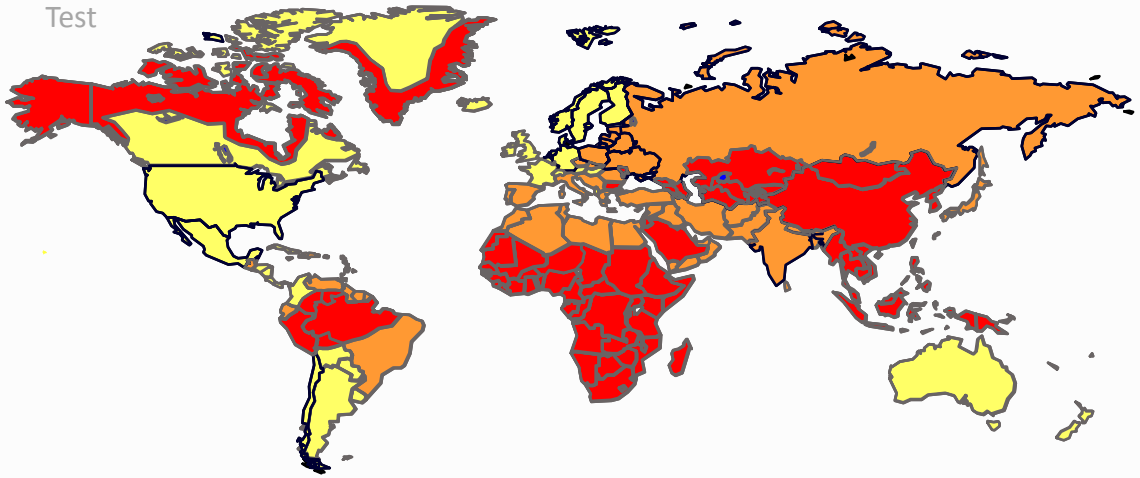
Geographic Distribution of Chronic HBV Infection

Test



- Many of the data relating to the global distribution of HBV are over 10 years old
- More recent data suggest that this is an over-simplification
- **There is an increasing trend towards HBeAg-negative HBV in many areas**
- Global distribution of HBV is being affected by population movements from high prevalence areas

Chronic infection prevalence	Past infection prevalence	Predominant age at infection
≥ 8% – High	40– 90%	Perinatal and early childhood
2–7% – Intermediate	16– 55%	Early childhood
< 2% – Low	4– 15%	Adult

HBV: A Global Problem

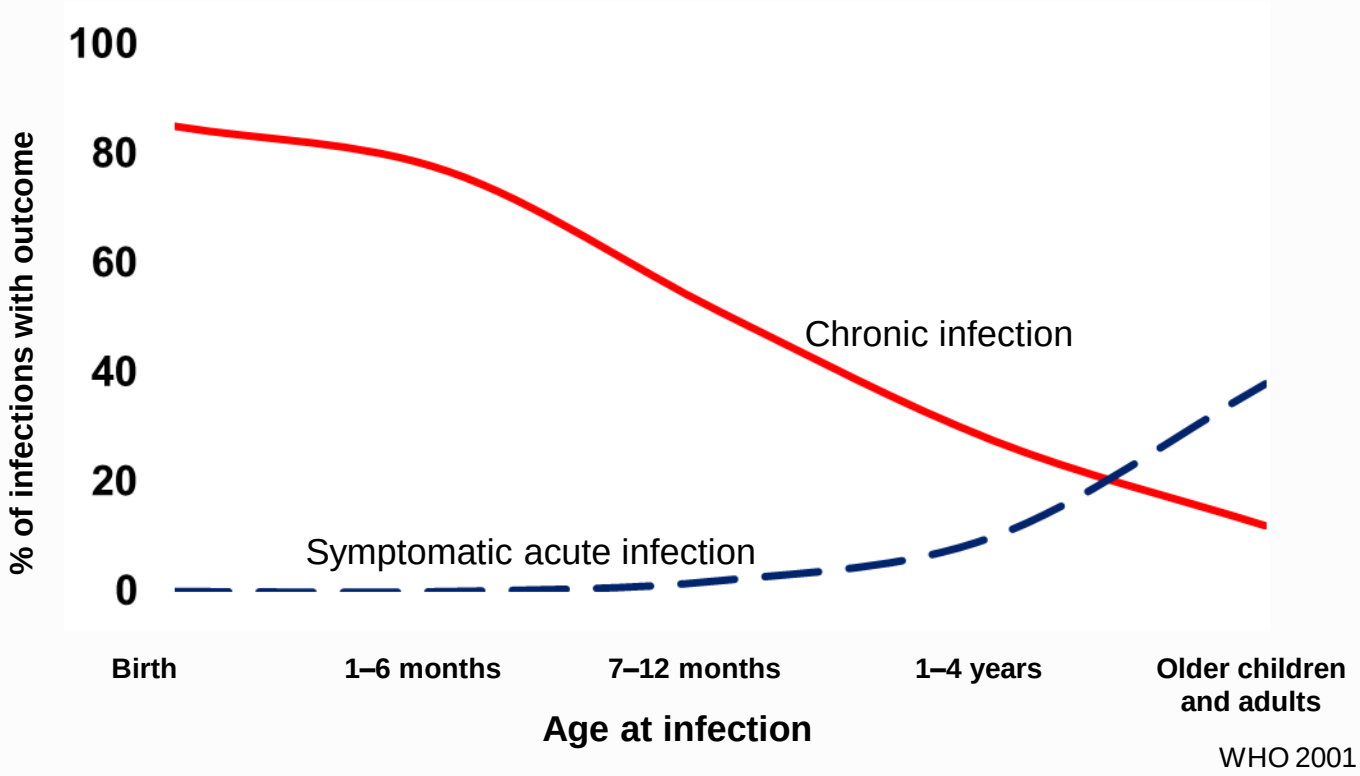
- Hepatitis B infection is of major global importance
  - **large pool of patients**
  - Serious nature of disease **squeal**
  - Difficult/impossible to **eradicate** once chronic infection established
  - Significant **economic** burden
- Urgent actions are needed to address the problem
  - **Immunization programmes**
  - **Therapeutic intervention for chronically-infected patients**
  - **Education initiatives to prevent transmission infection**

Transmission of HBV

- HBV is transmitted via contact with **blood or body fluids** in the same way as HIV. However, HBV is 50–100 times more infectious than HIV

- **Vertica**l : **Infected mother-to-infant**
- **Horizontal**
  - **Household exposure**
  - **Multiple sexual partners**
  - **Intravenous drug use**
  - **Contaminated blood transfusion**
  - **Contaminated needle and due to infected medical devices**

Outcome of HBV Infection According to Age at Time of Infection



WHO 2001

Risk Factors of HBV Infection / Iran

Risk factors in chronic hepatitis B-Iran

- Age, male sex, history of contact with hepatitis B infected subject, extramarital sexual activity, injection drug use, major surgery, experimental dentist visit and some jobs (**police, barber, and driver**) were found to be independent risk factors

- Risk factors in Iranian blood donors (1996-2000) in 2447 HBsAg + cases:
- **HBs Ag positivity in mother** and family, transfusion history, male gender, hospital admission, sexual contact, and more age were risk factors.

- Sali SH, Bashtar R, **Alavian SM**. Risk Factors in Chronic Hepatitis B Infection: A Case-control Study. Hepat Mon 2005

Alavian et al. Evaluation of Hepatitis B Transmission Risk Factors in Tehran Blood Donors [In Persian]. Govaresh 2004;3(9):169-75.

Characteristics of HBV Patients in Iran

- Most aged 30-50
- Most are not know about their infection- Asymptomatic
- We can not find the infected patients with history alone
- Variations are attributable to the differences in environmental factors and socioeconomic factors

National Vaccination of Infants in Iran

- In I.R. Iran mass vaccination of neonates against HBV infection was started from **1993** as a national program in routine neonates care.

- This program is supposed to affect the prevalence rate of HBV infection thorough the country and decrease the rate of infection.

Alavian SM, Fallahian F, Bagheri-Lankarani K. The Changing Epidemiology of Viral Hepatitis B in Iran. J Gastrointestin Liver Dis. 2007

Effectiveness of hepatitis B vaccination in children of chronic hepatitis B mothers

- Two group exposed and non-exposed:
- **Zero HBs Ag positivity** , 64.4% HBs Ab positivity , 1.2% HBc Ab positivity in non-exposed group.
- **14.3% HBs Ag positivity,** 49.5% HBs Ab positivity, 29.9% HBc Ab positivity in exposed group
- **Vaccination alone stopped transmission in the high-risk group partly, rather than completely.**

Table 1 - Prevalence of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and hepatitis B core antibody (HBcAb) in exposed and unexposed groups.

Serologic markers	Unexposed* (N=87)		Total n (%)	Exposed† (N=97)		Total n (%)	RR	95% CI
	Positive n (%)	Negative n (%)		Positive n (%)	Negative n (%)			
HBsAg	0	87 (100)	87 (100)	14 (14.3)	83 (85.7)	97 (100)	13.48	1.8 - 100.02
HBsAb	54 (64.4)	31 (35.6)	87 (100)	48 (49.5)	49 (50.5)	97 (100)	0.76	0.59 - 0.99
HBcAb	1 (1.2)	86 (98.9)	87 (100)	29 (29.9)	68 (70.1)	97 (100)	26.01	3.61 - 186.95

Adibi P, Ghassemian R, **Alavian SM**, et al. Effectiveness of hepatitis B vaccination in children of chronic hepatitis B mothers. Saudi Med J. 2004

Impact of adding HBIG to HBV vaccine for preventing perinatal transmission of the HBV in infants born to HBsAg positive mothers

Comparison of the prevalence of HBsAg, HBsAb, HBcAb, and HBeAg positivity between four groups

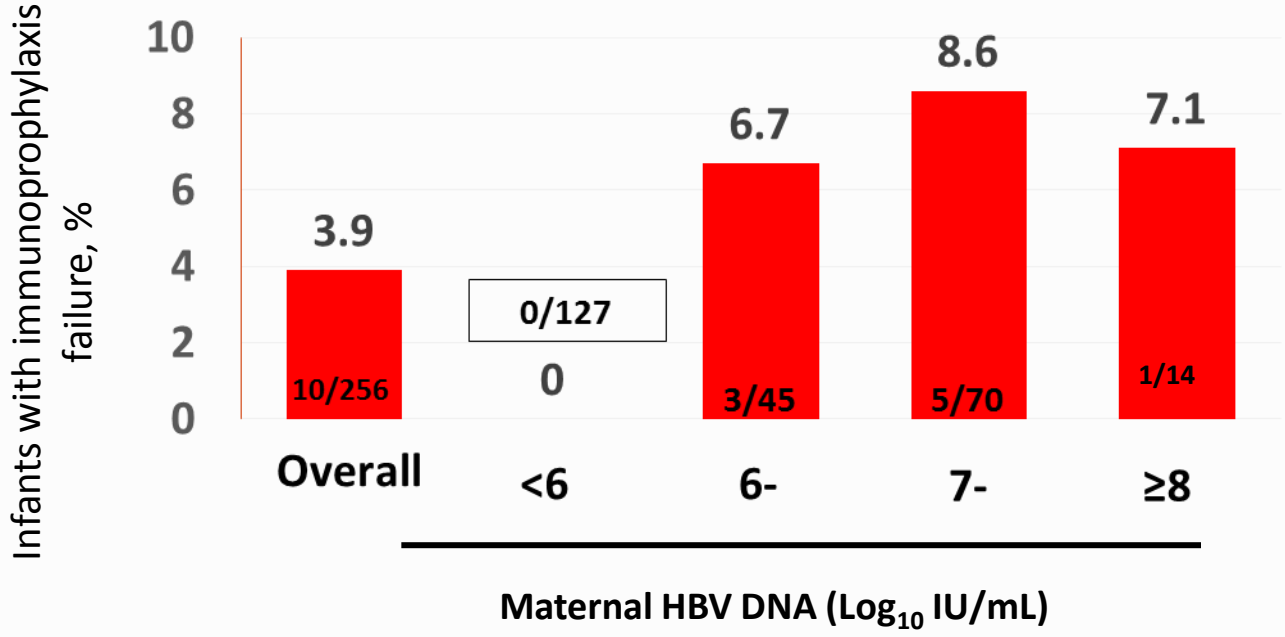
	Neither HB vaccine nor HBIG and aged > 16 No./total (%)	Neither HB vaccine nor HBIG and aged ≤16 No./total (%)	Only HB vaccine No./total (%)	HB vaccine and HBIG together No./total (%)	Sig.
HBsAg(+)	224/399 (56.1)	58/144 (40.3)	15/119 (12.6)	2/55 (3.6)	<0.001
Anti-HBsAb(+)	17/78 (21.8)	15/45 (33.3)	44/64 (68.8)	36/42 (85.7)	<0.001
Anti-HBcAb(+)	230/239 (96.2)	62/73 (84.9)	21/49 (42.9)	12/31 (38.7)	<0.001
Anti-HBs(+)/anti-HBc(+)*	3/23 (13)	4/23 (17.4)	7/23 (30.4)	9/23 (39.1)	NS#
Anti-HBs(+)/anti-HBc(−)[a]	2/38 (5.3)	2/38 (5.3)	16/38 (42.1)	18/38 (47.4)	<0.001
HBeAg(+)	20/59 (33.9)	10/17 (58.8)	6/8 (75)	2/2 (100)	0.041

Adding HBIG to standard HBV vaccination given to the infants of infected mothers significantly decreased the HBV infection rate in this high risk group. Therefore, the role of HBIG is very important.

- **Cohort study; Nov 2001-Dec 2003 with historical controls**
- 823 subjects from 264 families (mothers were HBs Ag positive)
- Children born before March 1993 who received neither HB vaccine nor HBIG and aged over 16 years
- Children born before March 1993 who received neither HB vaccine nor HBIG and aged 16 years or less
- Children after March 1993, HB vaccine in national plan
- Children after March 1993 who received both

Kabir A, **Alavian SM**, Ahanchi N, Malekzadeh R. Combined passive and active immunoprophylaxis for preventing perinatal transmission of the hepatitis B virus in infants born to HBs Ag positive mothers in comparison with vaccine alone. Hepatol Res. 2006

High maternal HBV DNA levels are associated with risk of failure of immunoprophylaxis



Liu CP, et al. Factors associated with mother-to-child transmission of hepatitis B virus despite immunoprophylaxis. Intern Med. 2015

Should antiviral therapy be recommended to reduce risk of perinatal transmission of HBV infection?

1 Yes

2. No.

Yes, the evidence in all studies show benefit without any danger

Treatment Options for HBV in Pregnancy

There is a growing body of literature to support both the safety and efficacy of antiviral therapy initiated in late pregnancy for reduction of MTCT among women in the highest risk for immunoprophylaxis failure (those with HBV DNA levels in the range of **10^7 log copies/mL and higher**). Treatment at **levels <10^6 log copies/mL** do not appear to be indicated unless the pregnant woman has liver disease for which viral suppression is indicated.

Antiviral Agent	FDA Pregnancy Category	Defects/Live Birth When Exposed During First Trimester, % (no./No.)	Defects/Live Birth When Exposed During Second/Third Trimester, % (no./No.)	Advantages/Disadvantages of Using During Pregnancy
Adefovir	C	0 (0/48)	0 (0/0)	• Not recommended
Entecavir	C	0 (2/58)	0 (0/2)	• Not recommended
Lamivudine	C	3.1 (143/4566)	2.8 (204/7193)	• Extensive human safety data • Not a preferred first-line agent in treatment guidelines • Associated with high rates of antiviral resistance
Telbivudine	B	0 (0/10)	0 (0/10)	• Positive human safety data; pregnancy class • Fewer data than lamivudine or TDF • Not a preferred first-line agent in treatment guidelines
TDF	B	2.3 (60/2608)	2.2 (24/1112)	• Extensive human safety data, pregnancy class B

If NA therapy only for prevention of perinatal transmission: May be discontinued within the first 3 months after delivery

EDITORIAL

Hepatitis Monthly 2007; 7(1): 3-5

Ministry of Health in Iran Is Serious about Controlling Hepatitis B

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Hepatitis B is one of the most common infectious diseases globally. It [illegible] cause of acute viral hepatitis in adulthood, chronic [illegible] and estimated that there are 350-400 m[illegible] hepatitis B virus (HBV) carriers w[illegible] whom 75% are Asians. About one-qu[illegible] will eventually die from the conseq[illegible] chronic infection. Iran is located in th[illegible] and has an intermediate prevalence of hepatitis B vaccination program launched in 1992 was not

Mass Vaccination against Adolescents in Iran

Mass Vaccination Campaign against Hepatitis B in Adolescents in Iran

- Since 2007, Iran's Ministry of Health carried out a nationwide hepatitis-B vaccination campaign for 17-year-old adolescents in **four stages**.
- The target population for the four consecutive campaign years (2007–2010) is all 17-year-olds.
- Passive, media-oriented, approach for mass HBV vaccination
- With more than 70% coverage rate.
- A study was done before it and it showed that 12% of these group had history of HBV vaccination and did not came to recive the HBV vaccine
- More than 82% vaccinated

Alavian SM, et al. Mass Vaccination Campaign against Hepatitis B in Adolescents in Iran. Hepat Mon. 2009
Alavian SM, et al.. Hepatitis B vaccination of adolescents: a report on the national program in Iran. J Public Health Policy. 2010

Impact of HBV Vaccination on Prevalence of Hepatitis B Virus Infection in Blood Donors in Iran

Table 2. Overall Prevalence of Hepatitis B virus and Hepatitis C Virus Infections in Nonconcurrent Controls [a]

Age at Donation Time , y	Sample Size	No. of Donors With Positive HBsAg	Prevalence in 10^5 (95% CI)	No. of Donors With Positive HCV Ab	Prevalence in 10^5 (95% CI)
17	321	1	311 (261-361)	0	0
18	4441	27	608 (594-622)	3	67 (60-74)
19	10433	38	364 (355-373)	4	38 (34-42)
20	13595	36	265 (258-272)	2	15 (13-17)
21	17372	60	345 (338-352)	6	34 (31-37)
22	20138	70	347 (340-354)	10	50 (47-53)
Total	66300	232	350 (346-354)	25	38 (36-40)

[a] Abbreviations: CI, confidence interval; HBsAg, hepatitis B surface antigen.

HBV prevalence was significantly lower among blood donors born during 1989-1993, which reflected the positive impact of EPI program and extended mass vaccination against HBV.

Mirrezaie SM, Saber HR, Hajibeigi B, Salekmoghaddam E, Abbasian A, **Alavian SM**. Impact of HBV Vaccination on Prevalence of Hepatitis B Virus Infection Among Volunteer Blood Donors in Tehran-Iran. Shiraz E-Med J. 2014

Recommendations for Control of HBV
Vaccination of High Risk Groups

- Mass vaccination in high risk group and susceptible groups, mainly women at reproductive ages, youth and high risk job workers such as health care providers, barbers, drivers, prisoners and intravenous drug abusers.

A prevention & Control Strategy Should Include Surveillance

Detection of viral hepatitis, Screening and finding the patients in early stages and asymptomatic phase, Educating the people, especially at risk group, Implementing strategies to prevent the transmission to others and start of therapy with good outcome

Monitoring of chronic liver disease

Evaluation of the effectiveness of activities

- Vaccination, Blood screening, Injection safety, infection control, Safe sex, Counseling of injection drug users

Decision making (burden, trends, risk factors)

Avoid heterogeneity in availability/quality of data

New Viral Hepatitis Infections Continue to Occur

- ✓ Horizontal and perinatal transmission
- ✓ Persons who participate in high risk sexual practices
- ✓ Unscreened blood transfusions or blood products
- ✓ Failure to sterilize medical equipment
- ✓ Dental and “traditional” medicine
- ✓ Injection drug users
- ✓ Exposed health care workers
- ✓ Hemodialysis or unsafe injections

Nosocomial Infection

- Transmission generally occurs from patient to patient or from patient to health care personnel via contaminated instruments or accidental needle stick.

- Healthcare workers, particularly surgeons, pathologists, and physicians working in hemodialysis and oncology units, have the highest risks of HBV infection.

Post-exposure Prophylaxis

- Is recommended for all non-vaccinated individuals who are exposed to blood or infectious secretions.
- The first dose vaccine should be given as early as possible and within 12 hours of exposure.
- If the source is known to be HBs Ag positive, one dose of HBIG should be administered at the same time in another site. The other two doses of vaccine should be administered according to the usual schedule.

Who to test for HBV infection

- WHO guidelines recommend offering focused testing to individuals from populations most severely affected by HBV infection.

- -Who are either part of a **population with higher seroprevalence** or have a history of exposure to or high-risk behavior for HBV infection).
- In settings with a ≥2% seroprevalence of HBsAg , it is recommended that all adults have routine access to and be offered testing (**a general population testing approach**).

- Routine HBsAg screening of **all pregnant women** is recommended.

- **Overall, these different testing approaches should make use of existing facility-based or community-based testing opportunities and programmes.**

Progress Toward Eliminating HBV

WHO HBV Elimination Targets

- Goal: **eliminate viral hepatitis** as a public health threat by 2030[1]
- 90% reduction in new chronic viral hepatitis infections
- 65% reduction in mortality related to viral hepatitis

Updated Recommendations	
CDC 2022	**HBV screening** with 3-test panel (HBsAg, anti-HBs, and total anti-HBc) at least once during adults' lifetime[2]
ACIP 2022	All adults aged 19-59 yr should receive **HBV vaccine**[3,4] ▪ Should vaccinate if aged ≥60 yr with risk factors (eg, sexual or household contacts of people who are HBsAg+, previously diagnosed with diabetes, HIV, or chronic liver disease) ▪ May vaccinate if aged ≥60 yr without risk factors


Line 3 - Azadegan


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