ISTM

TranSmedcon2016

सुरक्षित रक्त - हर जीवनदायिनी बूँद से स्वस्थ भारत

Safe Blood - Making every blood drop count for healthy India.

5th Annual Conference of
Indian Society of Transfusion Medicine

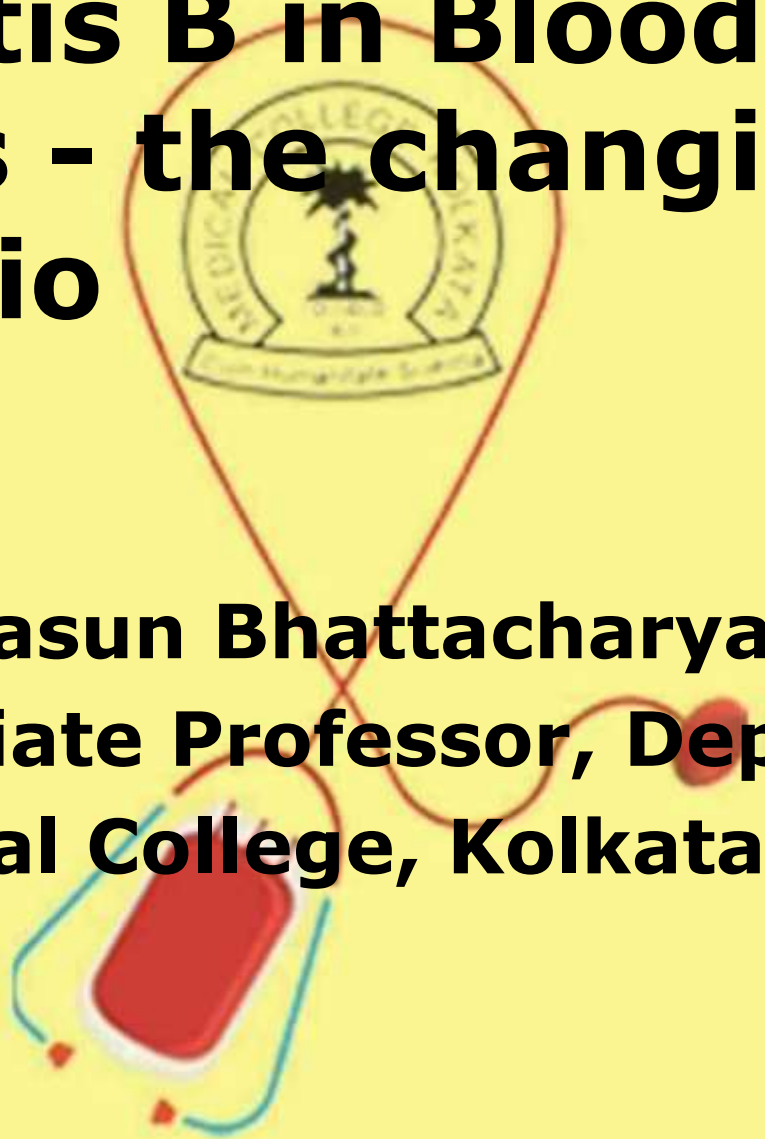
TRANSMEDCON 2016
Safe Blood - Healthy India

Dr. Prasun Bhattacharya
Associate Professor
Dept. of Immunohaematology and Blood Transfusion
Medical College Hospital
Kolkata

Notable Honours/Achievements:

Life Member: ISBTI, ISTM, Member: TRG NACO, Member: Hemovigilance Programme of India, Member: Expert Committee of blood group reagents
NABH Certified Assessor of Blood Bank and blood Transfusion Services

Hepatitis B in Blood Donors - the changing Scenario



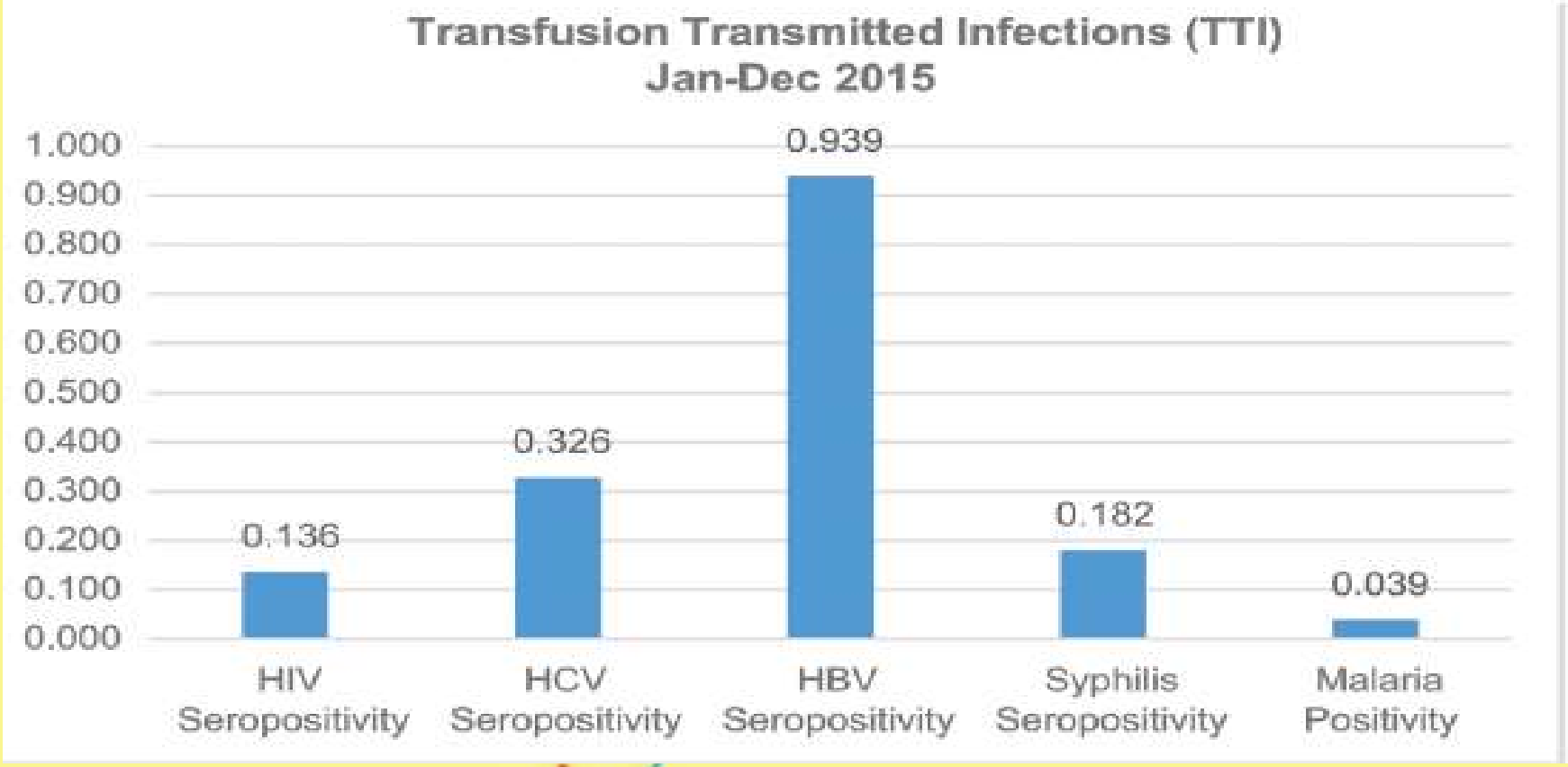
Dr. Prasun Bhattacharya
Associate Professor, Dept. IHBT
Medical College, Kolkata

Hepatitis B virus (HBV) infection is one of the major threats to human health worldwide, especially to the population.....

- 2 billion people worldwide; including an estimated 400 million chronically infected cases
- Individuals with chronic infection have a high risk of developing liver cirrhosis and hepatocellular carcinoma
- Evaluation of data on the prevalence of these transfusion transmitted infections (TTIs), namely HBV, HCV, HIV and syphilis, among blood and plasma donors permits an assessment of the occurrence of infections in the blood donor population and consequently the safety of the collected donations.
- It also gives an idea of the epidemiology of these diseases in the community

Over all prevalence of Hep.B in Blood donors

Fig-6 Transfusion Transmitted Infections (%)



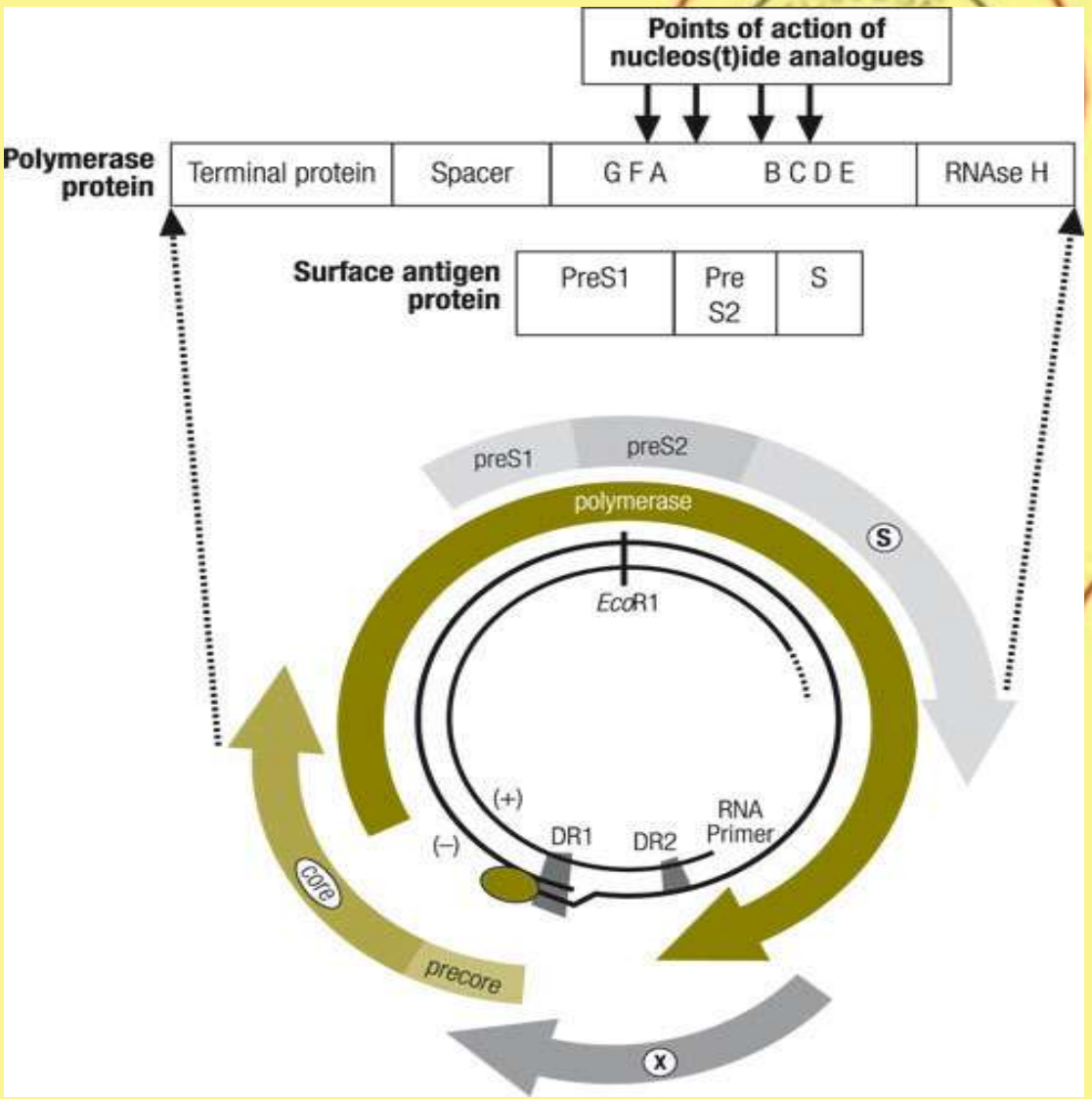
***Assessment of NACO supported blood banks

Studies reported across the country....

Table 3. Comparison of HBsAg prevalence rate in different parts of India

Place	Prevalence	Reference
New Delhi	< 2.5%, 2.23%, 2.76%	3,4,5
Kerala	3.1%	6
Madurai	4%	7
Rural India, Ambajogai Voluntary Replacement	 2.78% 4.84%	8
Maharashtra	2.15%	1
Tamilnadu Voluntary Replacement	 1.37% 2.96%	9
Dehradun	0.99%	10
Kolkatta	1.66	11
Kanpur	2.25%	12
Bangalore	1.86%	13
Coastal Karnataka	0.62%	Present study

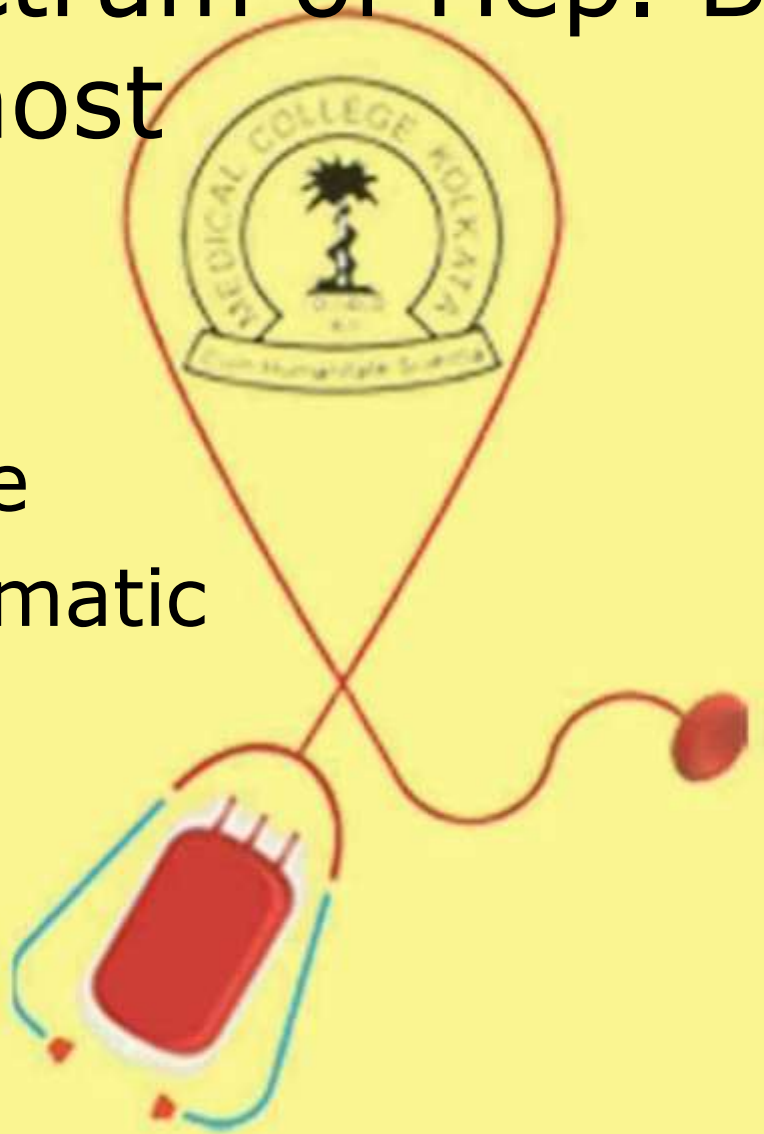
The Hepatitis B viral genome



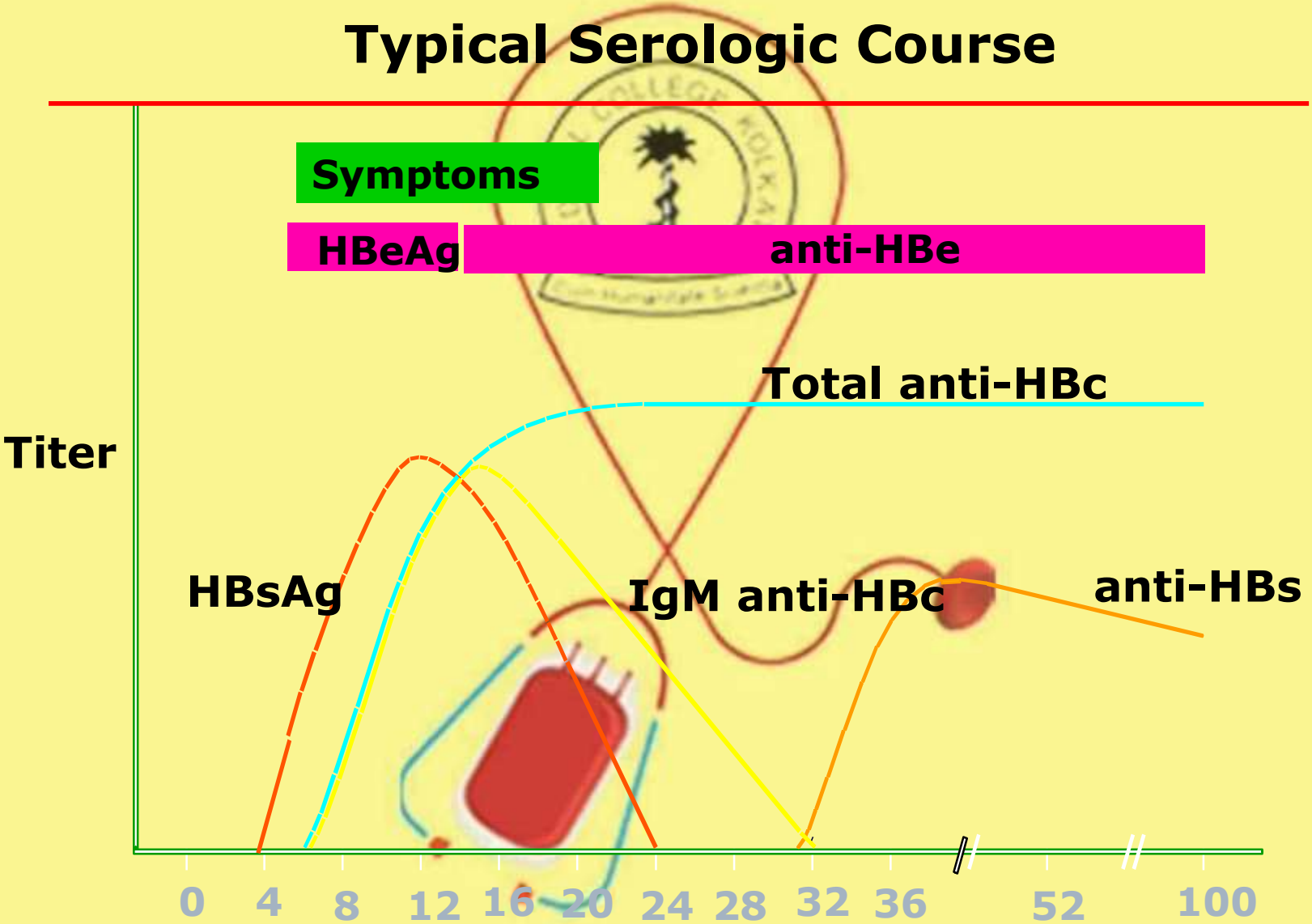
- HBV is a partially double stranded DNA virus of 3.2 kilo base length
- 4 partially overlapping genes: Surface antigen (S), Core (C), Polymerase (P) and carcinogenesis (X) gene
- On comparison of complete genomes with more than 8% nucleotide divergence, on the basis of which 10 genotypes have been defined: HBV/A to HBV/J

The spectrum of Hep. B virus in human host

- Acute
- Chronic
- Fulminate
- Asymptomatic
- Occult



Acute Hepatitis B Virus Infection with Recovery
Typical Serologic Course



**T. Mazzulli
Department of Microbiology
UHN/Mount Sinai Hospital

How we begin our journey 2004 onwards.....

- 2004, a survey of 500 thalassemia day-care patients - **a high prevalence (8%) Hep B** and of them >50% were vaccinated

My questions were

1. Was the pre-vaccination **HBsAg serology** report of these children were correct?
2. Is the vaccine at all is protective?
3. Is the test procedure of donated blood screening is proper?
4. **Is HBsAg screening only is adequate?**

Significant increase in HBV, HCV, HIV and syphilis infections among blood donors in West Bengal, Eastern India 2004-2005: Exploratory screening reveals high frequency of occult HBV infection

Table 1 Prevalence of TTIs among the blood donors in the years 2004 and 2005

	Total No of samples studied		No of samples reactive (%)		Statistical significance	
	2004	2005	2004	2005	RR (95% CI)	*P* values
HBsAg	113051	106695	1448 (1.28)	1768 (1.66)	1.29 (1.21-1.39)	< 0.001
Anti-HCV	113051	106695	314 (0.28)	372 (0.35)	1.26 (1.08-1.46)	0.003
Anti-HIV	113051	106695	262 (0.23)	374 (0.35)	1.51 (1.29-1.77)	< 0.001
Rapid plasma reagin (Syphilis)	113051	106695	772 (0.68)	853 (0.80)	1.17 (1.06-1.29)	0.001

World J Gastroenterol 2007 July 21; 13(27): 3730-3733
World Journal of Gastroenterology ISSN 1007-9327

Detection of HBV DNA in antiHBc positive blood donors

Sam colle in t ye	Total	Number of anti HBc		Number of 'anti HBc	
20					
2005	463	93(20.08%)	17(18.3%)	25(5.4%)	8(32%)
Total	**1027**	**188(18.3%)**	**40(21.3%)**	**61(5.9%)**	**19(31.14%)**

Our study raises serious concerns regarding the safety of the blood supply in our community, even after donor screening for HBsAg. In India transfusion associated HBV is estimated to be approximately 50% or more in multiply transfused patients and approximately 1.5% in post surgical

The uniqueness of Hep. B

In order to contain cost, NAT screening is frequently carried out by pooling samples from 6–50 blood donations. Furthermore, HBV DNA and/or anti-HBc testing are increasingly added to the panel of screening tools. Unlike that of HIV and HCV, the residual risk of HBV infection is not limited to window phase donations (estimated to be of 59 days to HBsAg conversion and of 21 days to a positive ID-NAT result [3]), but extends to those collected from donors with occult HBV infection (OBI). Donors with OBI lack detectable serum HBV surface antigen (HBsAg), but can still transmit infection by transfusion despite low levels of viraemia (<100–200 IU/ml) that often fluctuate over time [4,5]. Given the

Mechanisms of Occult Hepatitis B

Several possible hypothesis had been postulated

- mutations of HBV-DNA sequence
- formation of HBV-containing immune complex
- interference of HBV by other viruses
- integration of HBV-DNA into host's chromosomes
- infection of peripheral blood mononuclear cells by HBV
- **The occurrence of escape mutants interfering with HBsAg synthesis or detection by various serological assays**

Hu KQ. Occult hepatitis B virus infection and its clinical implications. J viral Hepat. 2002;9(4):243-57

van Hemert et al; in 2008 proposed an evolutionary scenario for occult HBV infection. They identified a novel RNA splicing event (deleting nucleotides **2986-202**) that abolishes surface protein gene expression without affecting polymerase, core or X-protein related functions. This **2986-202** splicing generates intracellular virus particles devoid of surface protein

Occult hepatitis B infection: an evolutionary scenario. Virol J. 2008;5:146

Hepatology Research 2009; 39: 53–59 doi: 10.1111/j.1872-034X.2008.00403.x

Original Article

Frequency and distribution of hepatitis B virus genotypes among eastern Indian voluntary blood donors: Association with precore and basal core promoter mutations

Avik Biswas,[1] Partha K Chandra,[1,2] Sibnarayan Datta,[1] Rajesh Panigrahi,[1] Arup Banerjee,[1,3] Shekhar Chakrabarti,[4] Kalidas Biswas,[5] Dipak Patra,[5] Prasun Bhattacharya,[6] Kuntal Biswas[5] and Runu Chakravarty[1]

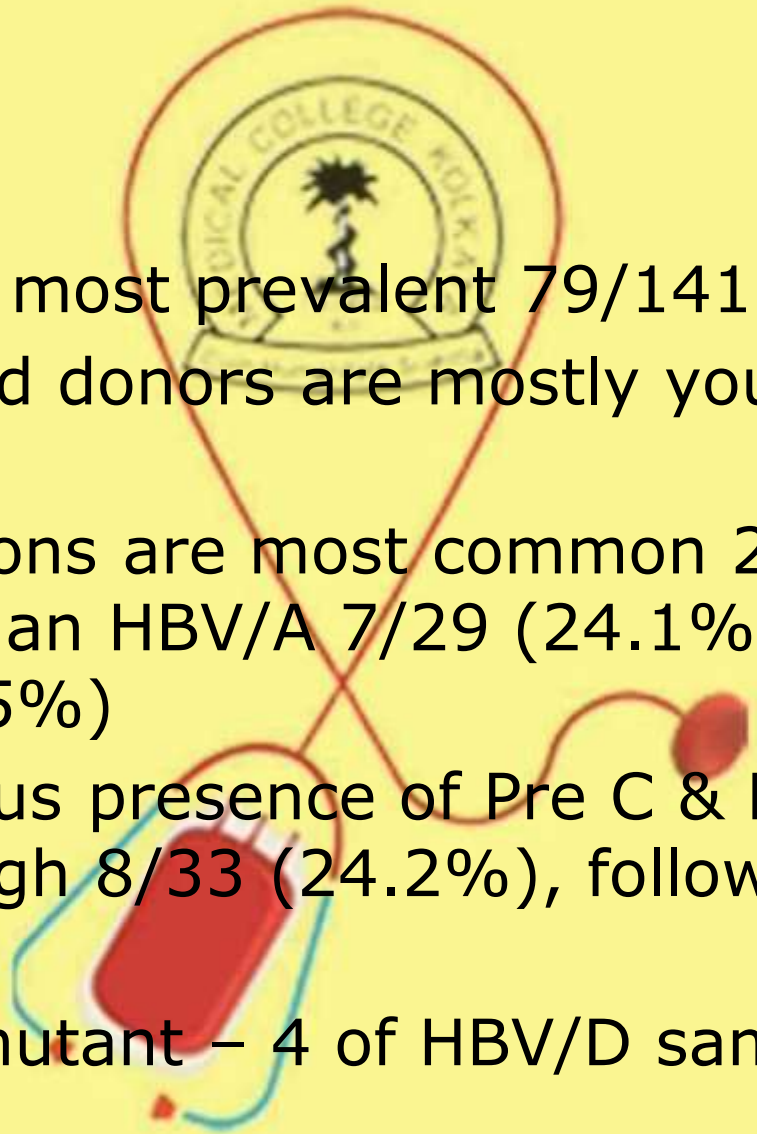
[1]*ICMR Virus Unit,* [4]*National Institute of Cholera and Enteric Diseases,* [5]*Medical College and Hospital,* [6]*Institute of Blood Transfusion Medicine and Immunohematology, Kolkata, India,* [2]*Department of Pathology & Lab Medicine, Tulane University School of Medicine, New Orleans, Louisiana 70112, and* [3]*Division of Infectious Diseases and Immunology, Saint Louis University, St. Louis, Missouri 63104, USA*

Table 1 Demographic, biochemical and virological characteristics of the blood donors

Variables	Total	Genotype		
		HBV/A	HBV/C	HBV/D
N (%)	141	29 (20.6)	33 (23.4)	79 (56.0)
Age (year)†	31.8 ± 9.4	31.9 ± 9.1	28.9 ± 8.8‡	33.0 ± 9.5‡
Sex (male/female)	135/6	29/0	30/3	76/3
ALT value†	36.6 ± 15.1	40.8 ± 9.1	32.7 ± 17.9	35.9 ± 16.0
HBeAg positive (%)	16 (11.3)	4 (13.8)	4 (12.1)	8 (10.1)
HBV-DNA† (log_{10} copies/ml)	5.39 ± 1.25	5.14 ± 1.14	5.94 ± 1.74	5.21 ± 1.01

†Mean ± SD (standard deviation).
‡HBV/C versus HBV/D, $P = 0.03$.
ALT, alanine aminotransferase

Results



- HBV/D was most prevalent 79/141 (56%)
- HBV/C blood donors are mostly young (18 -25 yrs)
- BCP mutations are most common 24/33 (72.7%) in HBV/C than HBV/A 7/29 (24.1%) and HBV/D 17/79 (21.5%)
- Simultaneous presence of Pre C & BCP mutation in HBV/C is high 8/33 (24.2%), followed by HBV/D 6/79.
- Wild type mutant – 4 of HBV/D samples

The diversity of chronic hepatitis B virus infections within blood donors in England and North Wales 2005 through 2010

TABLE 1. Ethnicity of chronically infected donors according to HBV genotype*

Donor demography	All		Genotype A		B		C		D		E	
Total	304		52	(20)	24	(8)	15	(5)	119	(45)	94	(32)
Ethnicity†												
Number	259		51		24		14		110		94	
White-British	21	(8)	9	(43)	0	(0)	1	(5)	10	(48)	1	(5)
White-Other	45	(17)	15	(33)	0	(0)	0	(0)	29	(64)	1	(2)
Black-African	65	(25)	12	(18)	0	(0)	0	(0)	1	(2)	52	(80)
Chinese	28	(11)	0	(0)	19	(68)	9	(32)	0	(0)	0	(0)
Indian/Pakistani/Bangladeshi	48	(19)	3	(6)	0	(0)	0	(0)	45	(94)	0	(0)
Asian-Other	34	(13)	4	(12)	4	(12)	4	(12)	22	(65)	0	(0)
Mixed and other	18	(7)	8	(44)	1	(6)	0	(0)	9	(50)	0	(0)

* Categorical variables are expressed as number (%) and were analyzed using the chi-square test.
† Excludes five donors with unknown ethnicity.

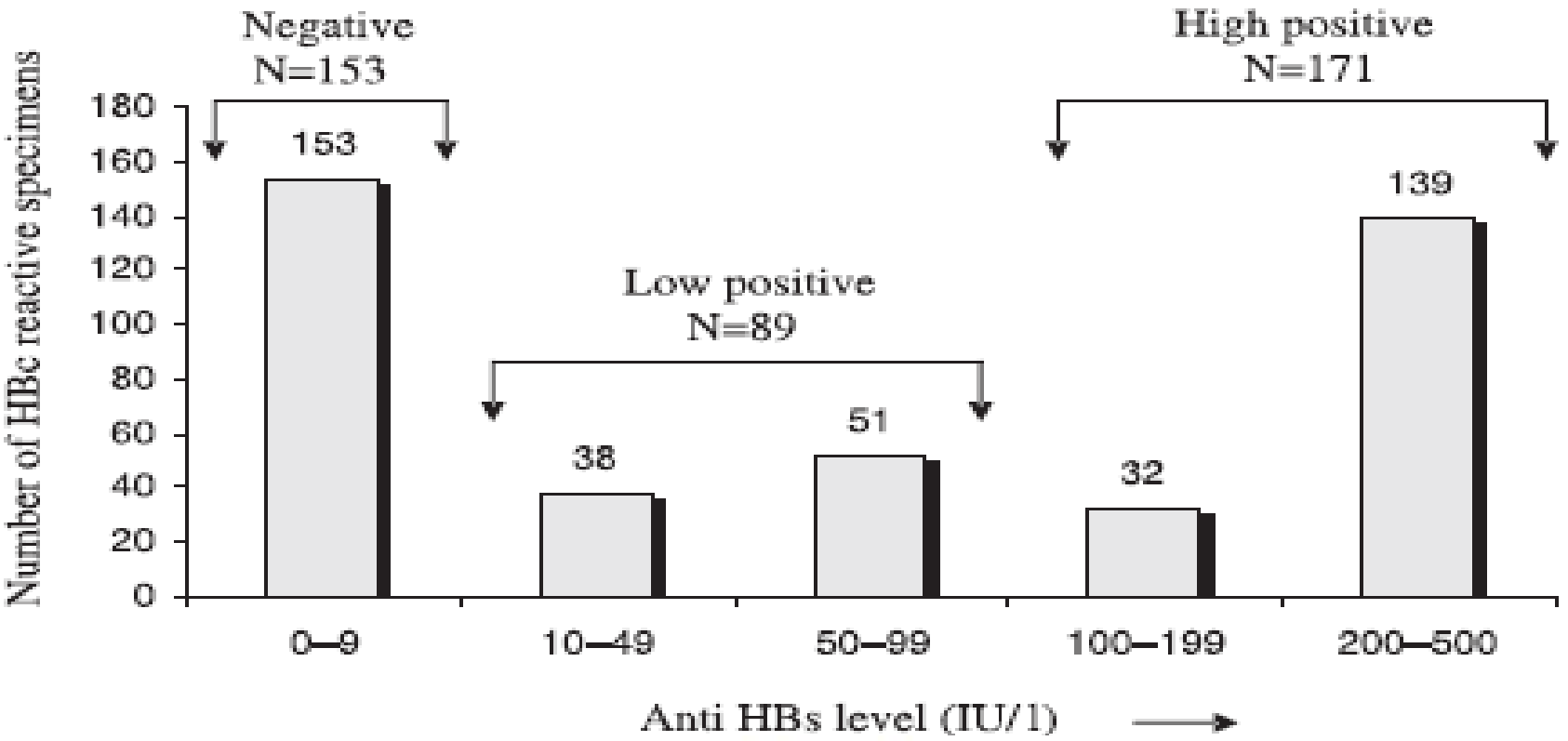
Possibilities of Post-transfusion Hep. B in-spite of HBsAg negative screening

(a) Sero non reactive donor (WP; early phase HBV infection).
(b) The donor is a typical OBI carrier with a wild type of virus in which replication activity and gene expression are suppressed.
(c) The donor is infected with variant HBV strains (S-escape mutant) that are replication competent but produce abnormal surface proteins which are not recognized by the commercially available HBsAg detection kits.

Serological characterization of occult hepatitis B virus infection among blood donors in India

Veena Doda *, Satyam Arora, Tapannidhi Kirtania

Significance of anti-HBc screening of blood donors & its association with occult hepatitis B virus infection: Implications for blood transfusion



*Department of Medicine, Maulana Azad Medical College, University of Delhi, New Delhi, India

Conclusion:

- A high percentage of anti-HBc in the donor population shall lead to a high discard rate

Conclusions: Viraemic blood donations from occult HBV infection carriers remain undetected by current minipool HBV DNA screening, and transfusion transmission of HBV continues to occur in susceptible patients. More effective individual HBV DNA screening and/or tests for antibodies to HBV core antigen should be considered to improve blood safety.

Poor efficacy of nucleic acid testing in identifying occult HBV infection and consequences for safety of blood supply in Italy

THANK YOU