Molecular epidemiology of HBV in SSA

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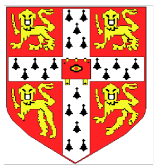
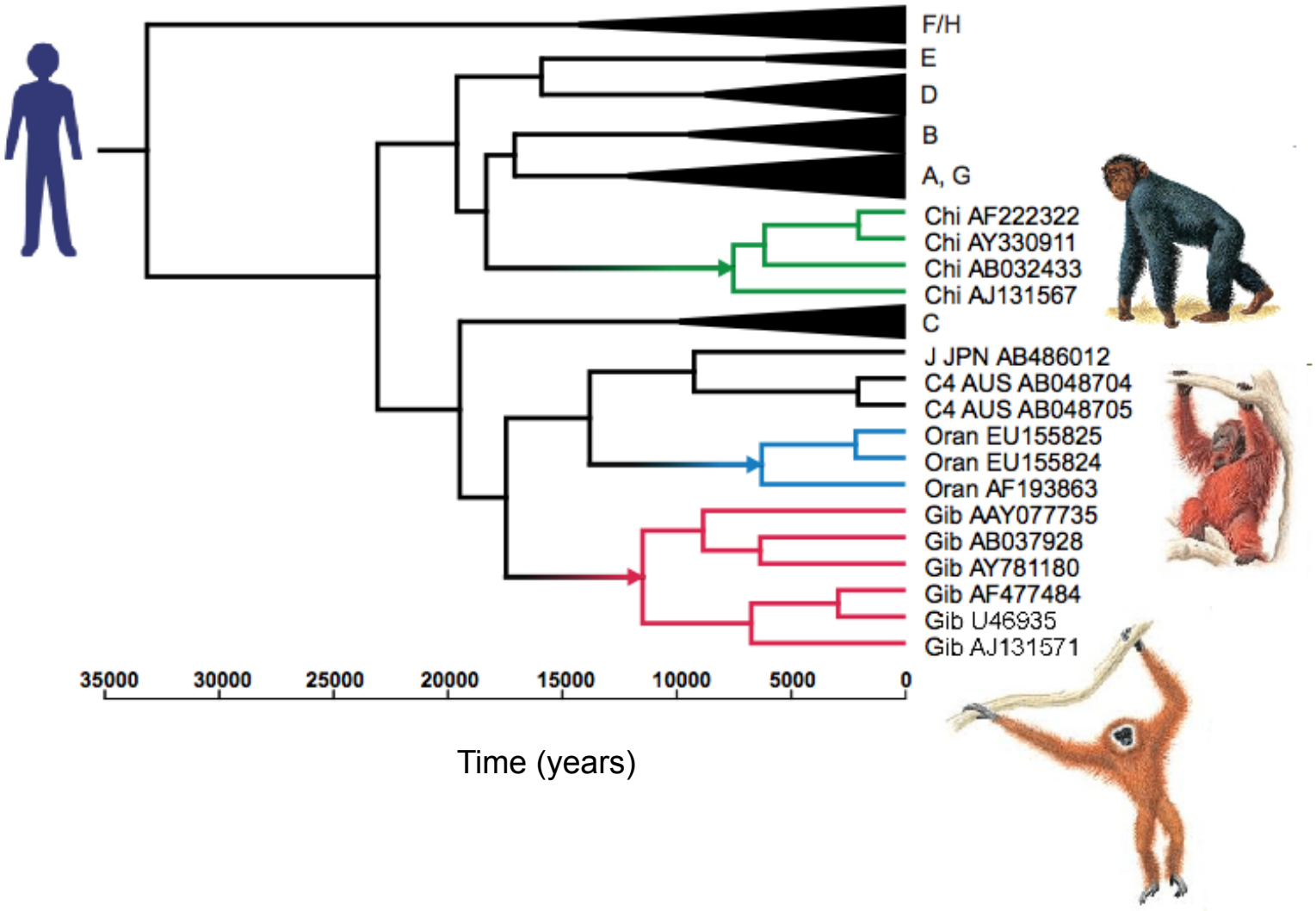
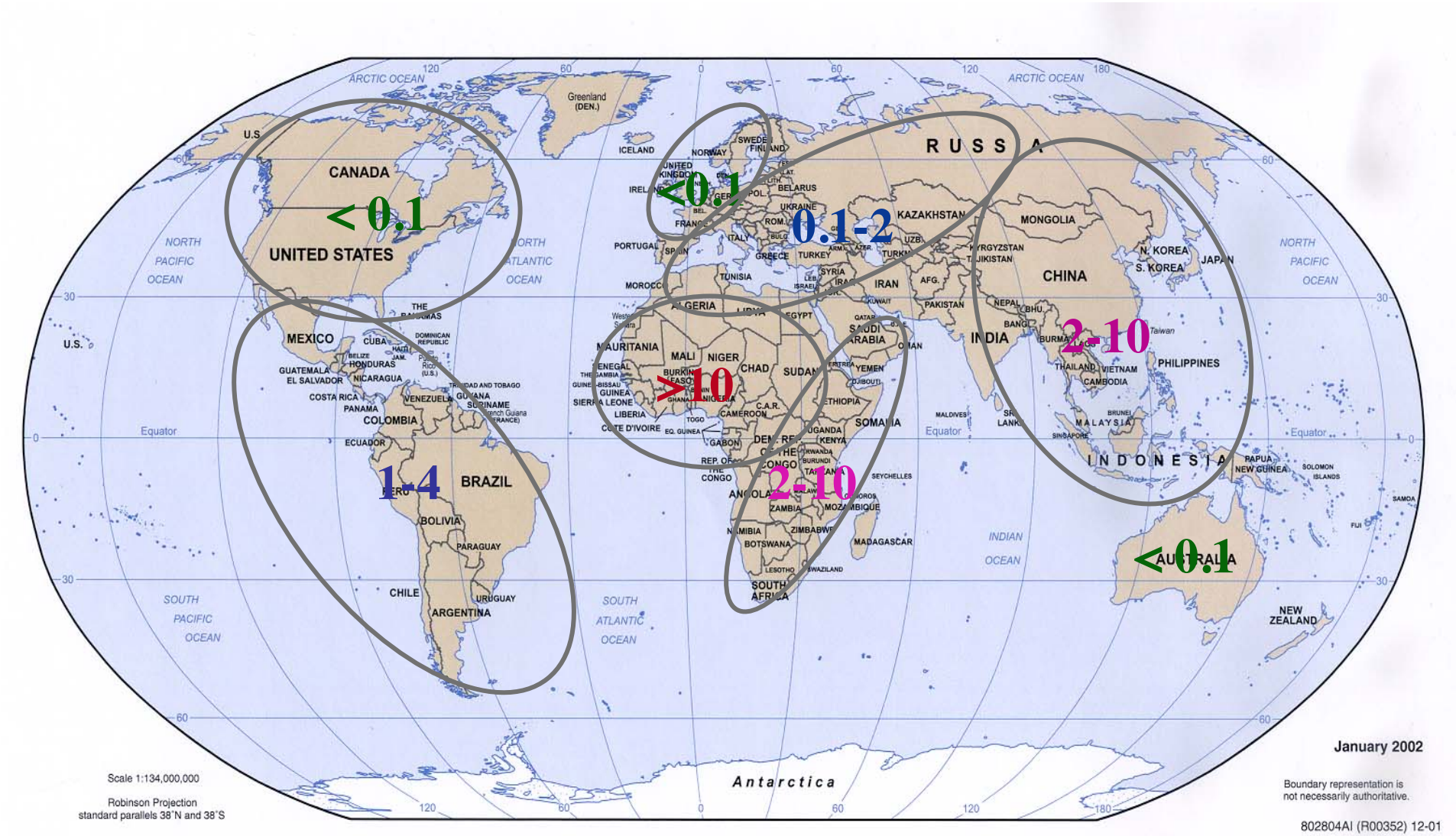


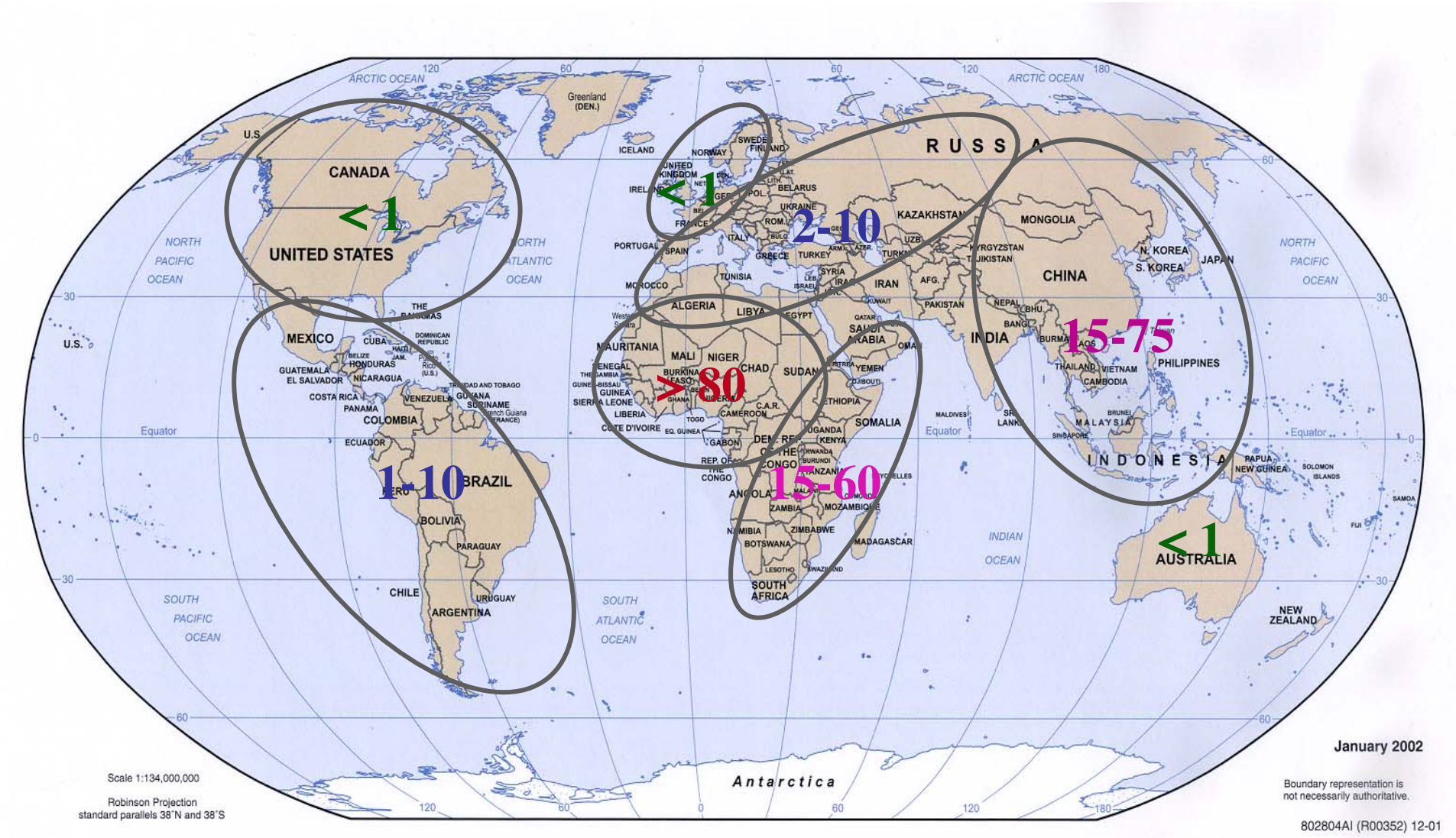
Phylogenetic analysis of human and ape HBV over time of evolution (Paraskevis D et al. Hepatol 2013)



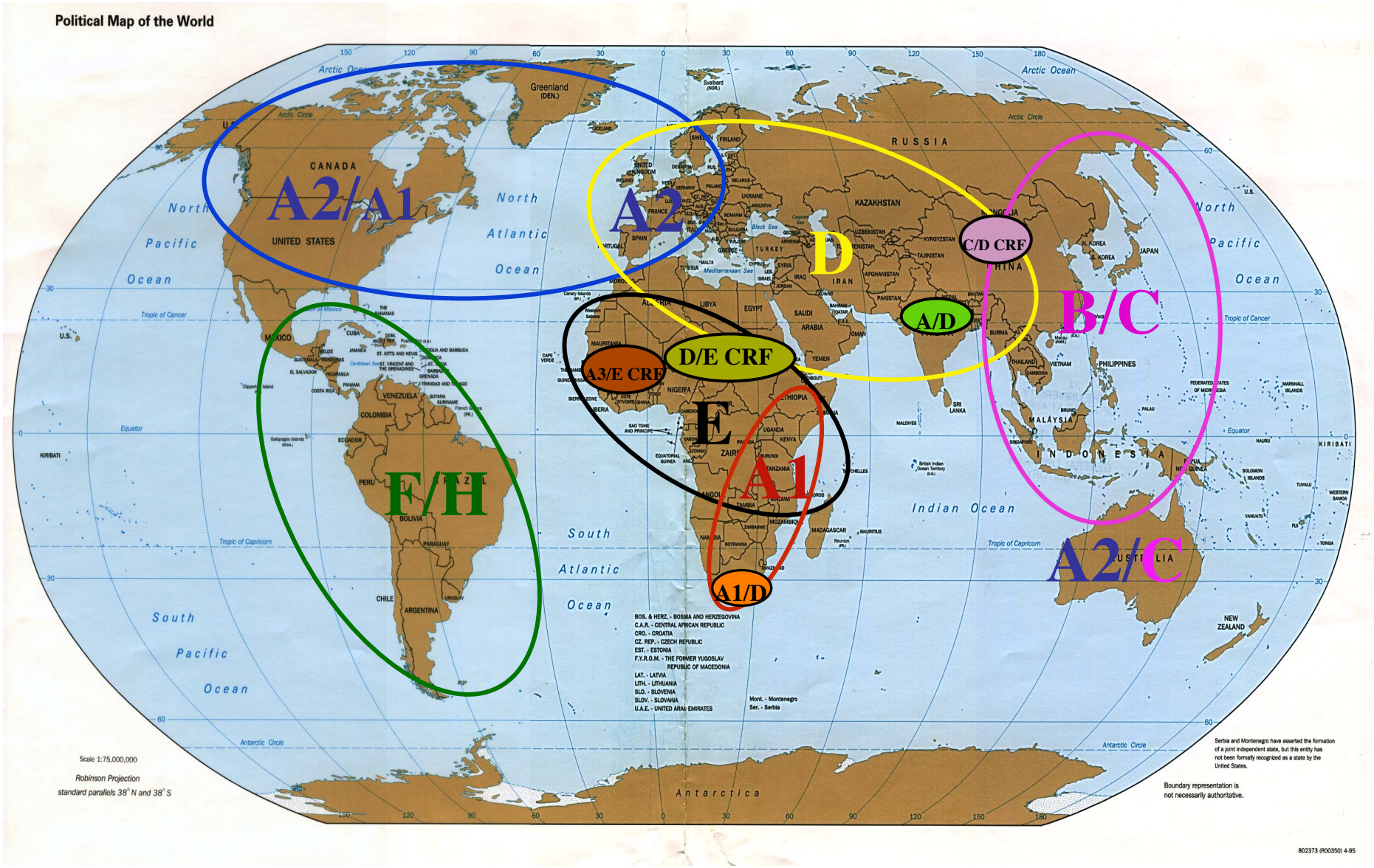
Prevalence of HBsAg in the world

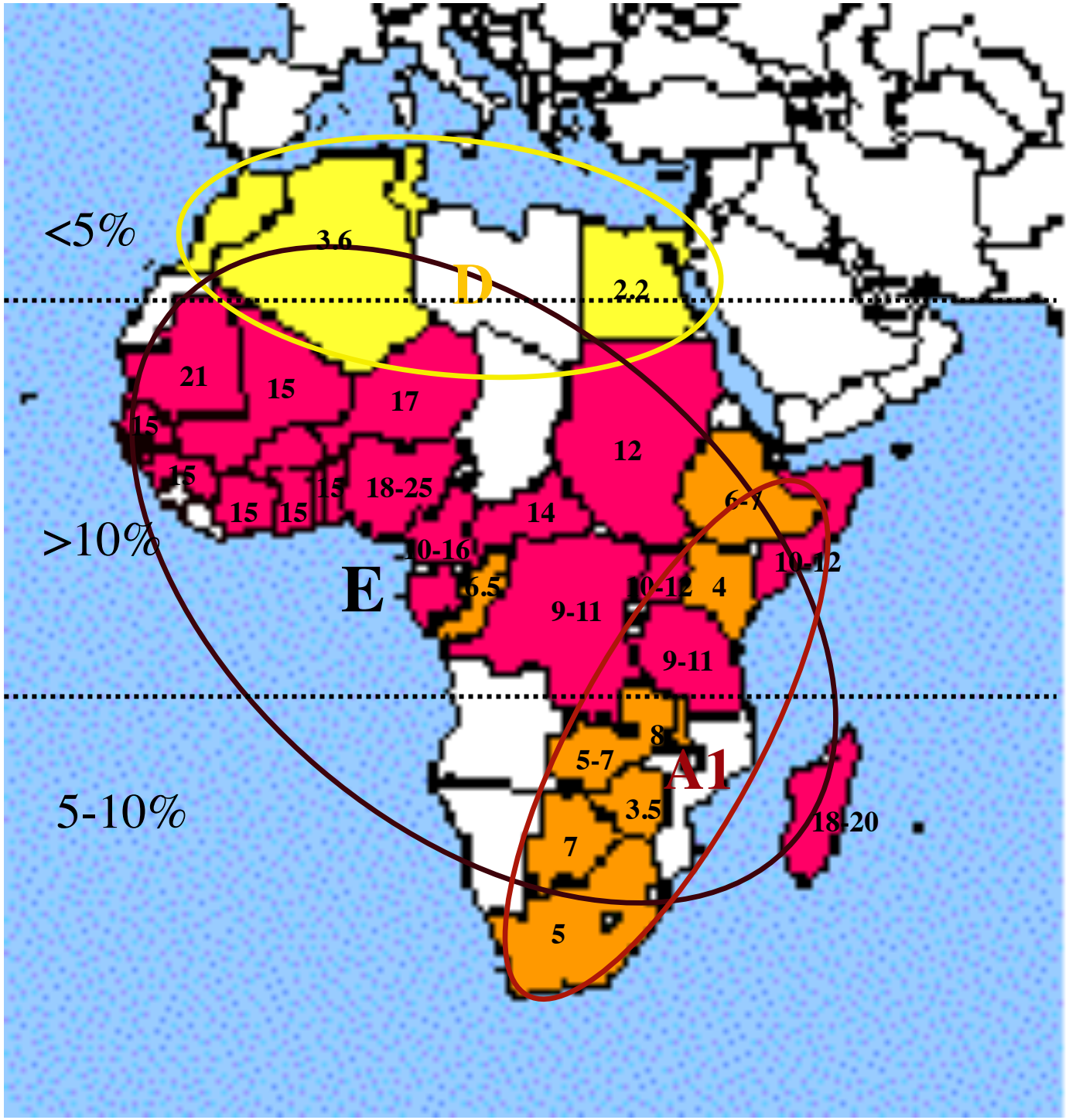


Prevalence of anti-HBc in the world



HBV inter-genotype recombinant forms

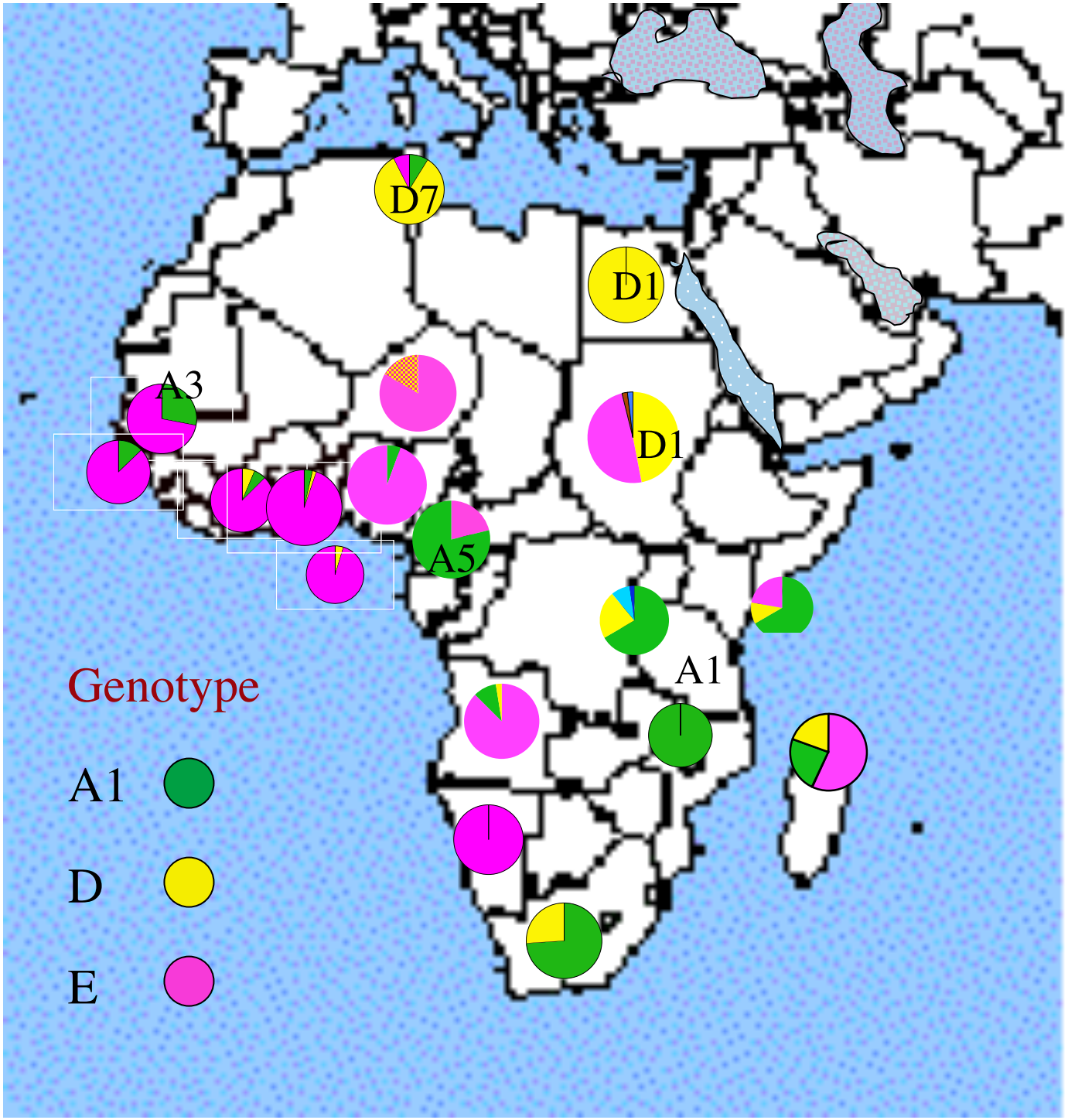




Distribution of HBsAg prevalence in first time blood donors in Africa

- <5 %
- 5-10 %
- >10 %

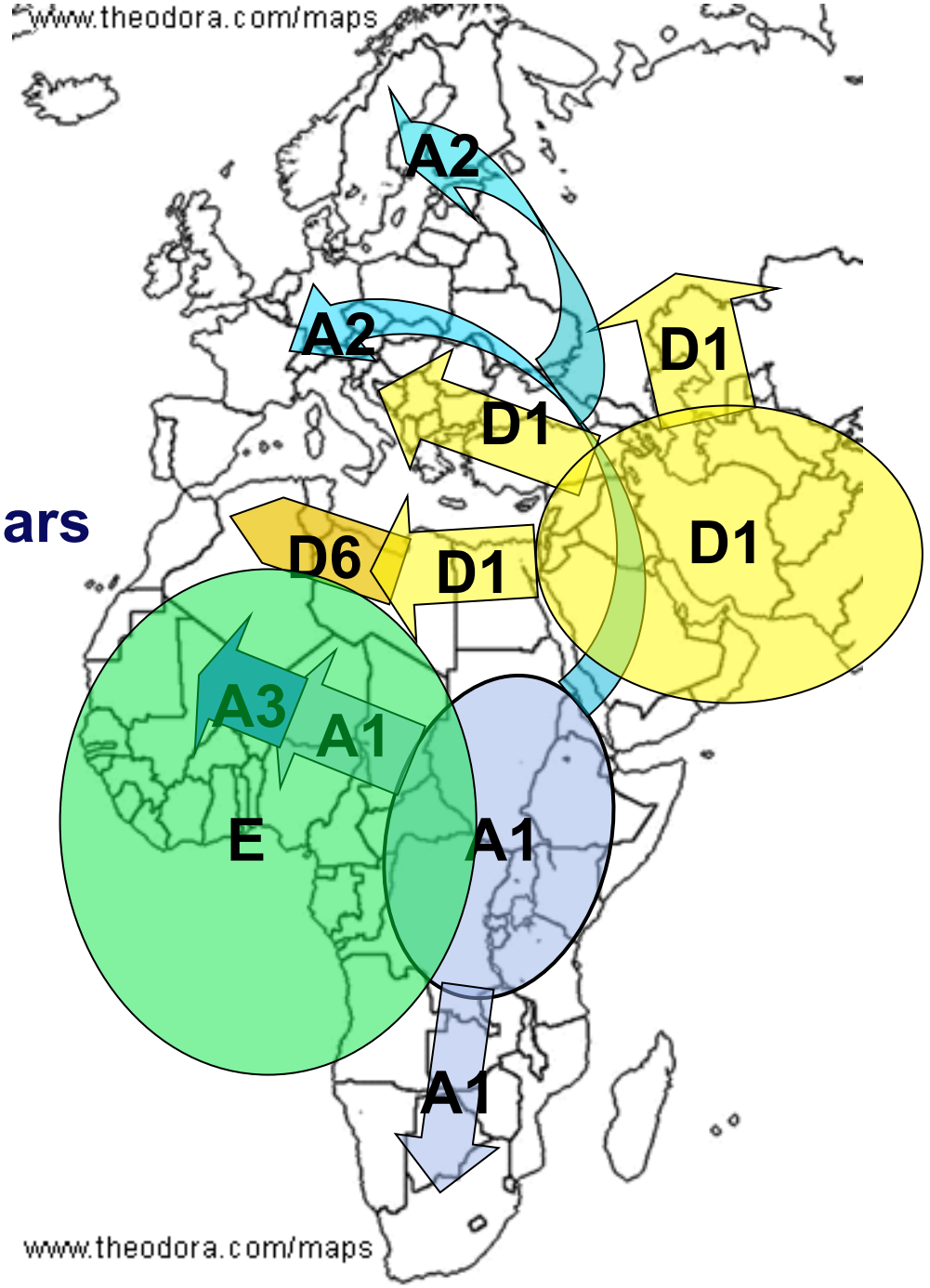
Distribution of HBV genotypes in Africa



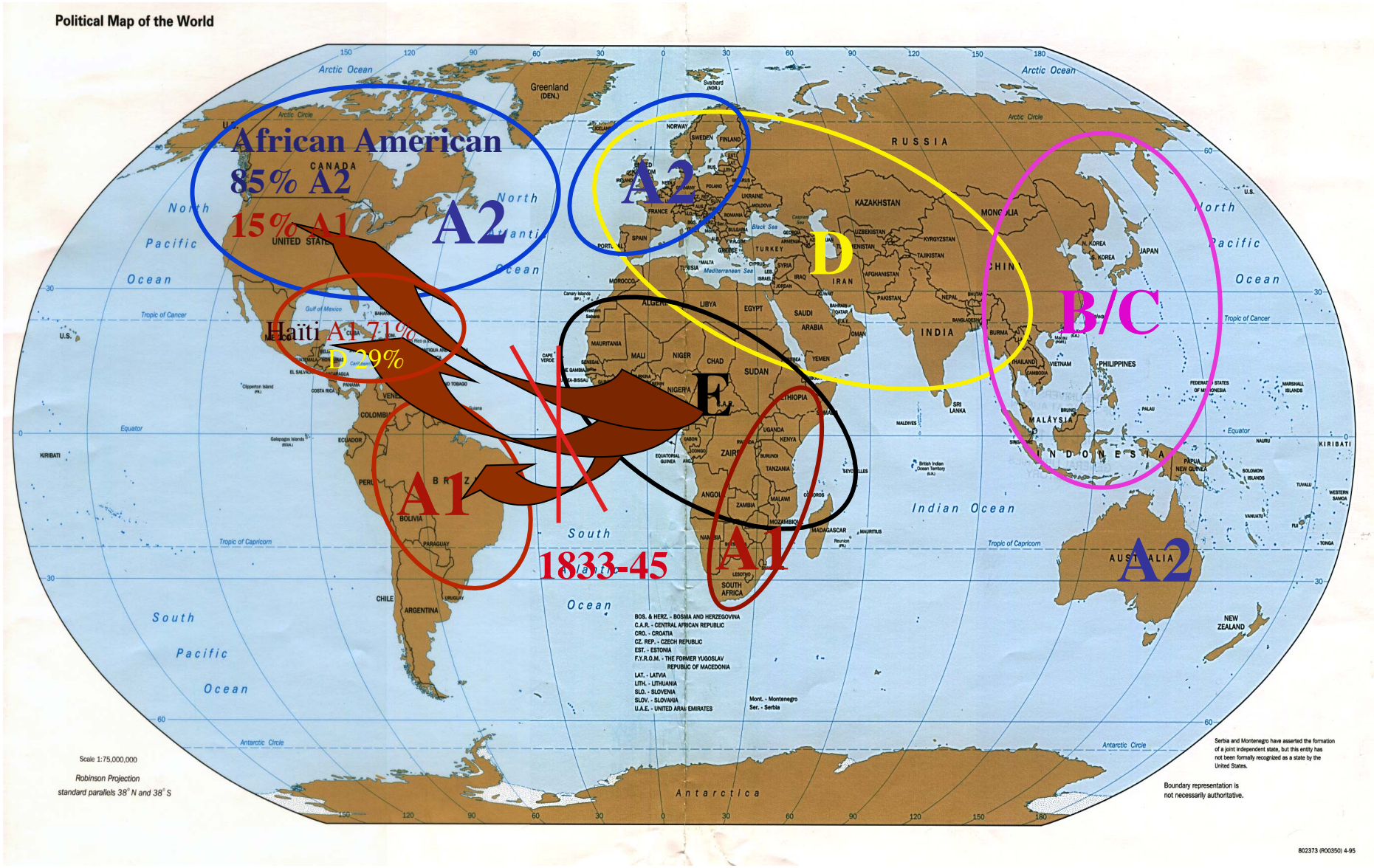
Number of samples

Tunisia = 79
Egypt = 105
Senegal = 32
The Gambia = 124
Côte d' Ivoire = 48
Ghana = 214
Benin = 20
Niger = 58
Nigeria = 163
Cameroon = 100
Kenya = 56; 18
Rwanda = 45
Malawi = 20
Angola = 40
Namibia = 23
South Africa = 23
Madagascar = 45

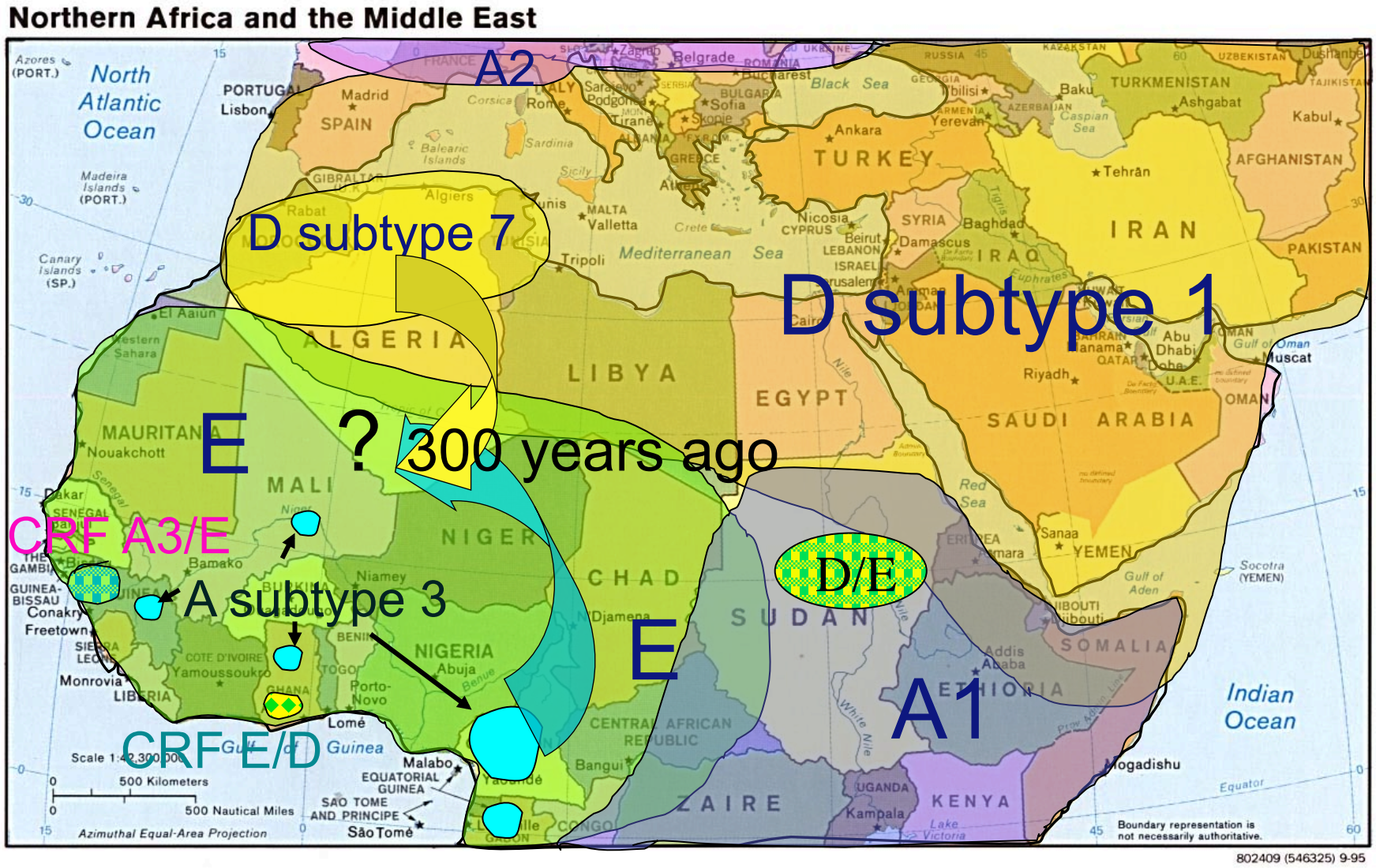
Potential historical evolution of HBV in the old world in the past 10,000 years



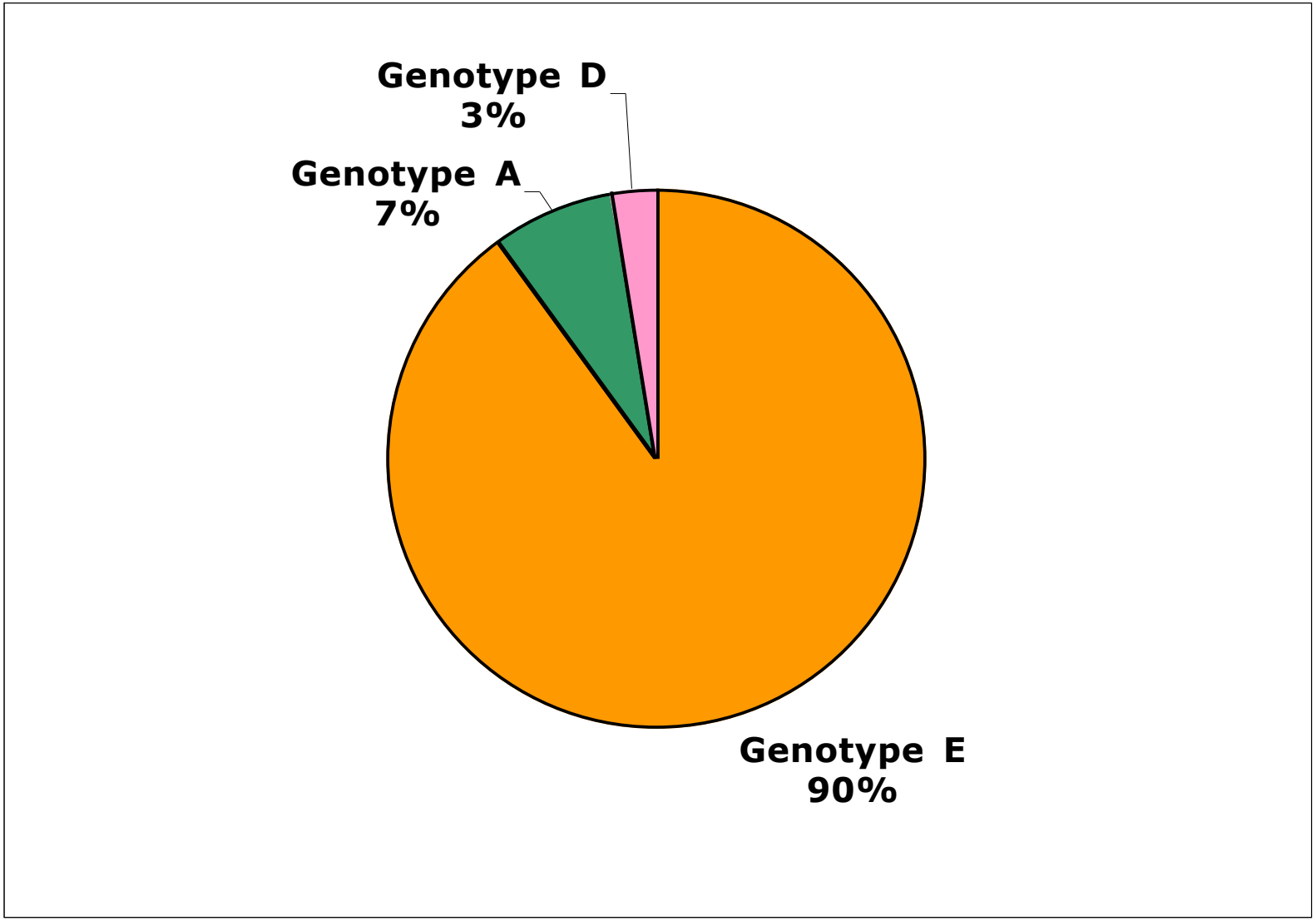
Distribution of HBV genotypes in Africans and African Americans



Possible evolution of HBV in the old world

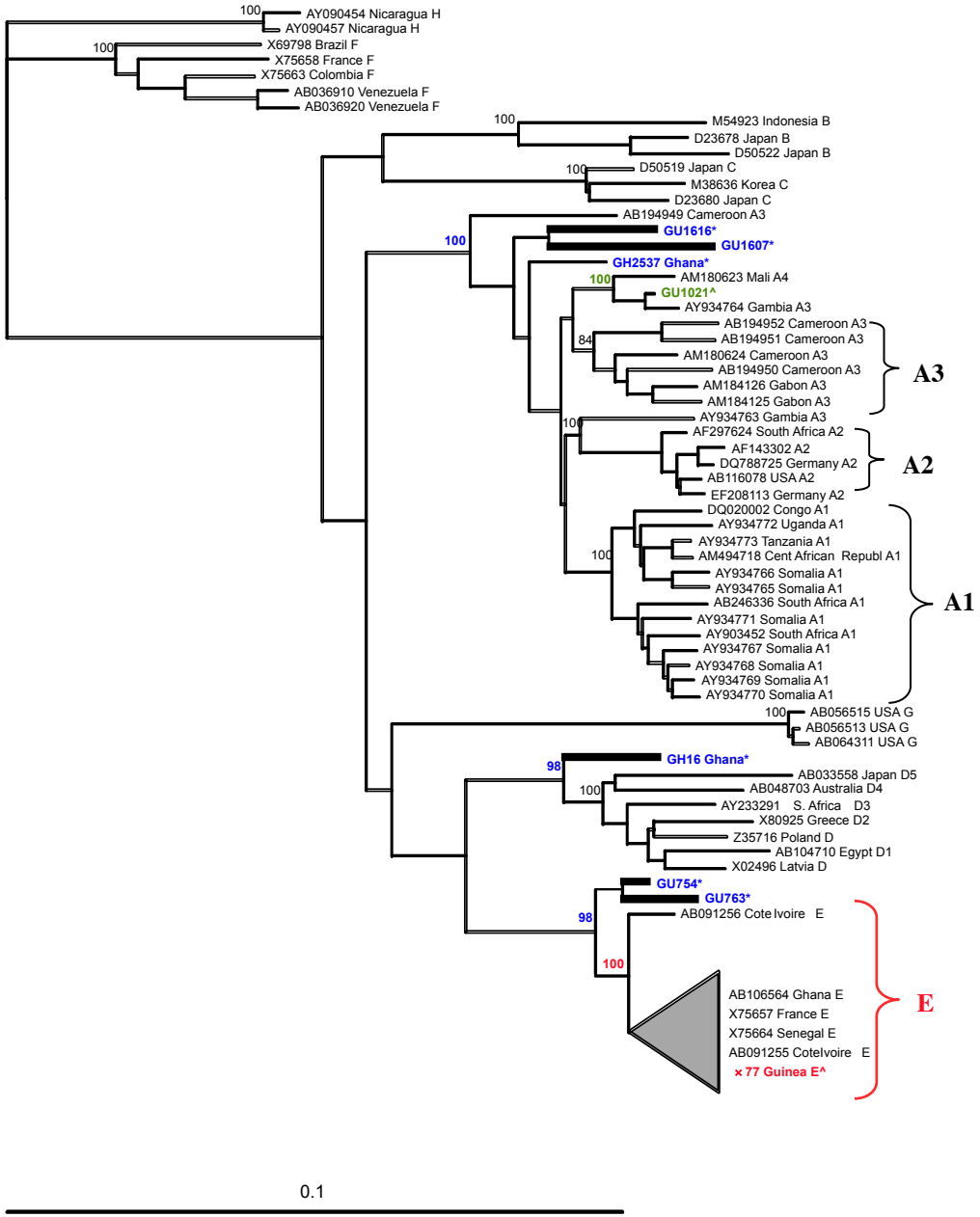


Distribution of HBV genotypes in Ghana in 110 HBsAg + blood donors (Allain et al. Blood 2003)

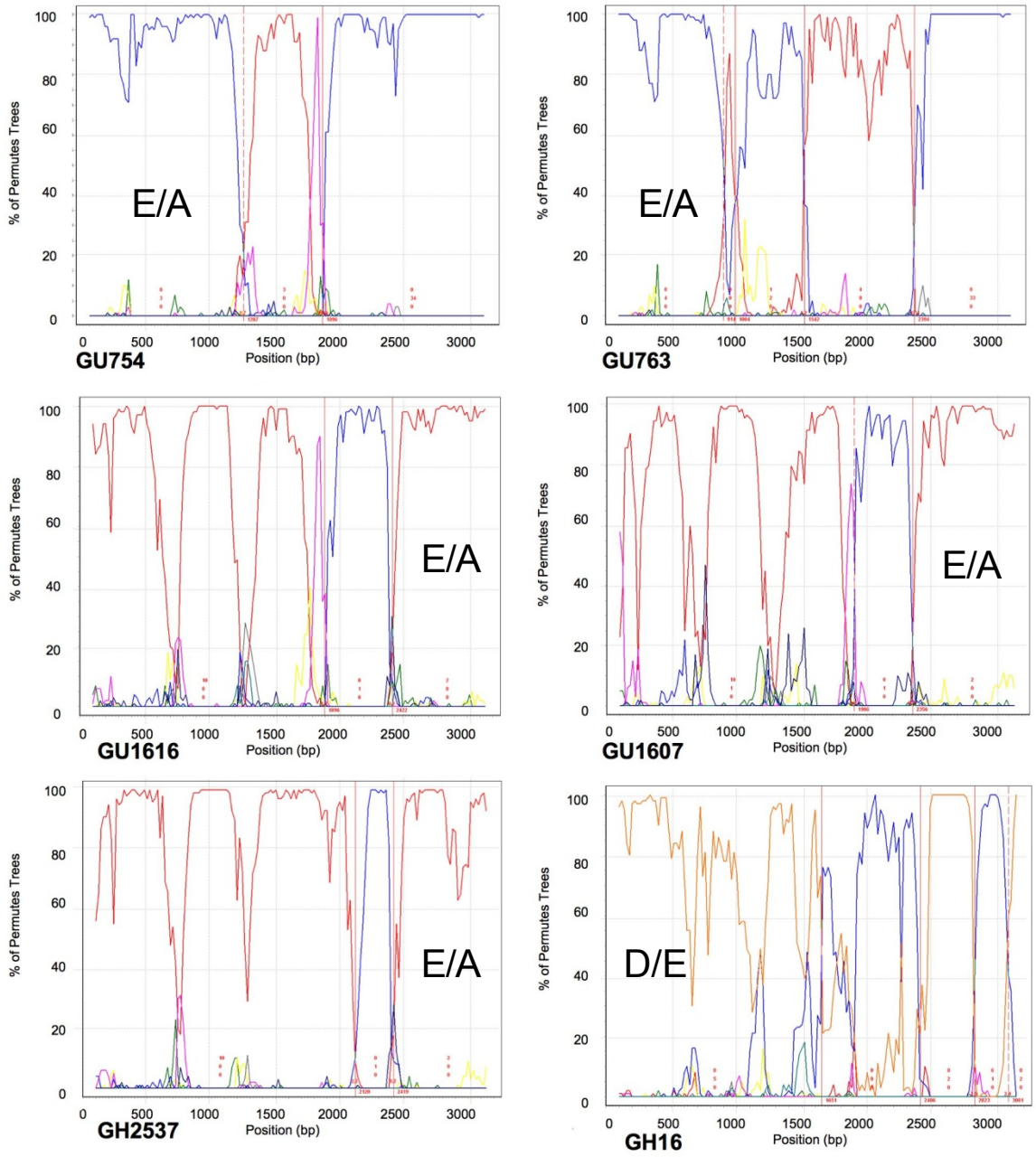


Phylogenetic analysis of full genome sequences from Guinea

Garmiri et al. J Gen Virol 2009; 90:2442-51



- 81 full genome sequences
- Genotype A3 : 1 seq
- Genotype E : 76 seq
- Seq in blue: Recombinants



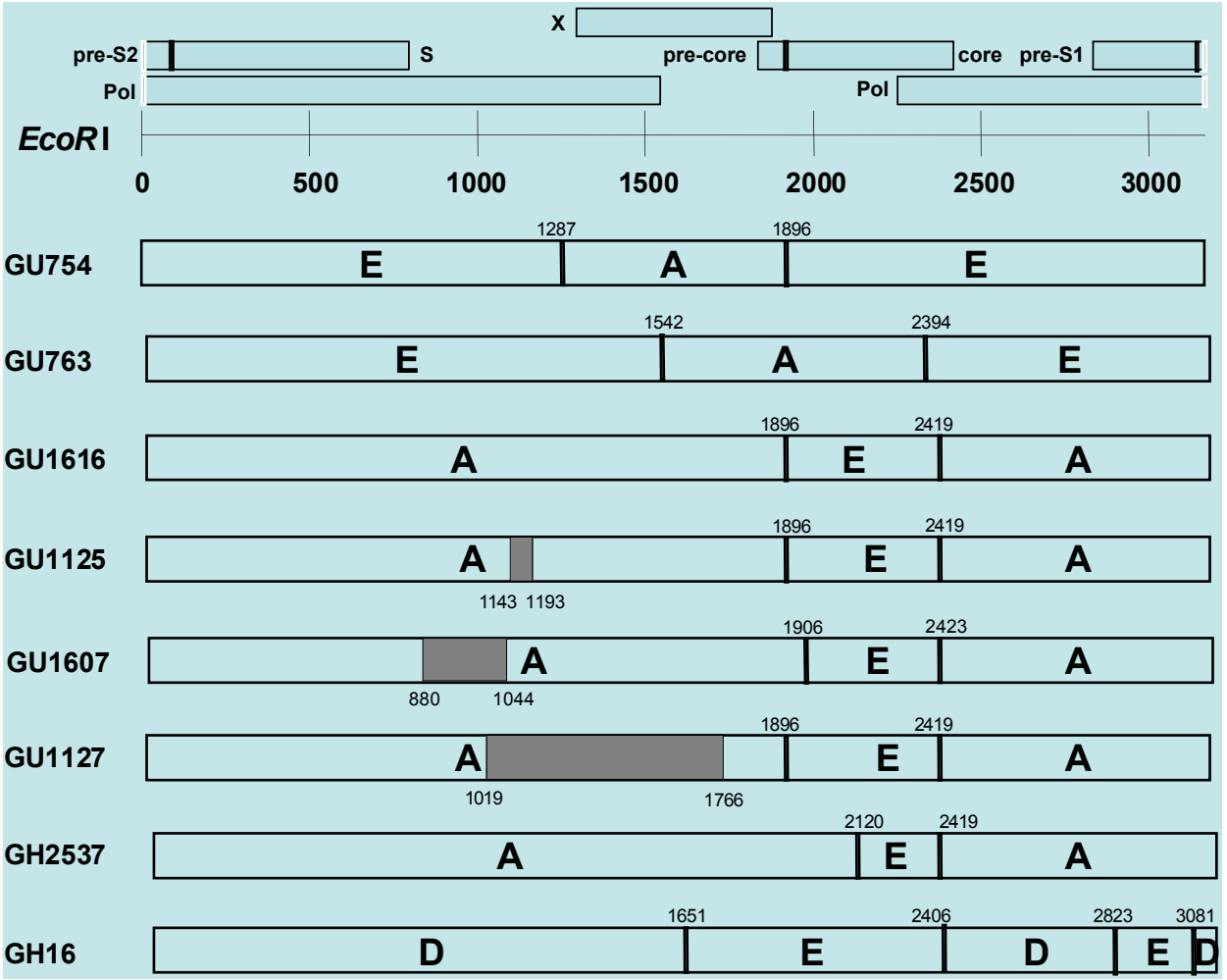
Evidence of recombination between HBV genotype E and A and E and D in strains originating from Guinea and Ghana

Red: genotype A

Blue: genotype E

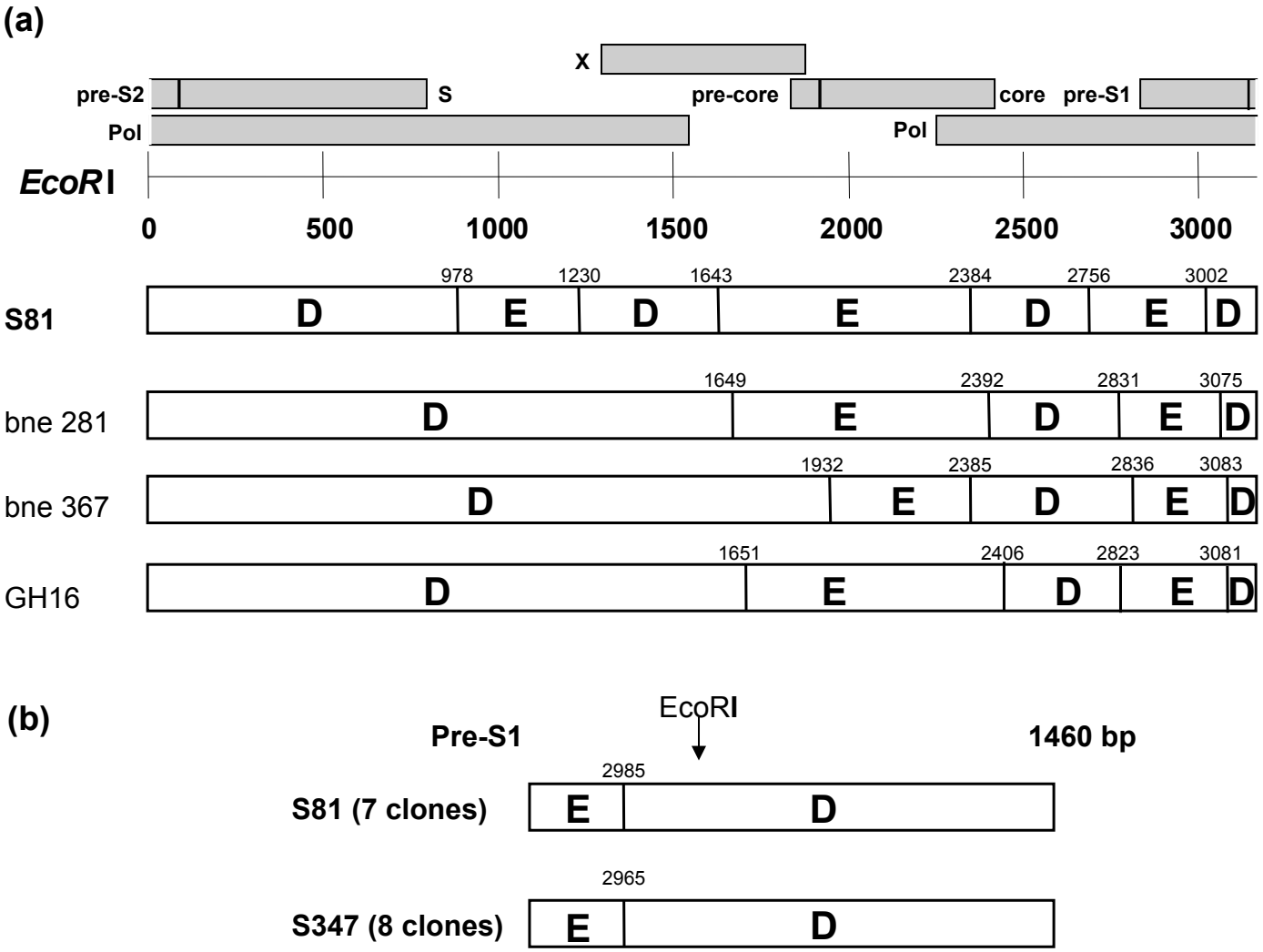
Orange: genotype D

Schematic representation of Guinean and Ghanaian HBV A/E and E/D recombinant strains



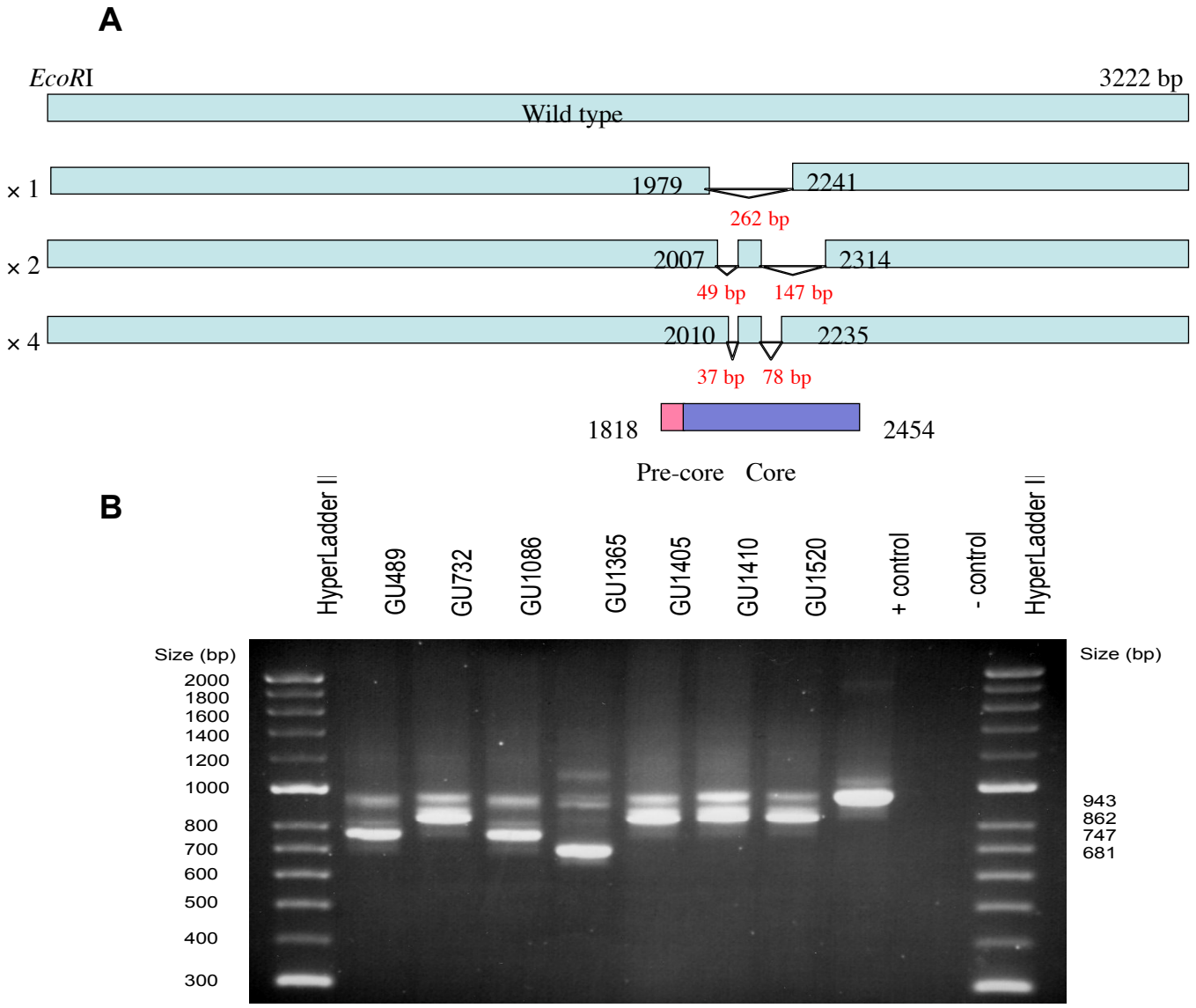
Recombinant D/E in blood donors in Khartoum, Sudan

Mahgoub S et al. J Clin Microbiol 2010; 49: 298-306

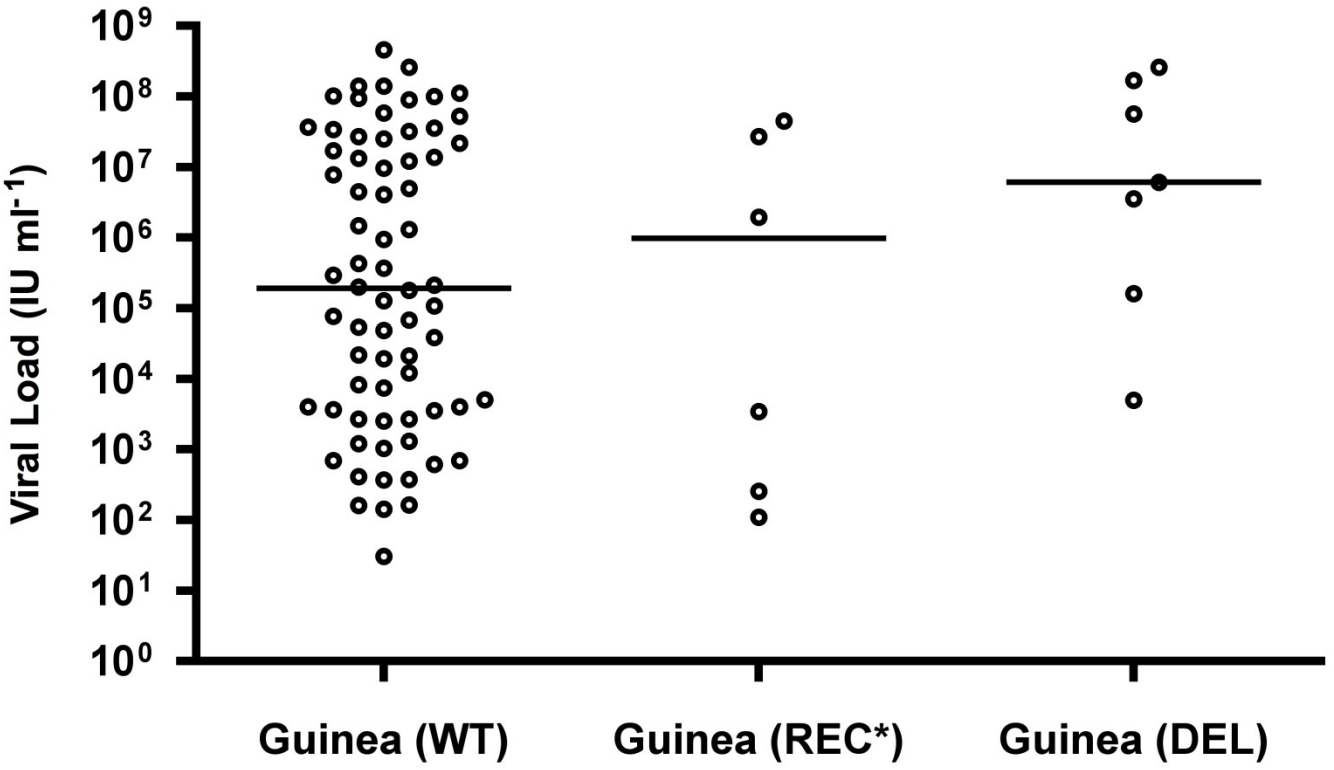


7 Guinean strains with core deletions

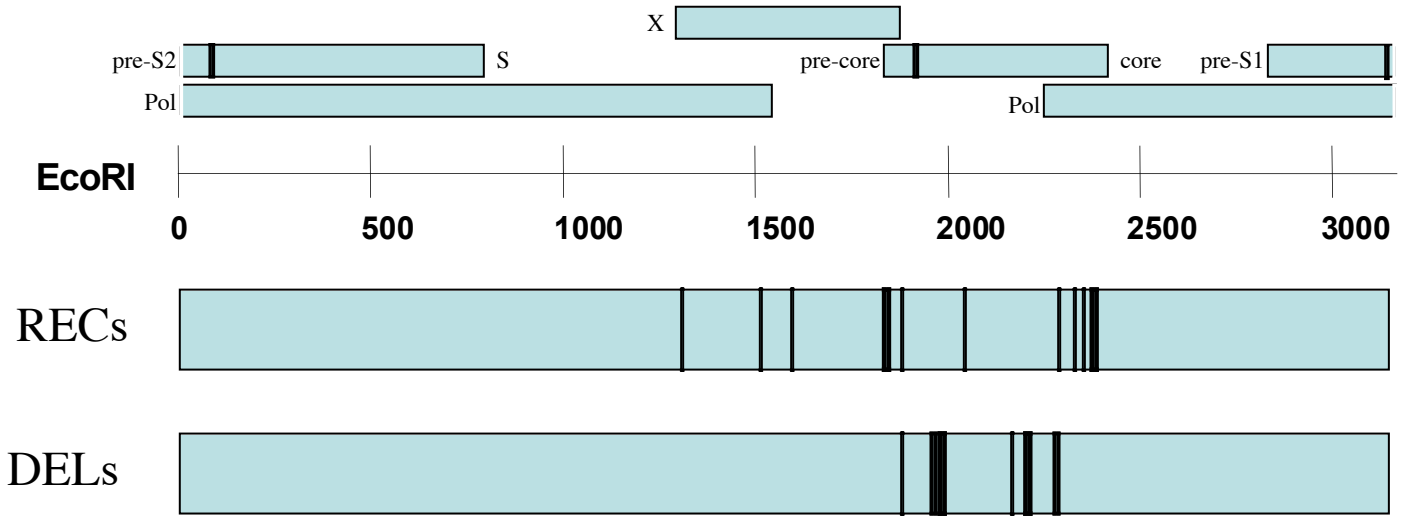
(Garmiri et al. J Gen Virol 2009; 90:2442-51)



Viral Load distribution of HBsAg+ Guinean samples



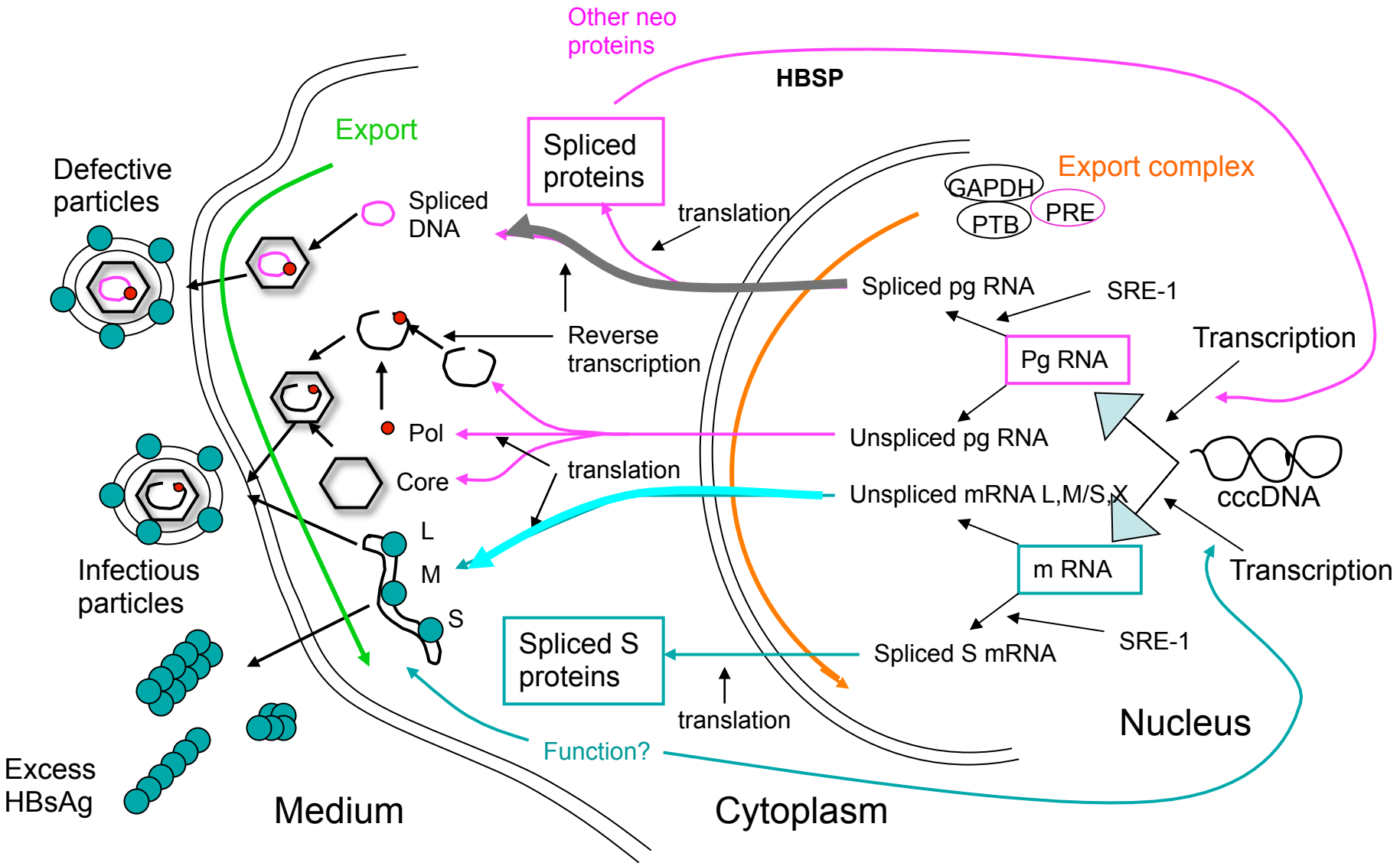
Overview of the recombination and deletion points in West African strains



Deletions and recombinations occur in similar core regions suggesting preferential DNA re-arrangement in this area of HBV genome

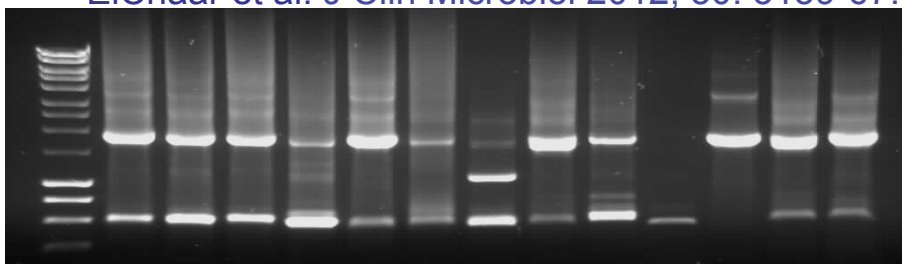
HBV splicing and mechanisms of replication and HBsAg production

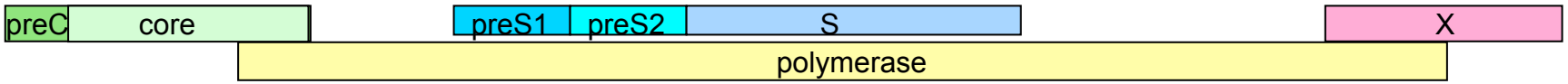
Allain & Cox Curr Opin Hematol 2011; 18: 461-6

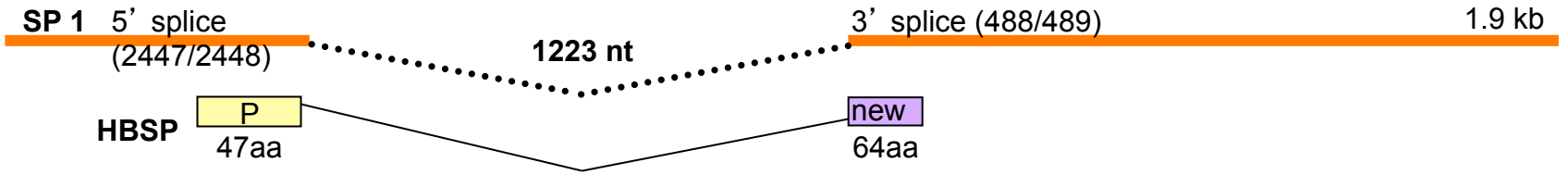


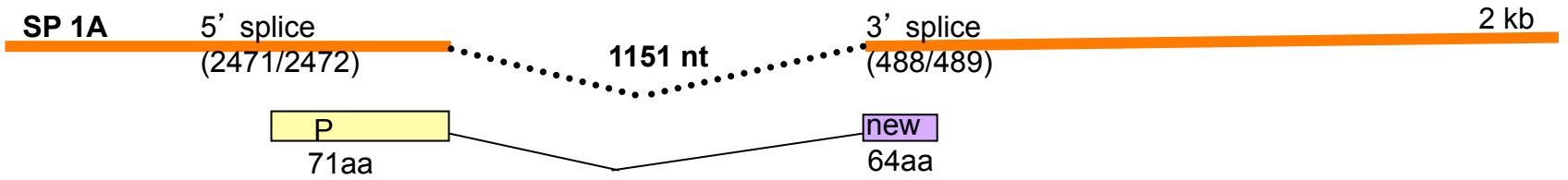
Splicing sites and neo-proteins observed in HBV genotype D

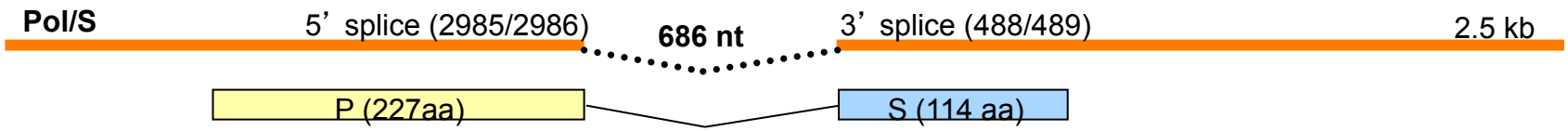
ElChaar et al. J Clin Microbiol 2012; 50: 3159-67.









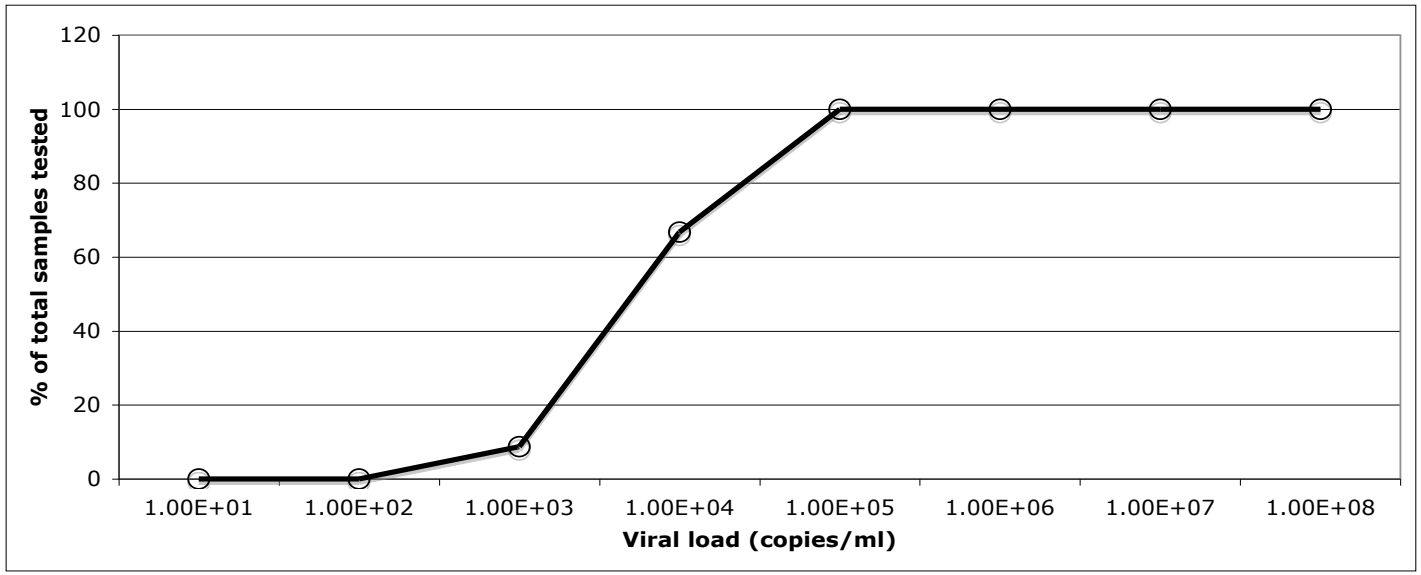


Total % splicing and % SP1 spliced DNA

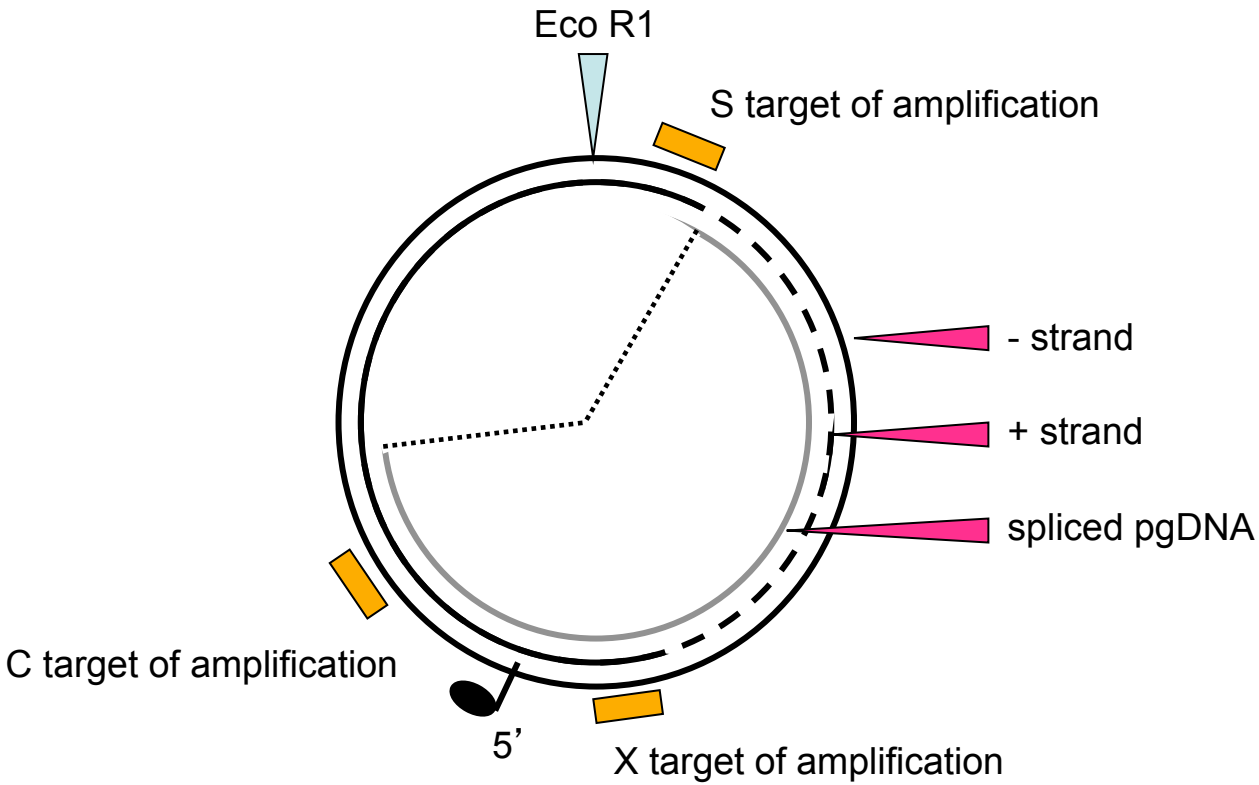
(ElChaar et al. J Clin Microbiol 2012; 50: 3159-67)

Genotype	Median viral load (IU/ml)	Mean % total spliced DNA	% Range	Mean % SP1 quantitative	Range % SP 1
20 A	$1.0x10^7$	5.6	0-24	0.15	0.01-1.0
20 B	$3.1x10^5$	36.7	0-91	1.7	0.01-9.9
20 C	$2.5x10^5$	6.2	0-56	0.43	0.1-1.2
20 D	$9.3x10^4$	55.9	0-95	10.3	6.1-91.4
20 E	$2.3x10^7$	16.9	0-67	0.1	0.01-0.8

N samples 2 15 23 6 7 8 26 13



Impact of spliced HBV DNA in viral load quantification and infectivity studies

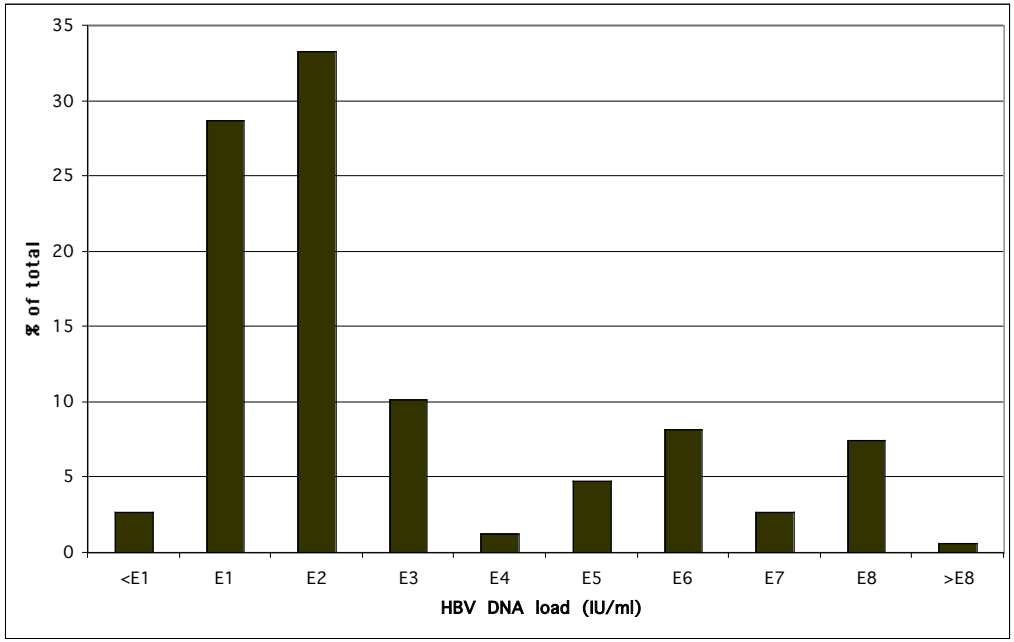


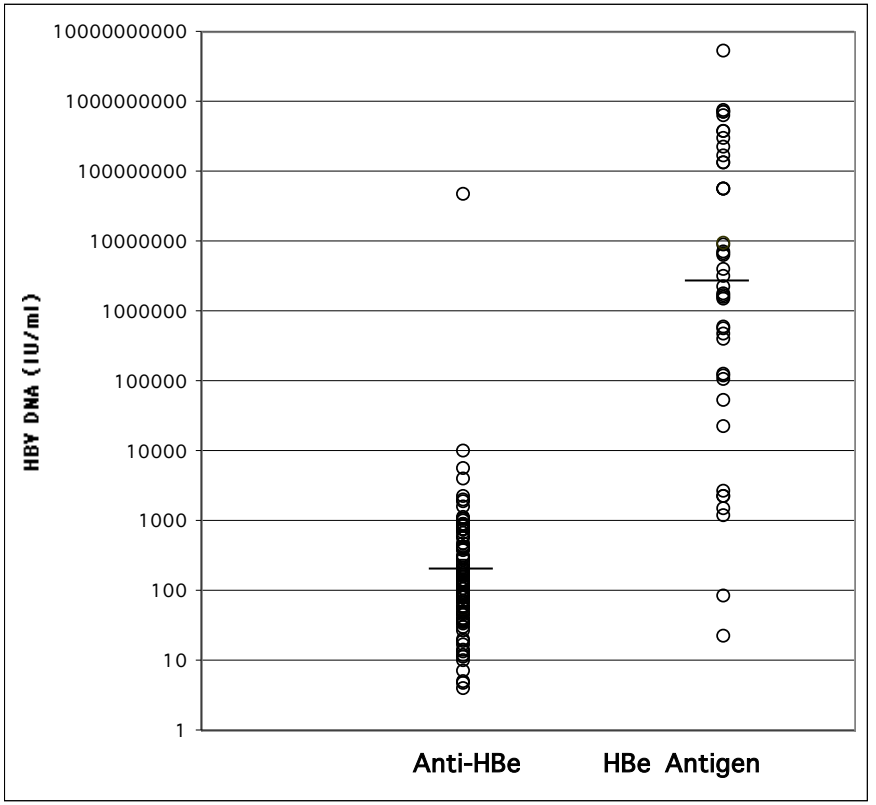
Modes of HBV transmission in various areas

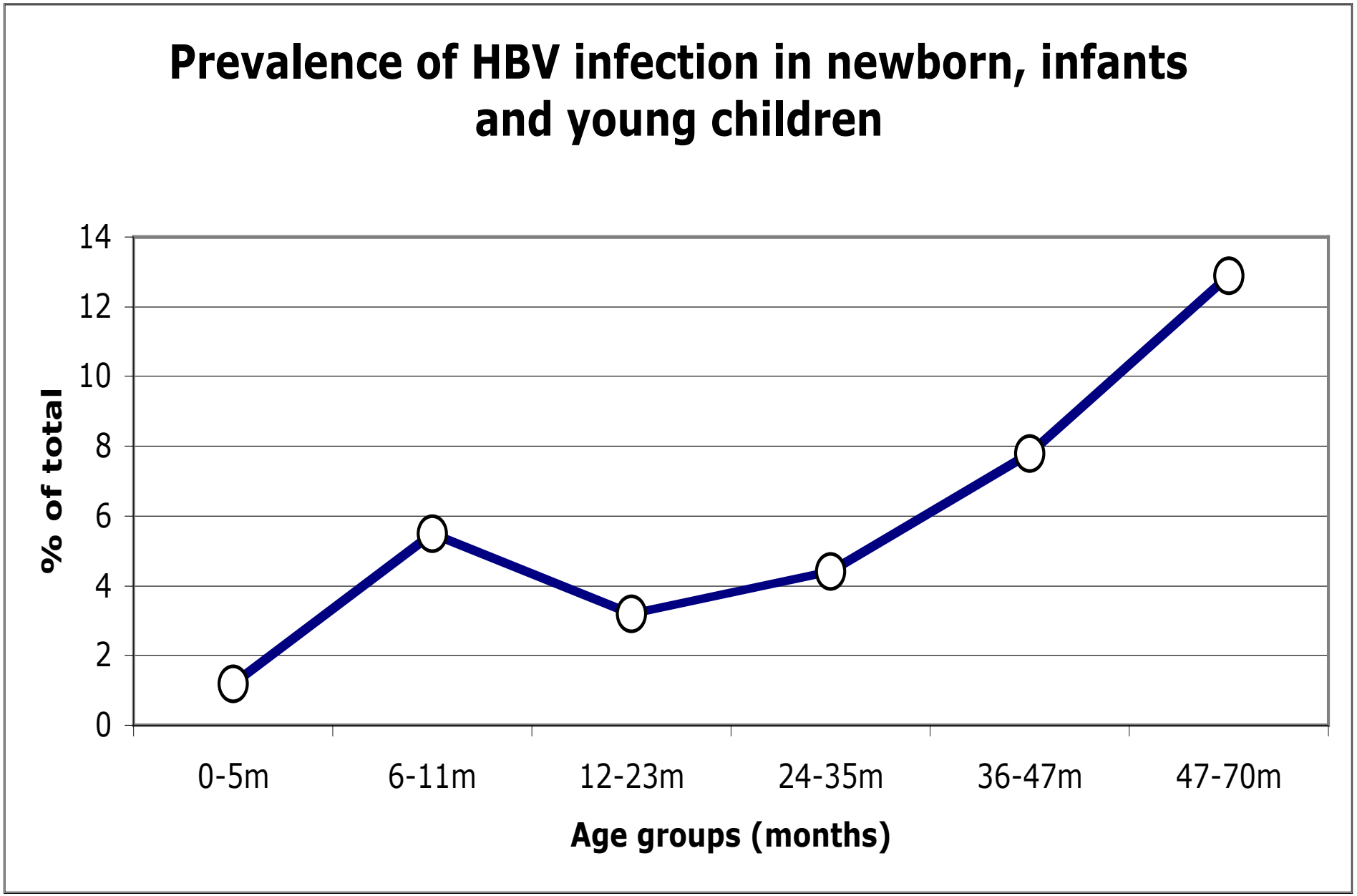
Mode of transmission		NW Europe	Mediterranean	Asia	Africa
Vertical		±	±	+++	+
Horizontal	- < 5years	-	-	+	+++
	- familial	-	-	±	±
Sexual	- hetero	+	++	+	+
	- homo	++	+	-	-
Blood	- IVDU	+++	++	-	-
	- tattoo/scar.	+	+	?	+
	- transfusion	-	±	+	+
Prevalent genotype		A/D	D/A	C/B	E/D/A

Distribution of HBV DNA load and relation to HBe Ag/Ab in HBsAg+ Ghanaian blood donors

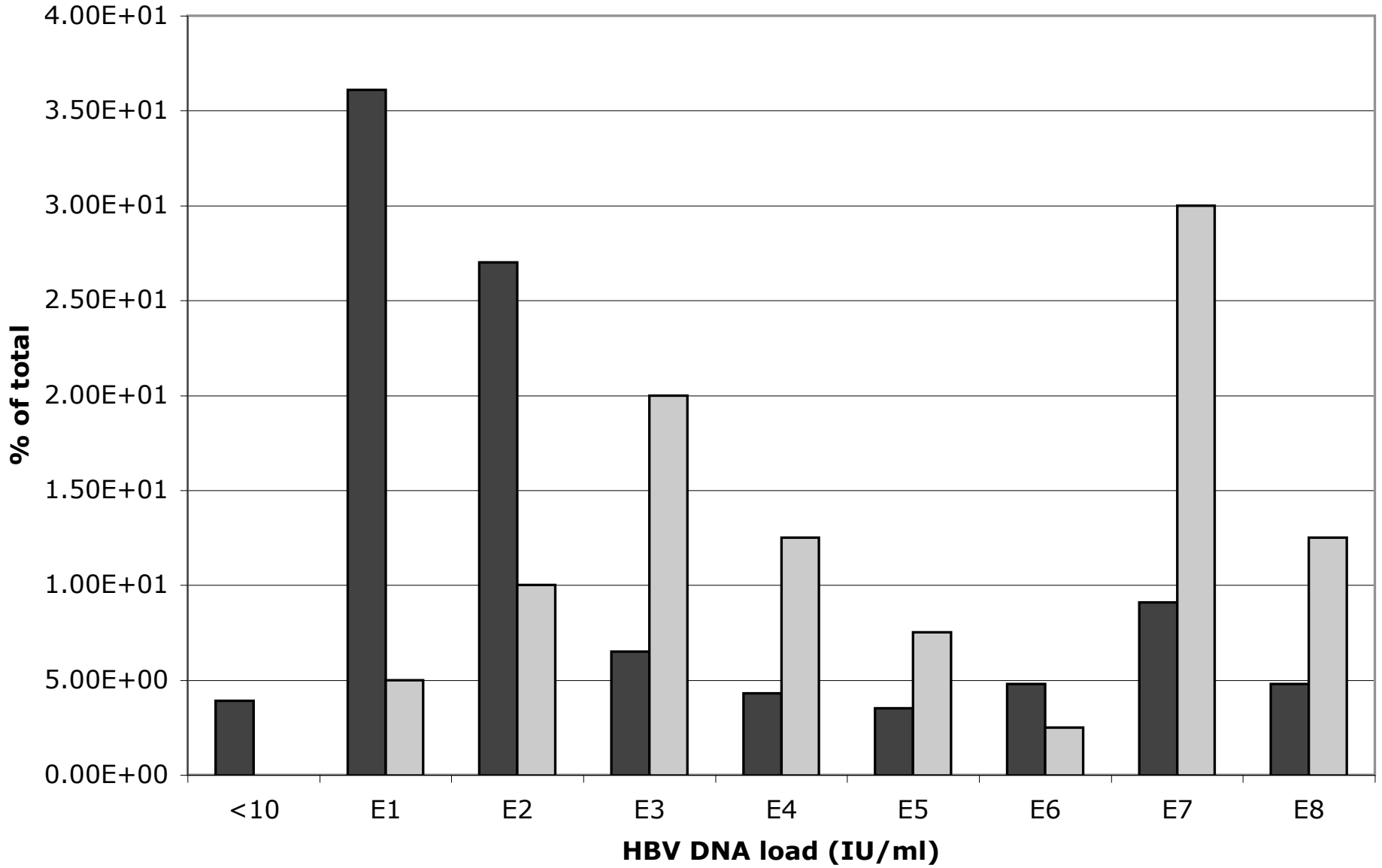
(Allain et al. Blood 2003)



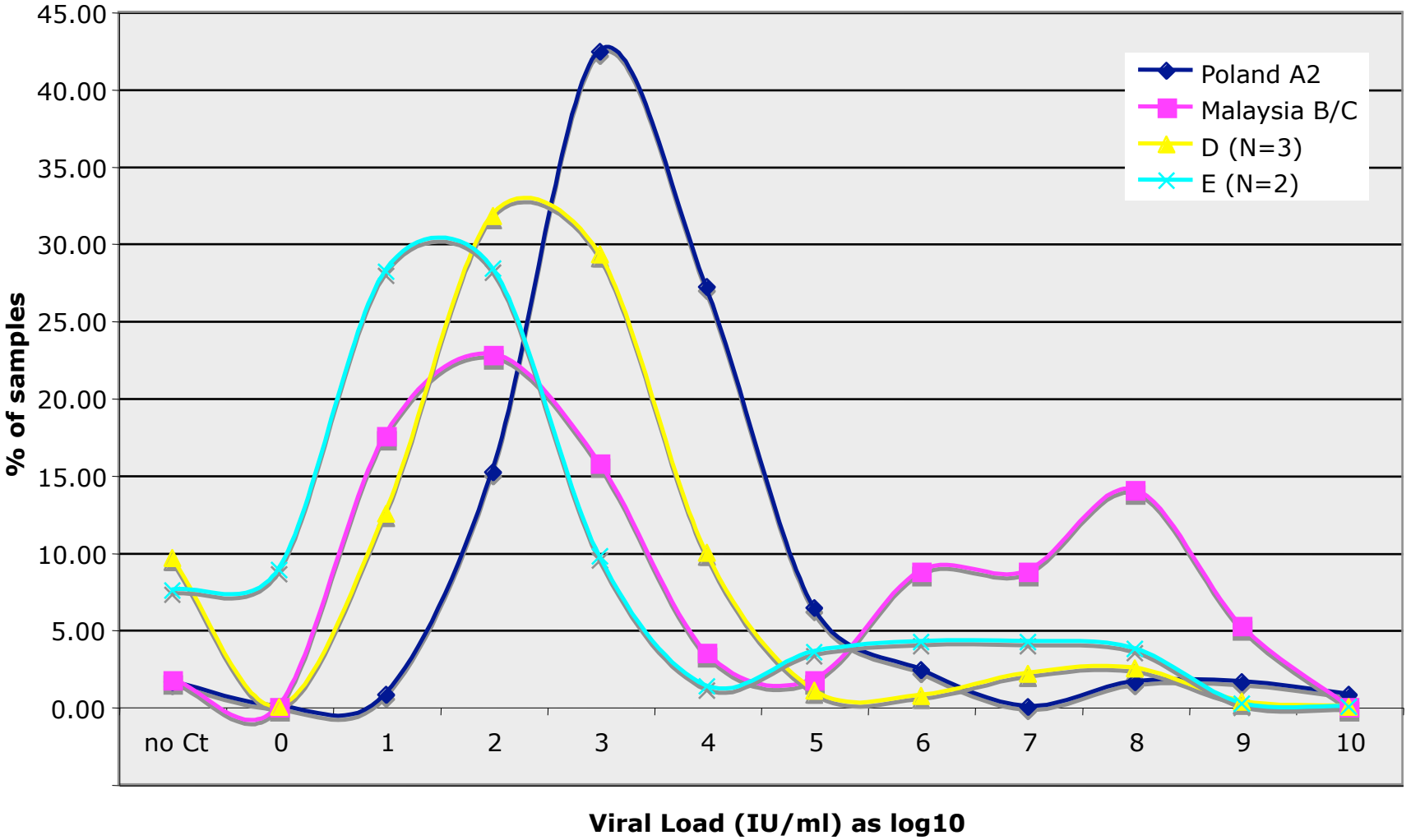



Prevalence of HBV infection in newborn, infants and young children
% of total
14
12
10
8
6
4
2
0
0-5m
6-11m
12-23m
24-35m
36-47m
47-70m
Age groups (months)

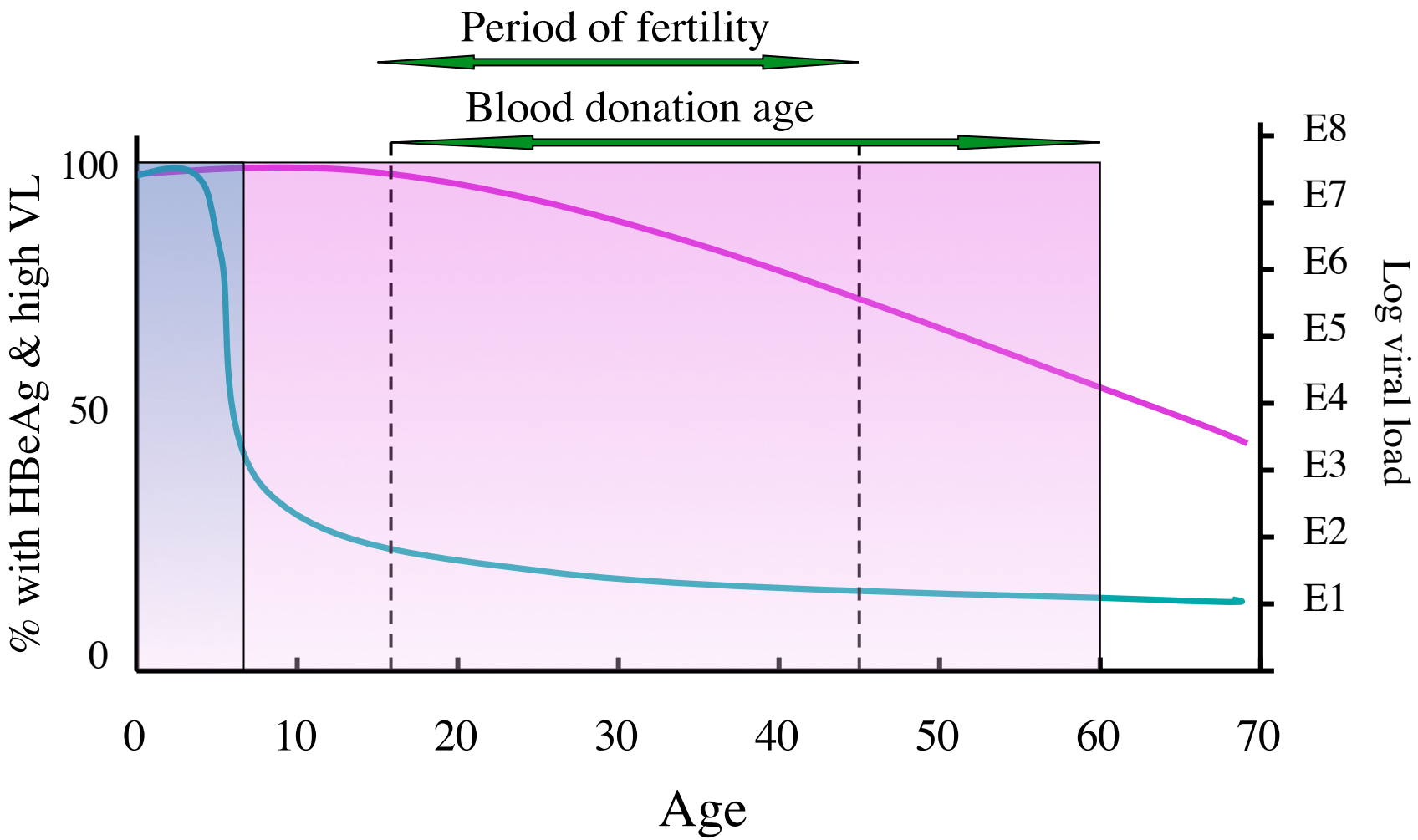
Distribution of HBV DNA load in adults (230) and children <6y (44)



Distribution of HBV Viral Load in HBsAg+ blood donors cumulative per Genotype

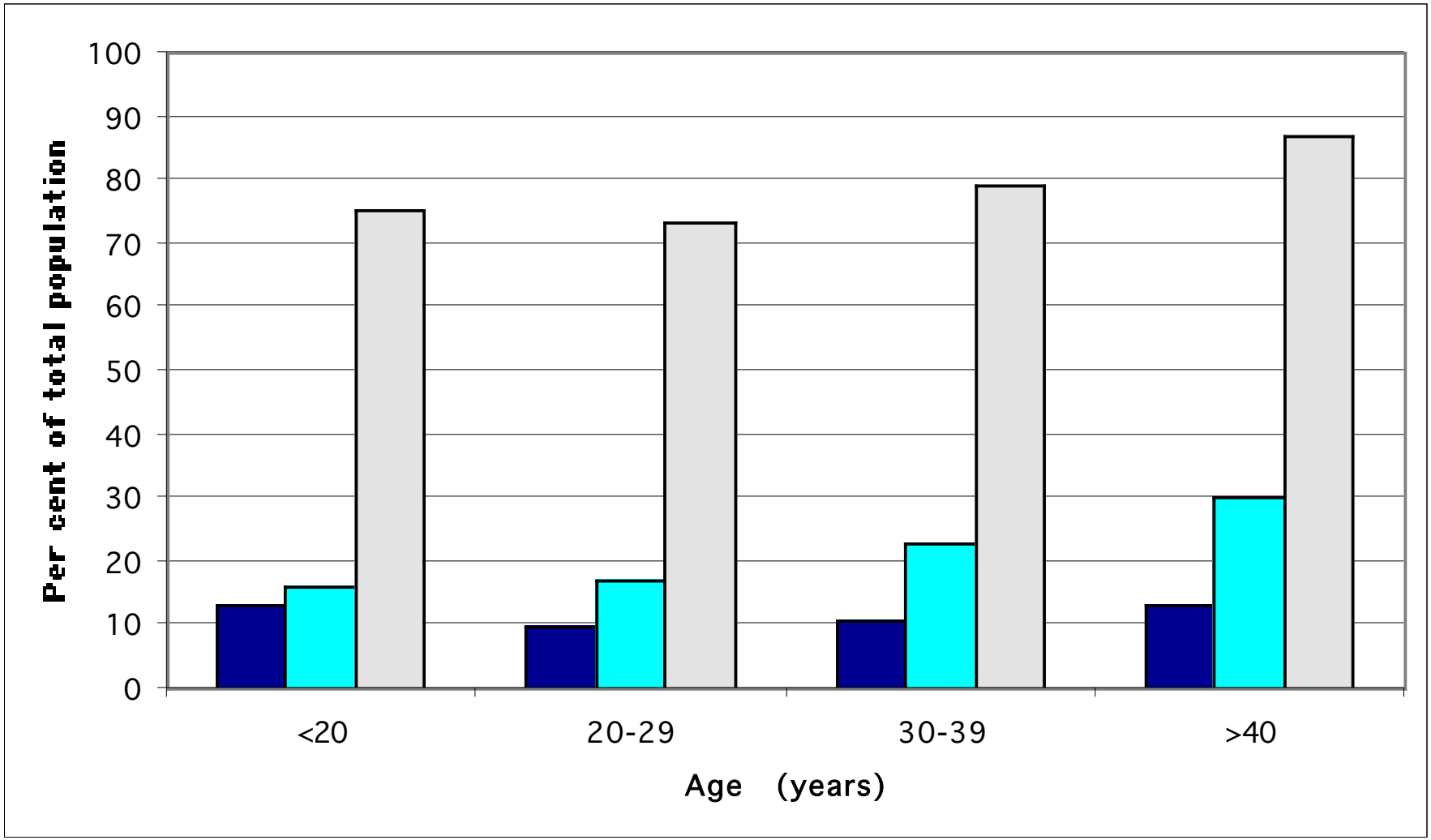


Comparing genotype C and E

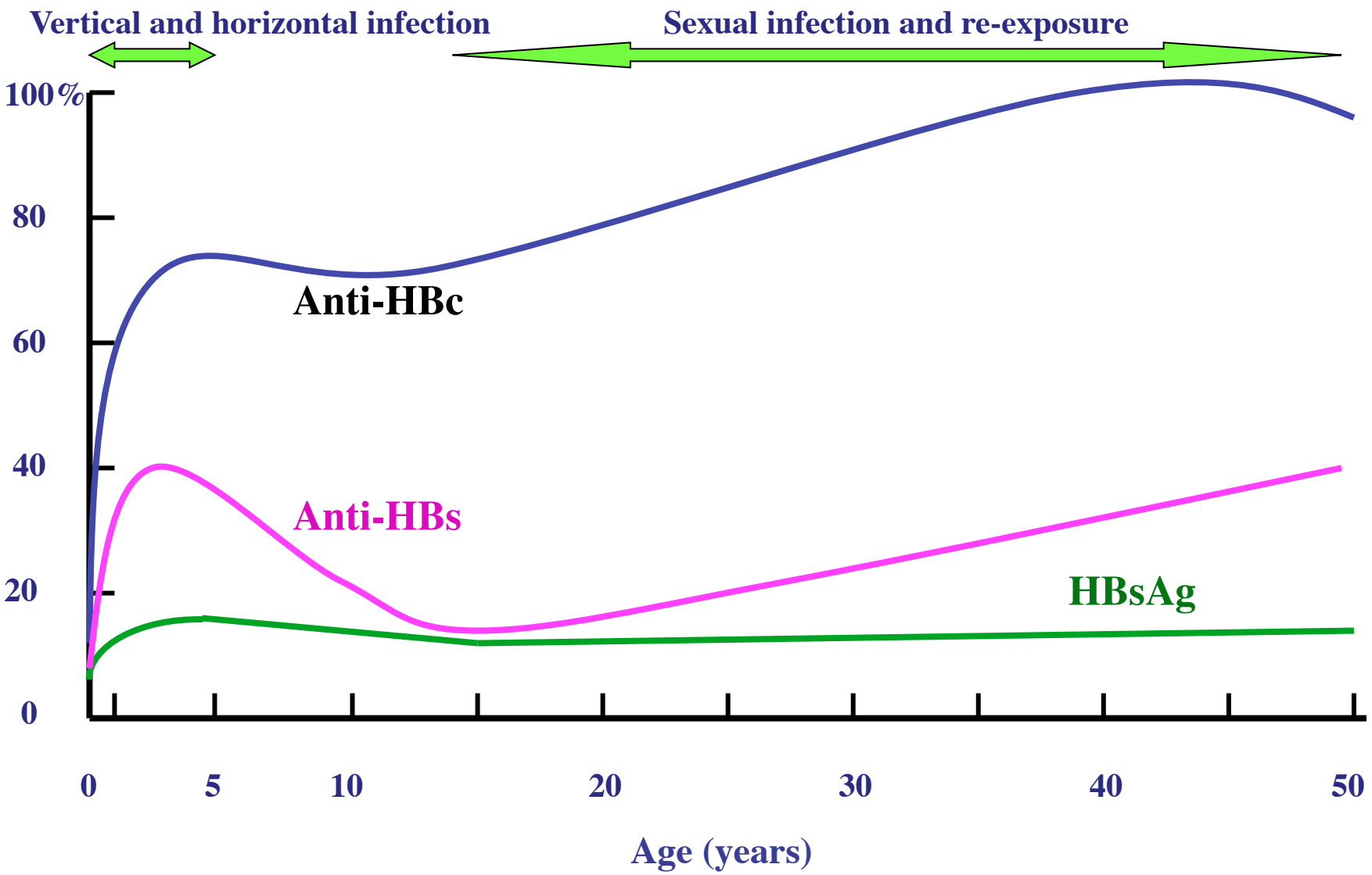


HBV markers in Ghanaian blood donors

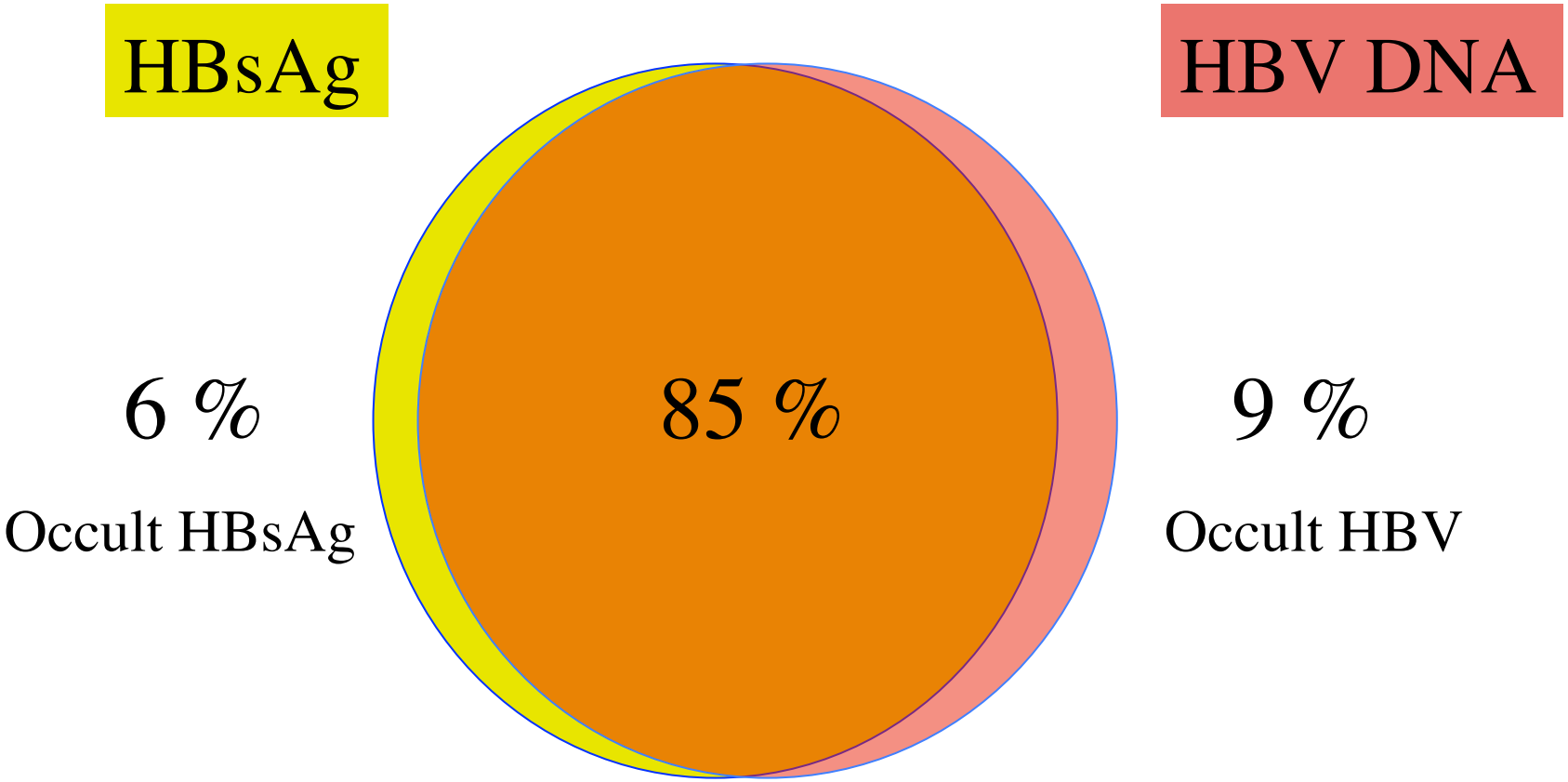
HBsAg Anti-HBs Anti-HBc



Natural history of HBV infection in Ghana



Viral markers of HBV infection in 217 Ghanaian pregnant women



Conclusions

- Genotype E infection generates frequent OBI of uncertain pathogenicity
- Pathogenicity of relatively frequent recombinant virus should be compared to genotype E
- 87.6% of infants being vaccinated, horizontal transmission should significantly decline (evidence?)
- Vertical transmission from few high VL mothers might remain a threat depending on vaccine schedule
- Most chronic infections having low VL, sexual transmission should remain low