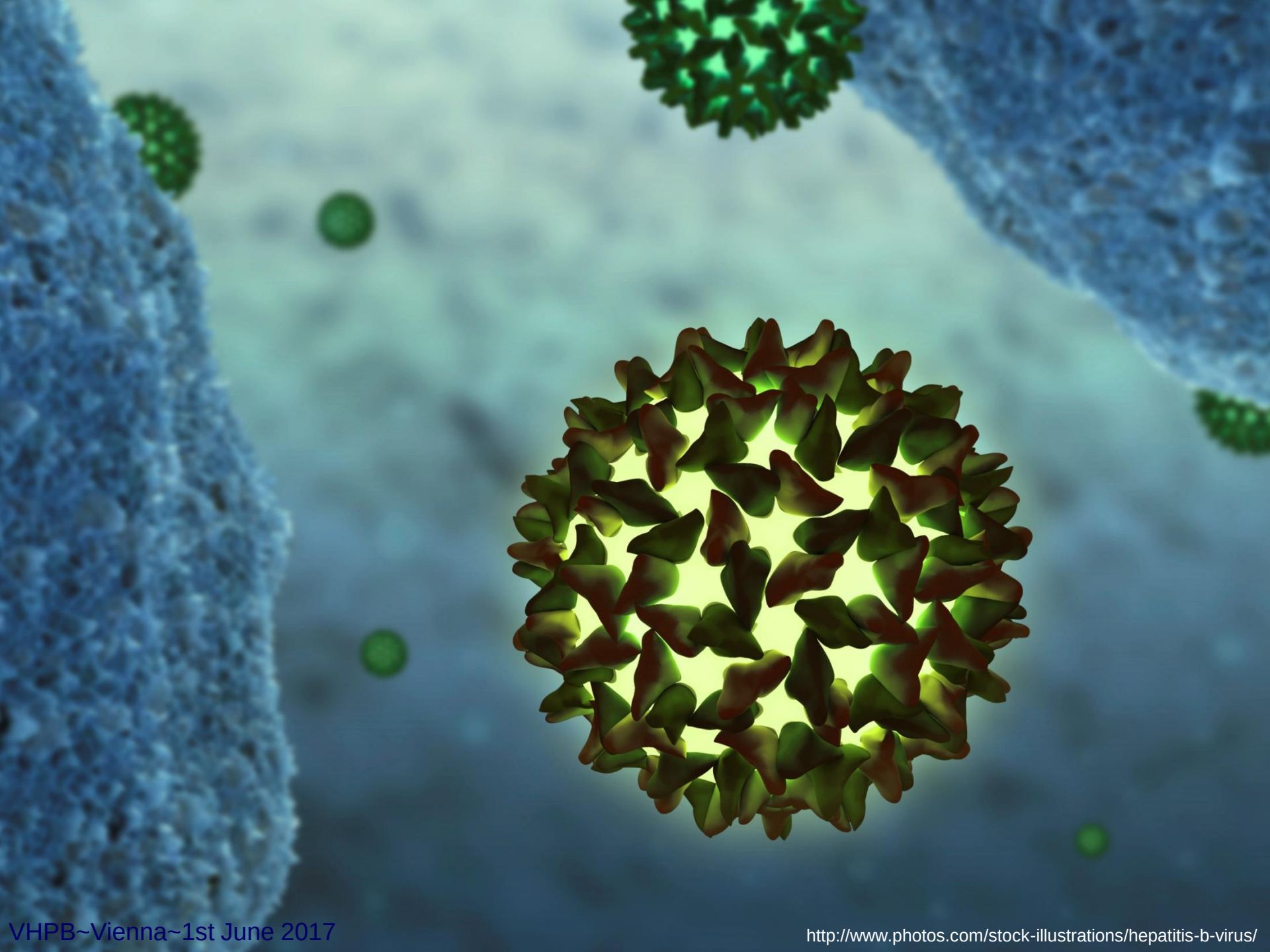

VHPB~Vienna~1st June 2017

http://www.photos.com/stock-illustrations/hepatitis-b-virus/

The Effect of Genotype/Subgenotype of Hepatitis B Virus on HBeAg Expression and Perinatal Transmission

Anna Kramvis

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University of the Witwatersrand

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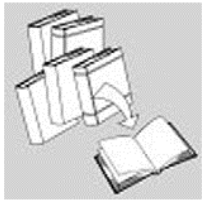
Rev. Med. Virol. 2016; **26**: 285–303.
Published online 3 May 2016 in Wiley Online Library
(wileyonlinelibrary.com)
DOI: 10.1002/rmv.1885

Reviews in Medical Virology

REVIEW

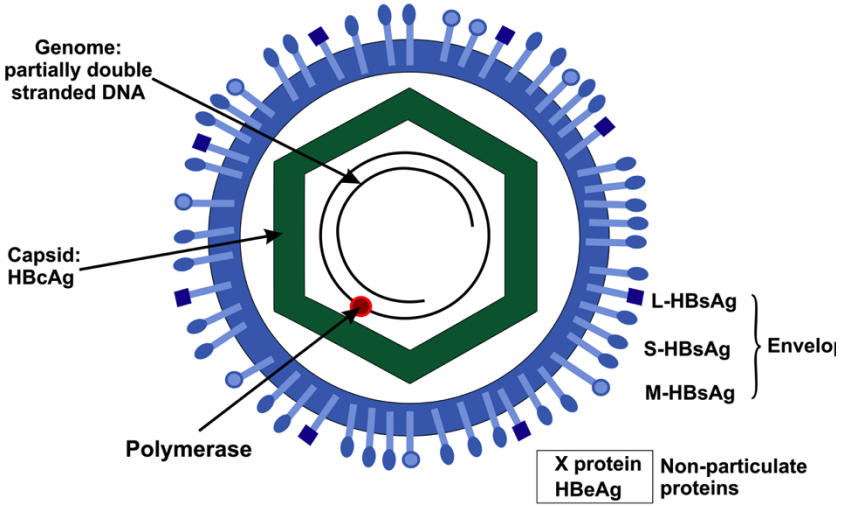


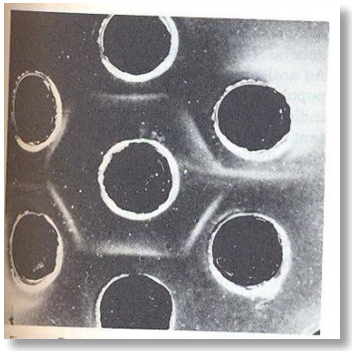
The clinical implications of hepatitis B virus genotypes and HBeAg in pediatrics

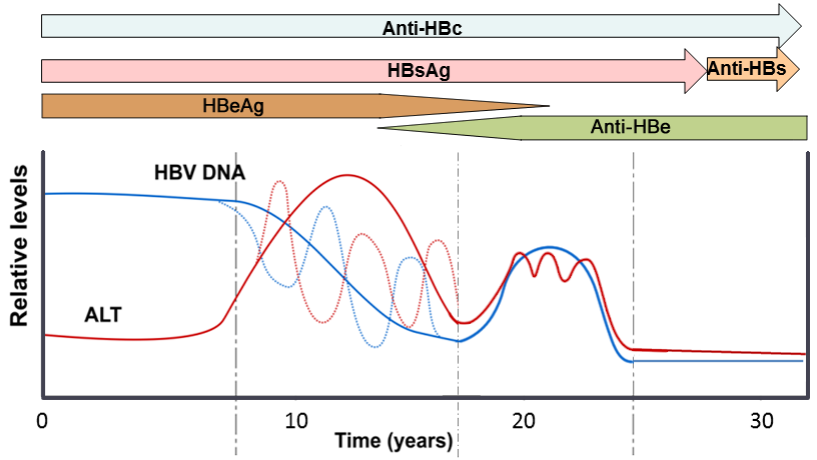
Anna Kramvis*

Hepatitis Virus Diversity Research Unit (HVDRU), Department of Internal Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

HBeAg







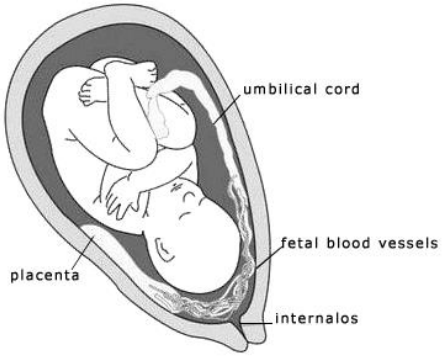
Liver activity	Mild or no necroinflammation	Moderate to severe necroinflammation	Necro-inflammation	Absent
Phase	High replicative/ low inflammatory	Immune clearance	HBeAg-negative Chronic Hepatitis	Non-replicative

Magnius & Espmark Immunology 1972; 109: 1017 – 1021
Kramvis 2016; Rev Med 2016 26(4):285-303

Function of HBeAg

- Not required for viral assembly or replication but is important for natural infection *in vivo.*
- Clinically
  - Index of viral replication
  - Infectivity
  - Severity of disease
  - Response to antiviral treatment

- **Immunoregulatory protein**
  - **Immunogen**
  - **Tolerogen**
  - **↓ Innate IR**



Milich, D & Liang (2003) Hepatology 38: 1075 – 1086Yang, CY et al (2006) J Biol Chem 281:34525 – 34536
1. Visvanathan, K et al (2007) Hepatology 45: 102 -110
https://classconnection.s3.amazonaws.com/129/flashcards/475129/gif/vasa_previa1352911684347.gif

HBeAg Expression and Mother-to-Child Transmission

746 THE NEW ENGLAND JOURNAL OF MEDICINE April 1, 1976

e ANTIGEN AND ANTI-e IN THE SERUM OF ASYMPTOMATIC CARRIER MOTHERS AS INDICATORS OF POSITIVE AND NEGATIVE TRANSMISSION OF HEPATITIS B VIRUS TO THEIR INFANTS

KIYOSHI OKADA, M.D., ICHIRO KAMIYAMA, M.D., MINAKO INOMATA, B.S., MITSUNOBU IMAI, B.S., YUZO MIYAKAWA, M.D., AND MAKOTO MAYUMI, M.D.

AMERICAN JOURNAL OF EPIDEMIOLOGY Vol. 105, No. 2

THE e ANTIGEN AND VERTICAL TRANSMISSION OF HEPATITIS B SURFACE ANTIGEN

R. PALMER BEASLEY,[1,2] CHRISTIAN TREPO,[3] CLADD E. STEVENS,[3] AND WOLF SZMUNESS[3]

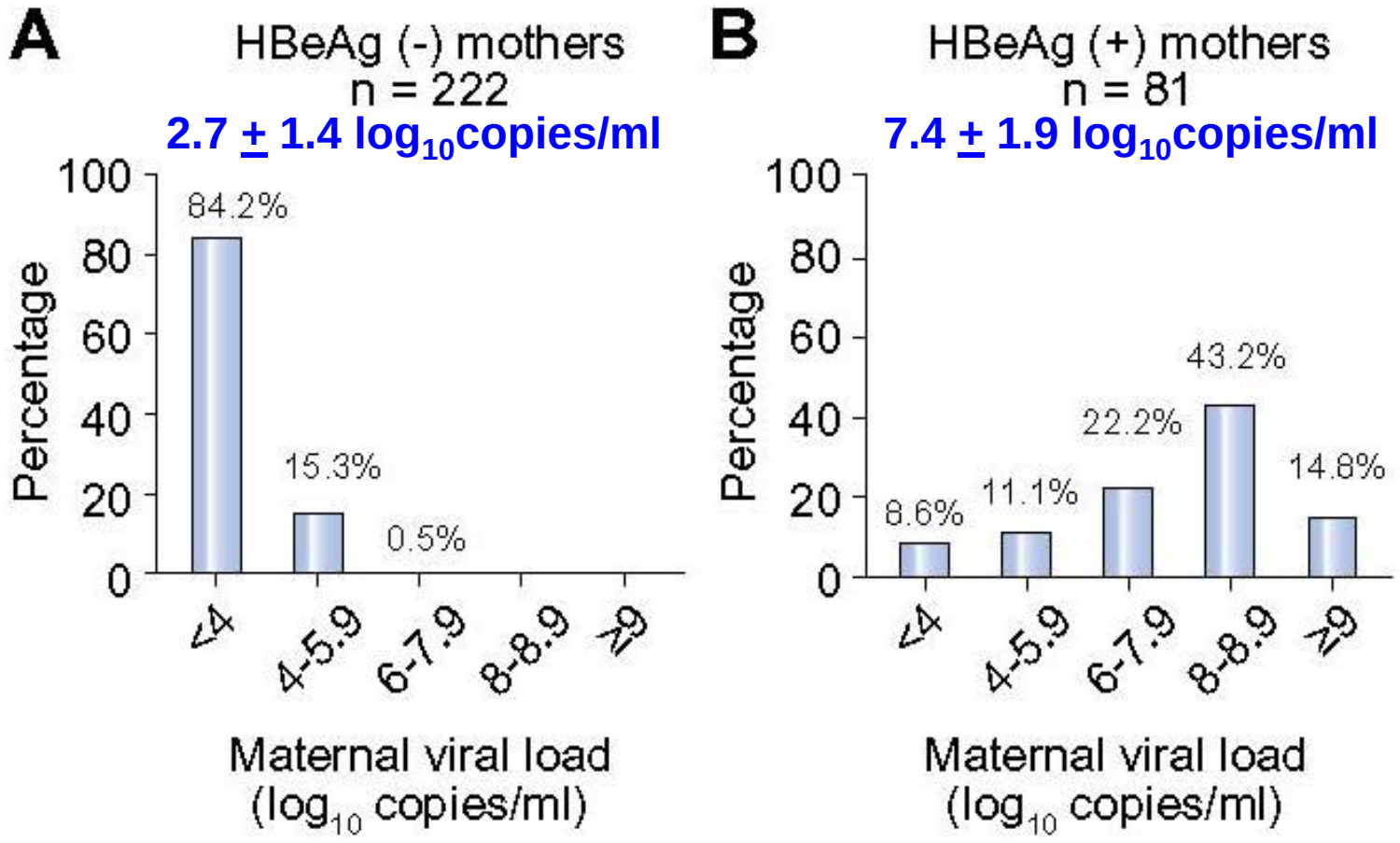
HBeAg and Anti-HBe Detection by Radioimmunoassay: Correlation With Vertical Transmission of Hepatitis B Virus in Taiwan

Cladd E. Stevens, Robert A. Neurath, R. Palmer Beasley, and Wolf Szmuness

HBeAg+ve vs HBeAg-ve
9.26% vs. 0.23%, p <0.001

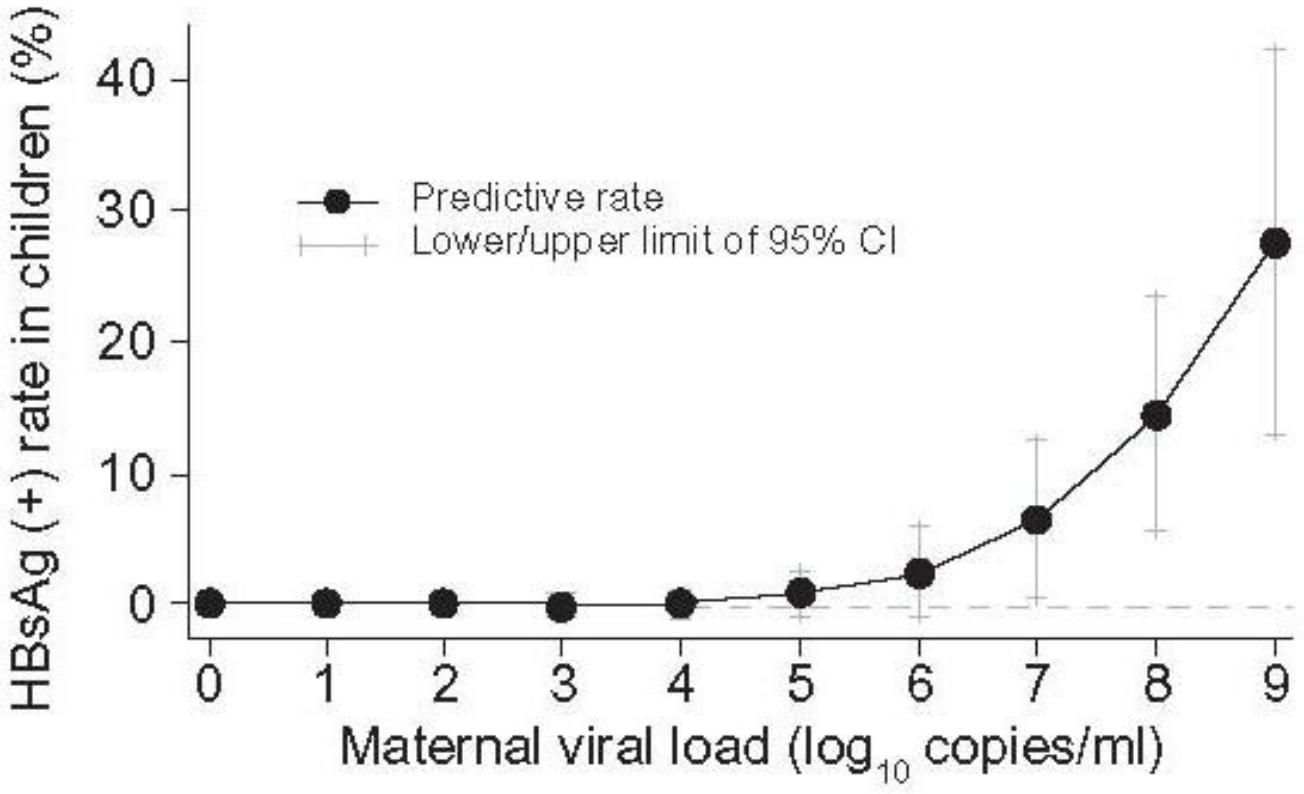
Chen et al Gastorenterology 2012; 142e772

HBV Viral Load
HBeAg-ve versus HBeAg+ve



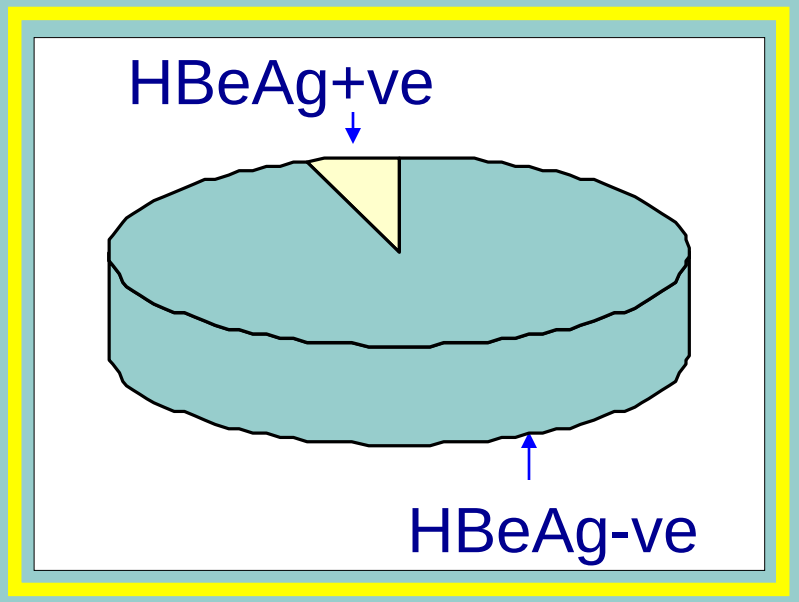
Wen et al, J Hepatol 2013; 59:24 -30

Predictive Rates of HBV Infection versus Maternal VL

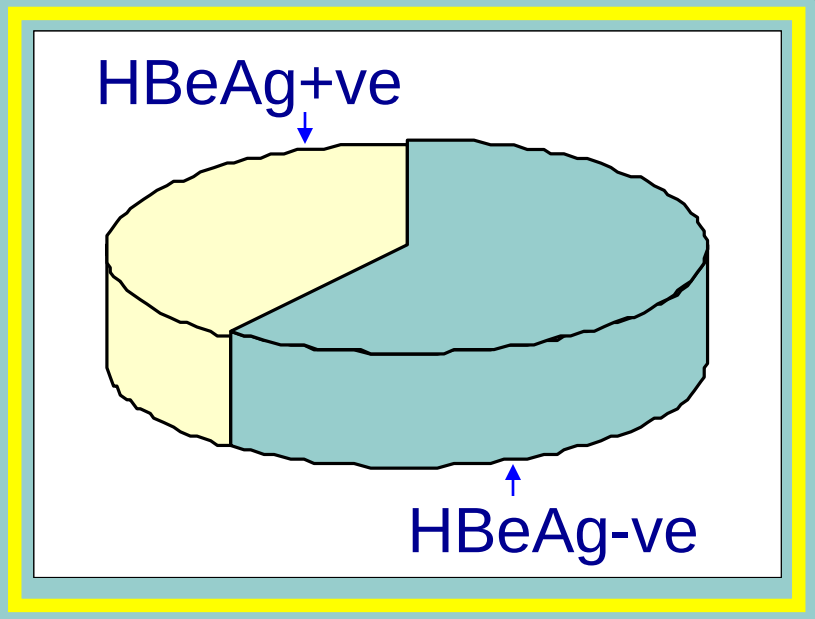


Wen et al, J Hepatol 2013; 59:24 -30

Regional Differences in HBeAg-positivity



Sub-Saharan Africa



South East Asia

Botha et al, Lancet 1984; 1(8388):1210-1212

HBeAg-positivity and Genetic Factors?

Perinatal transmission of hepatitis B virus in high-incidence countries

Y. Ghendon

World Health Organization, Geneva, Switzerland

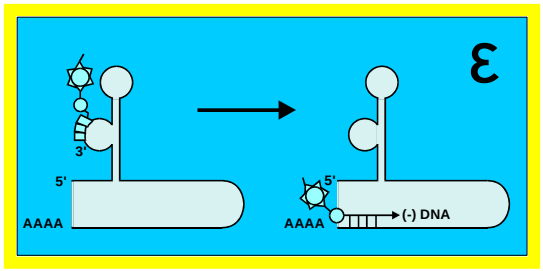
(Accepted 27 March 1987)

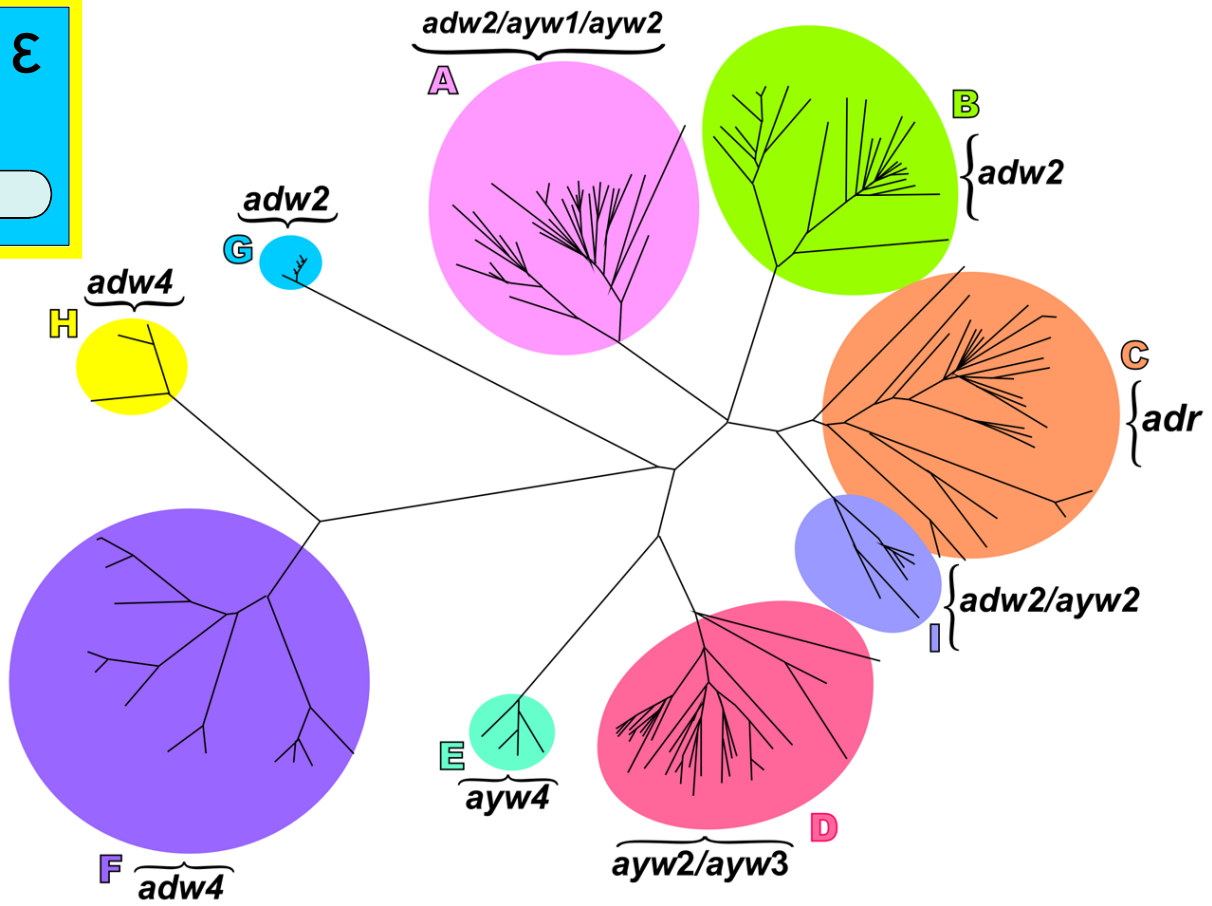
Genetic factors in perinatal transmission of HBV

The expression of HBeAg seems to be determined genetically: most Chinese carrier women but rather fewer African carrier women are HBeAg-positive and throughout children born to Chinese carrier mothers, 40–70% become carriers; to African mothers about 30%; to Asian mothers about 6–8% and to European mothers almost none (Derso et al., 1978; Stevens et al., 1975; Wong et al., 1980).

Ghendon, Y 1987; J Virol Methods 17: 69-79

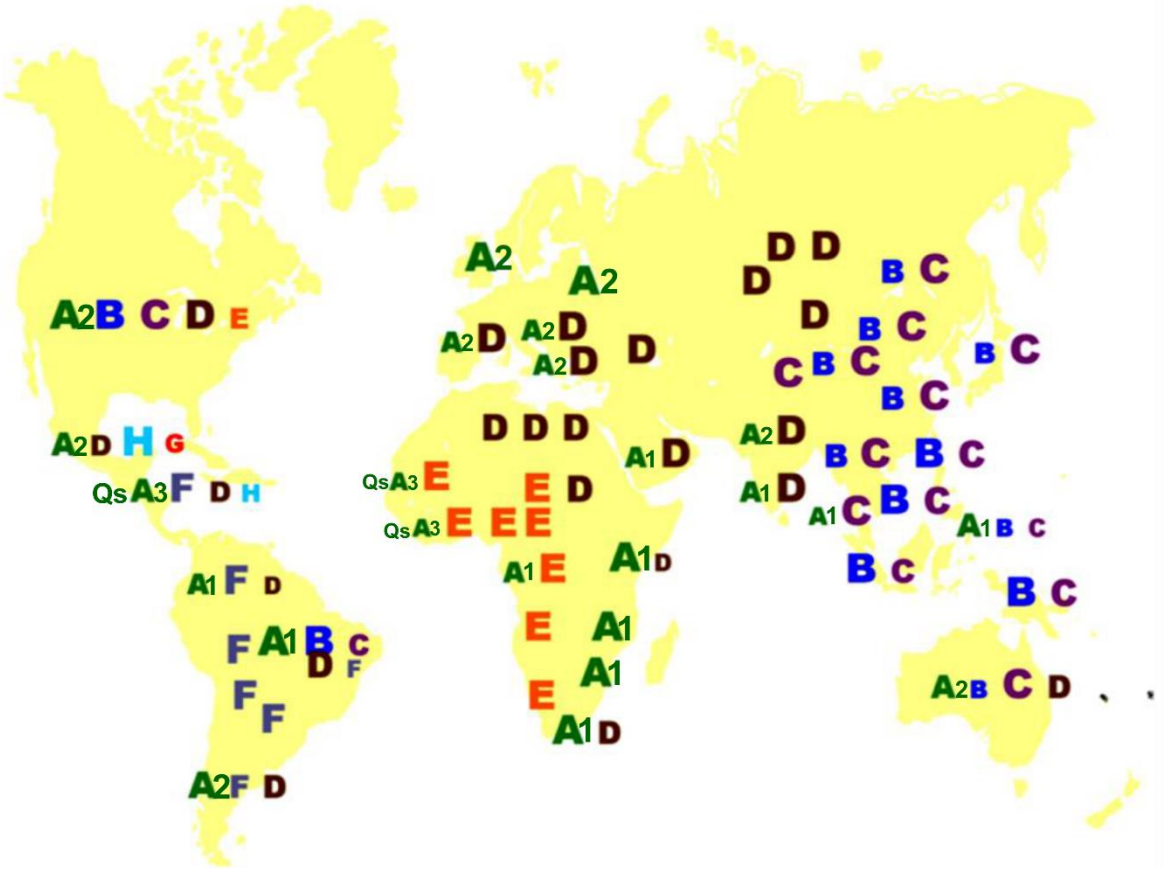
The Genotypes of HBV





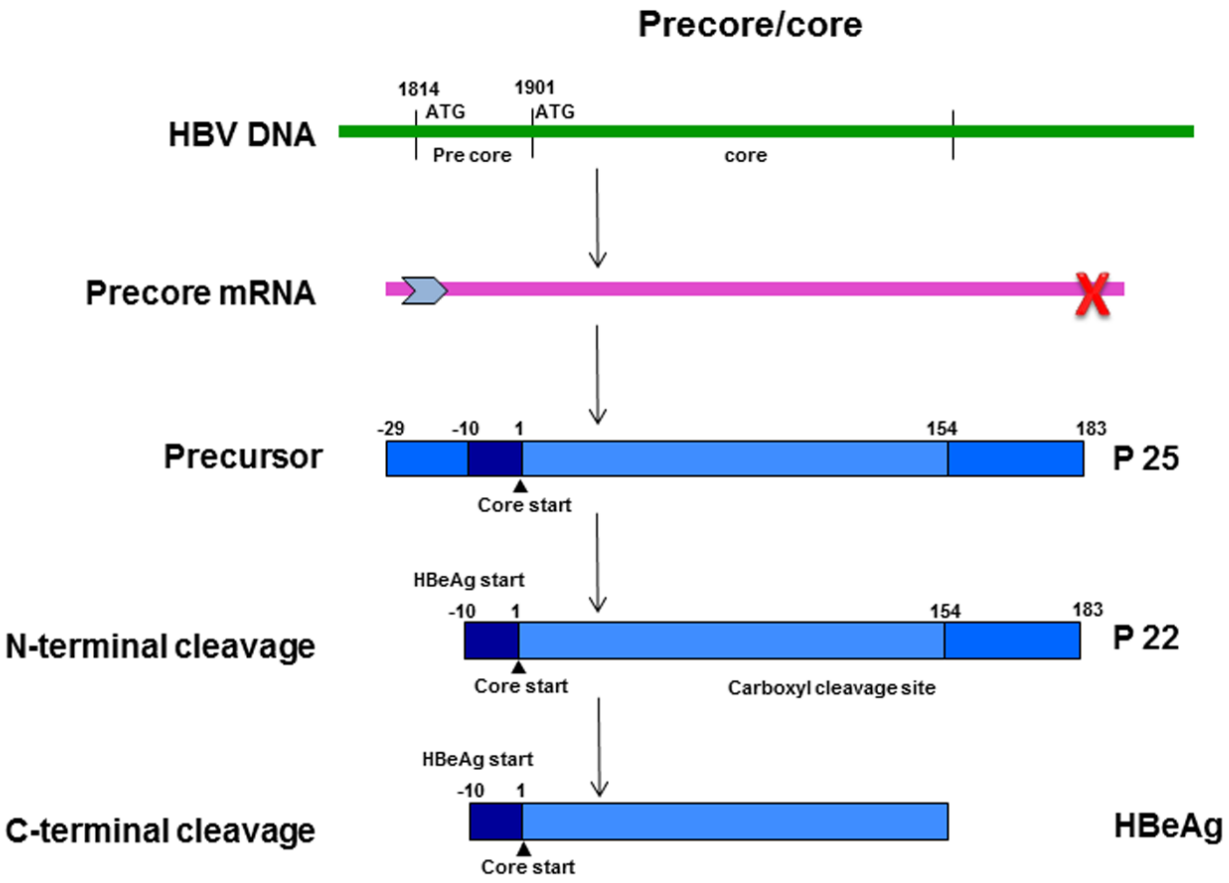
Kramvis & Kew J Viral Hepat 1998; 5:357-367
Kramvis et al Vaccine 2005;23:2409- 2423
Kramvis Intervirology 2014;57:141-150

Geographic Distribution of HBV Genotypes/Subgenotypes

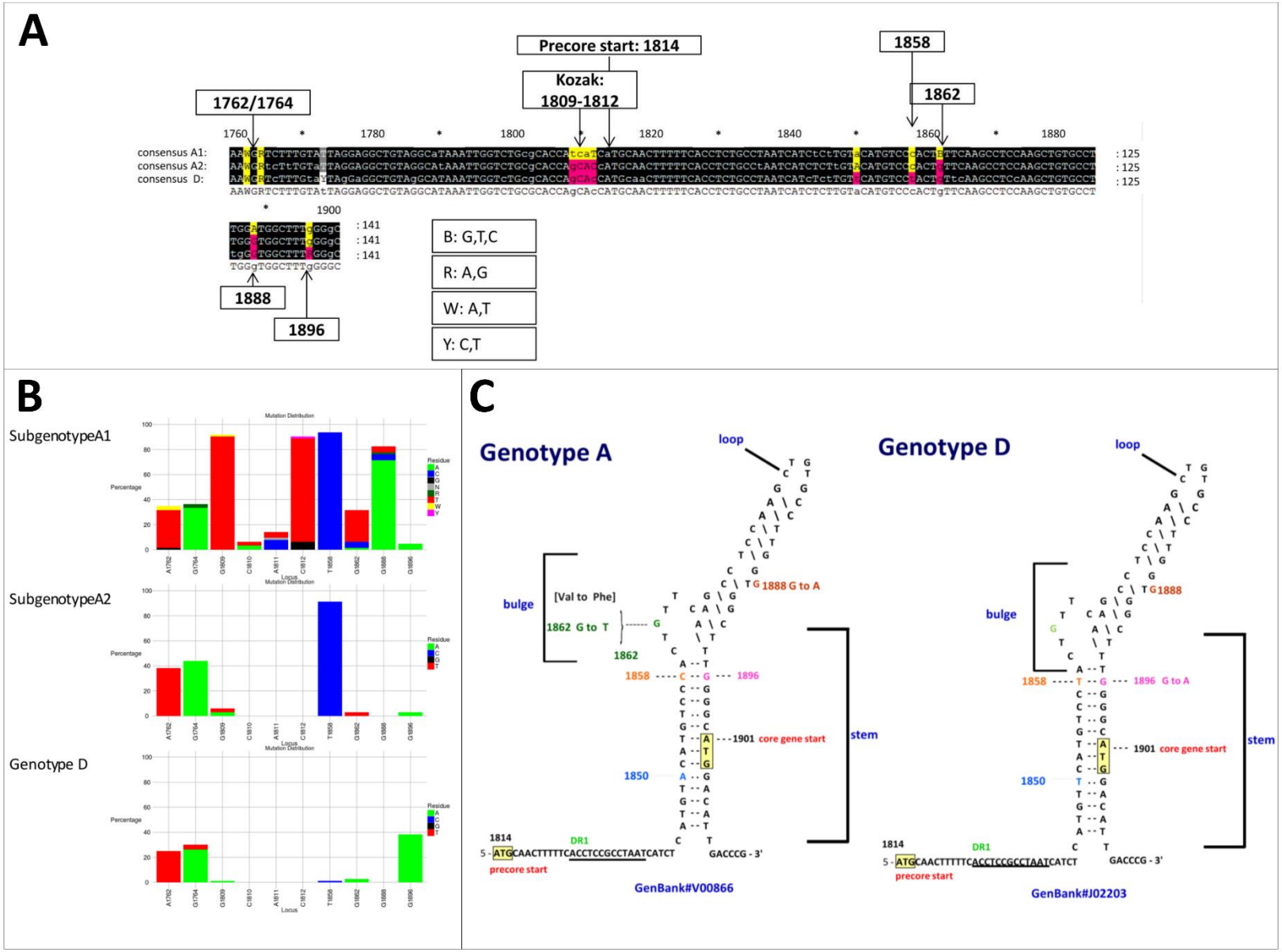


Kramvis Intervirology 2014;57:141-150
Kramvis 2016; Rev Med 2016 26(4):285-303

Expression of HBeAg

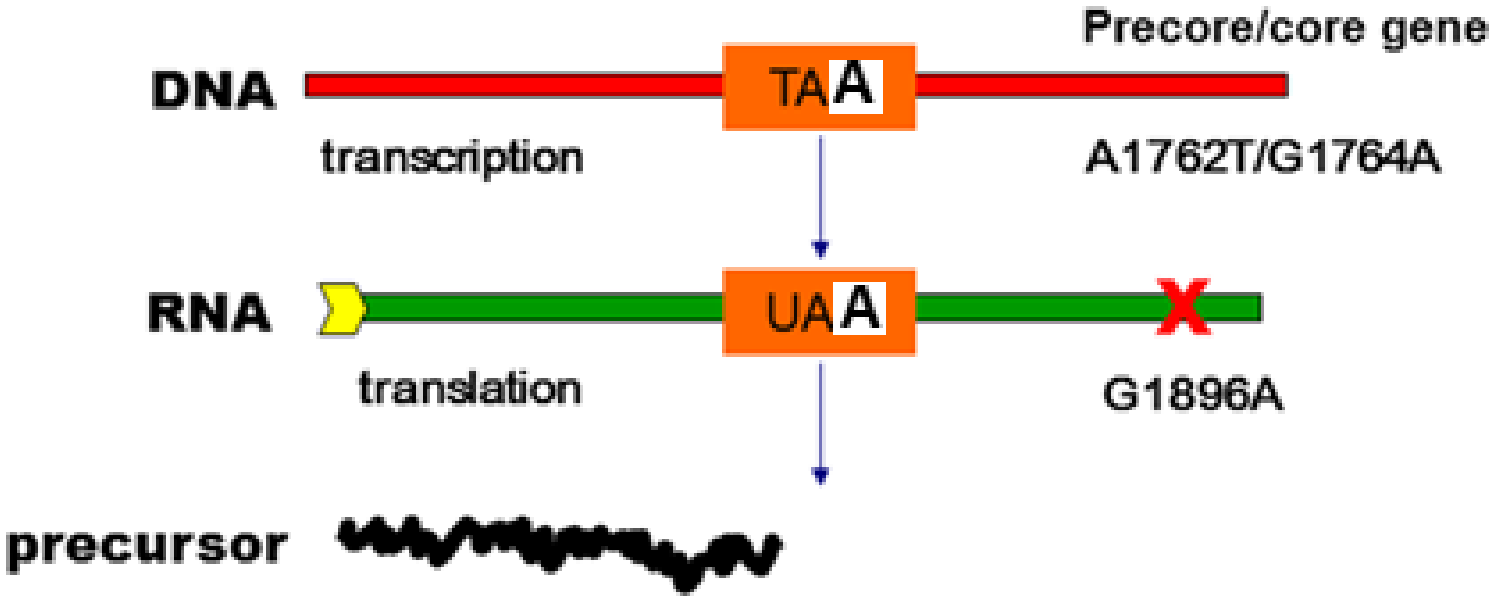


Revill….Kramvis J Med Virol 2010;82: 104-115
Kramvis; Rev Med 2016 26(4):285-303



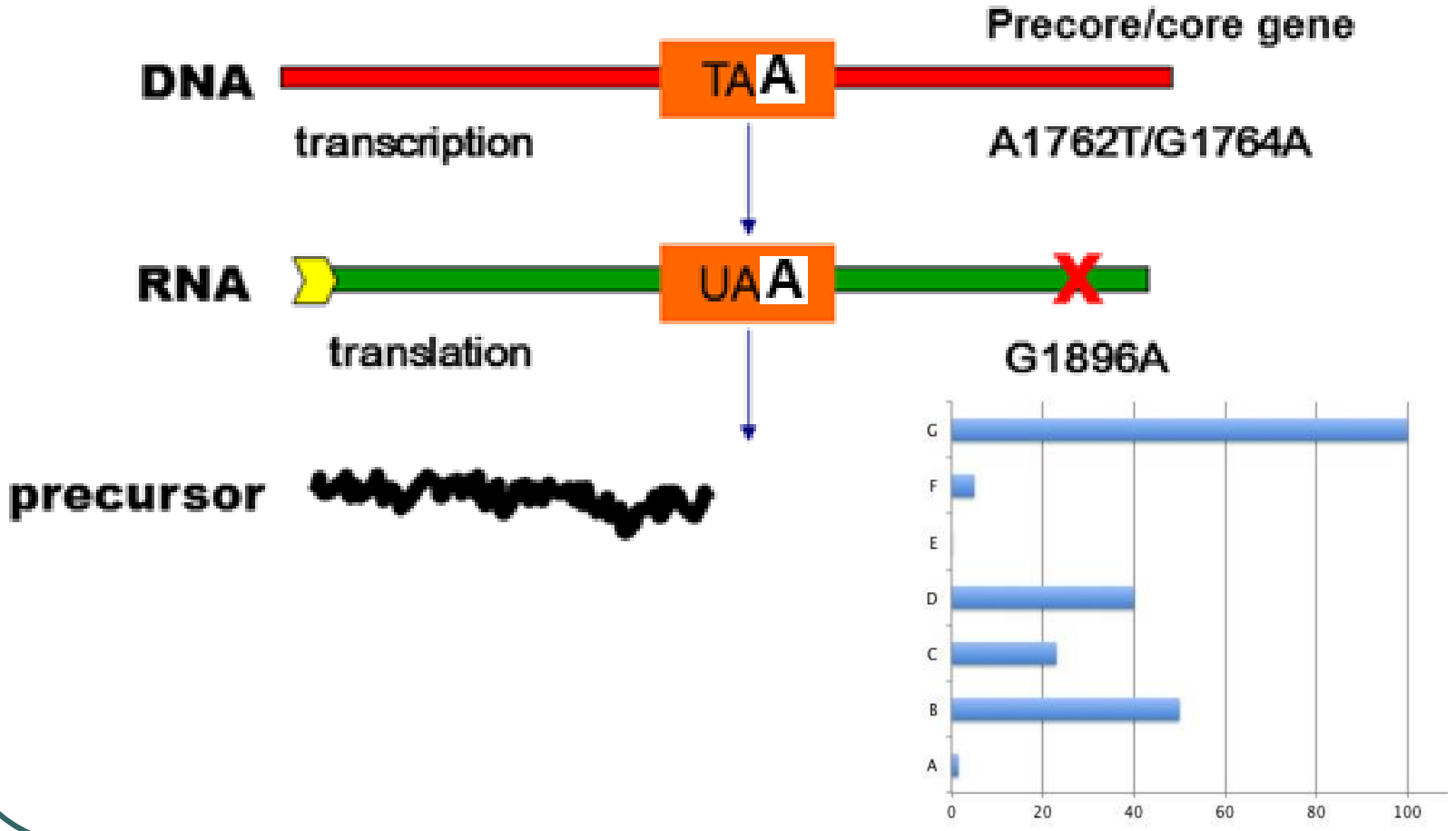
Kramvis 2016; Rev Med 2016 26(4):285-303

G1896A Mutation in Genotype D



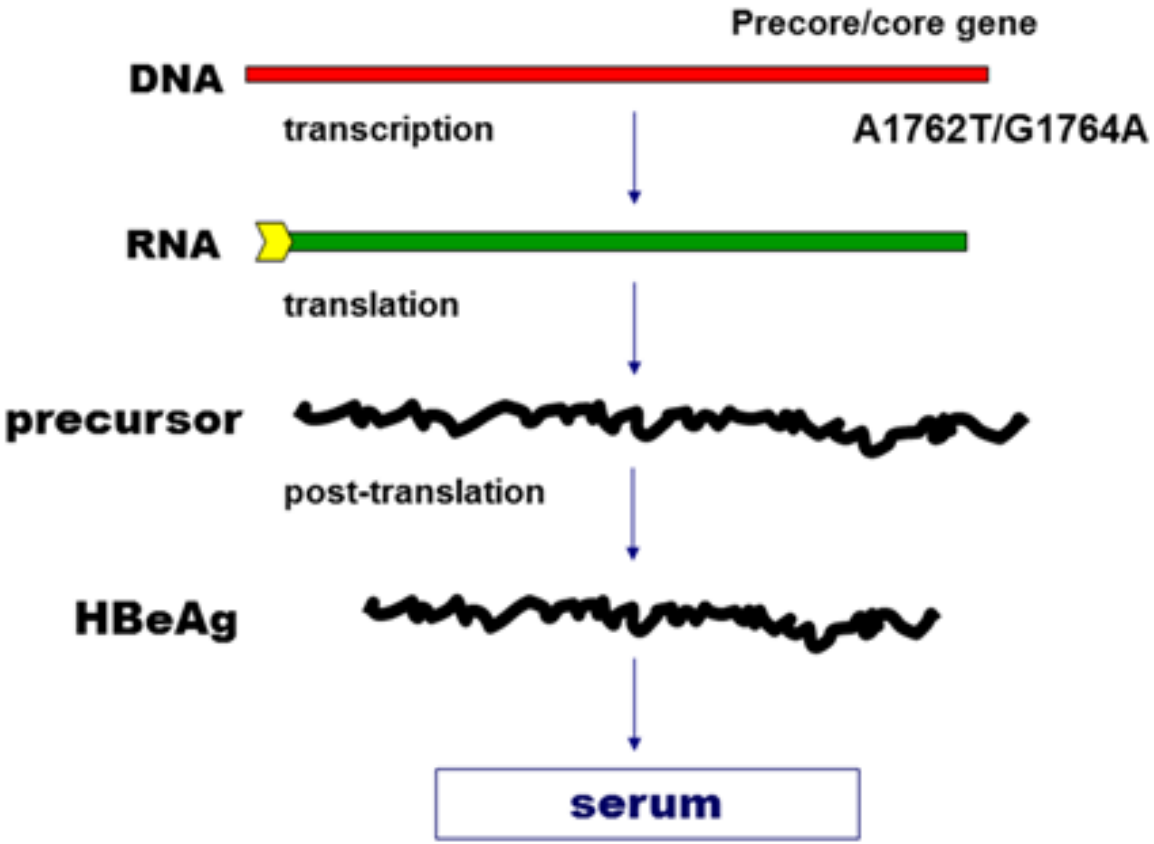
Carman et al Lancet 1989; **2**(8663): 588-591.

G1896A Mutation in Genotype D



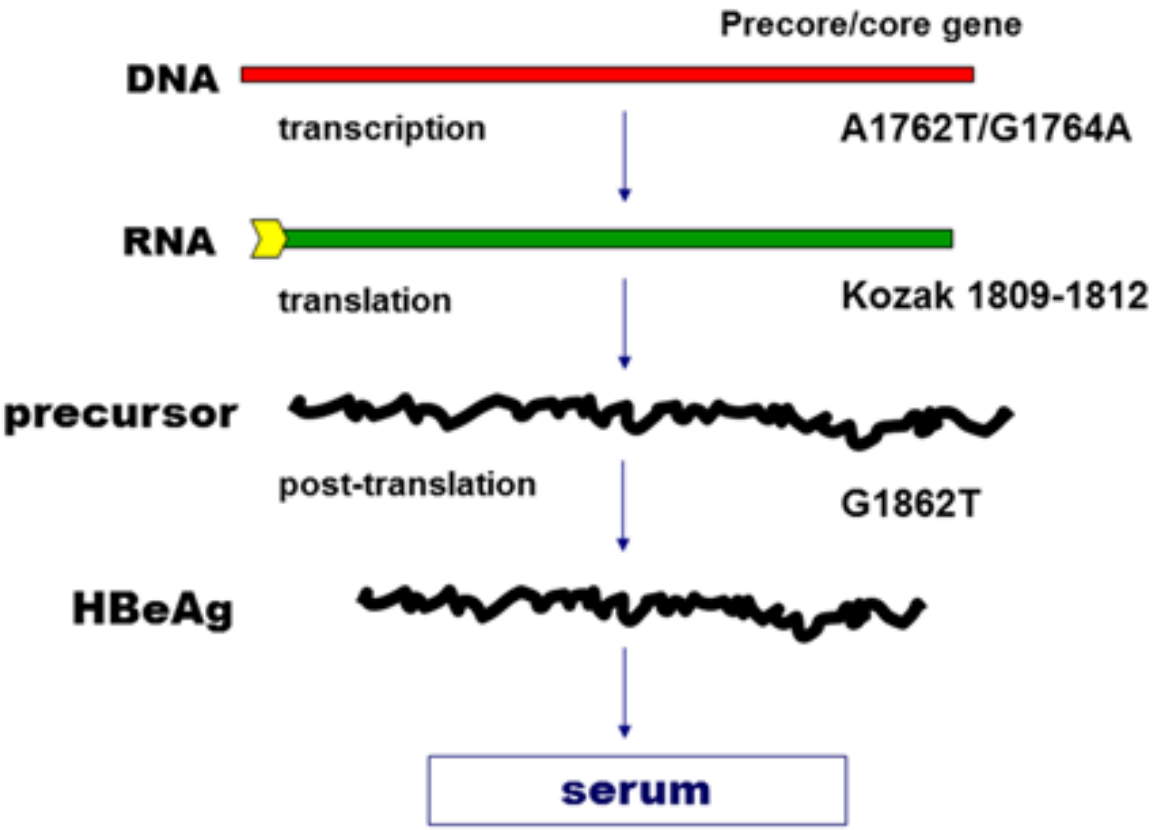
Carman et al Lancet 1989; **2**(8663): 588-591.
Revill….Kramvis J Med Virol 2010;82: 104-115

Subgenotype A2



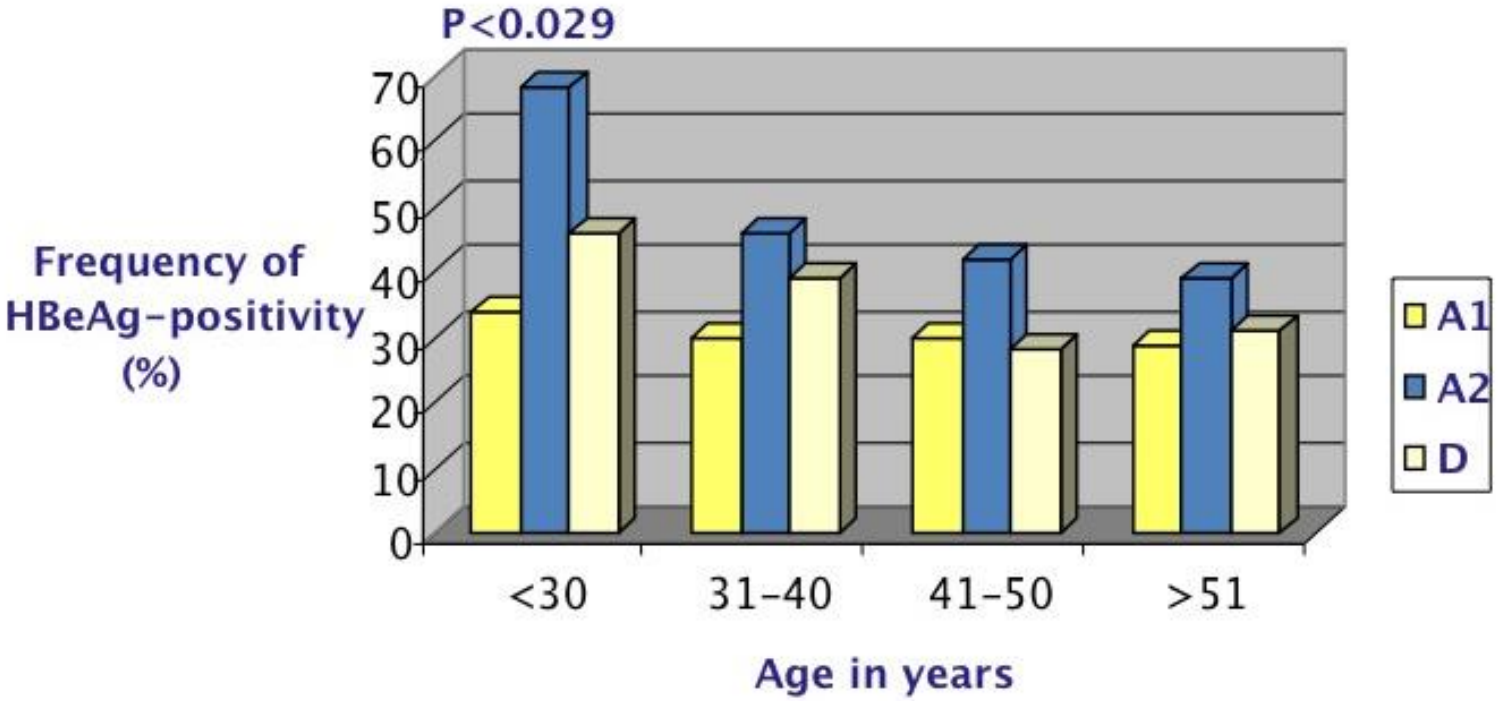
Kramvis 2016; Rev Med 2016 26(4):285-303

Subgenotype A1



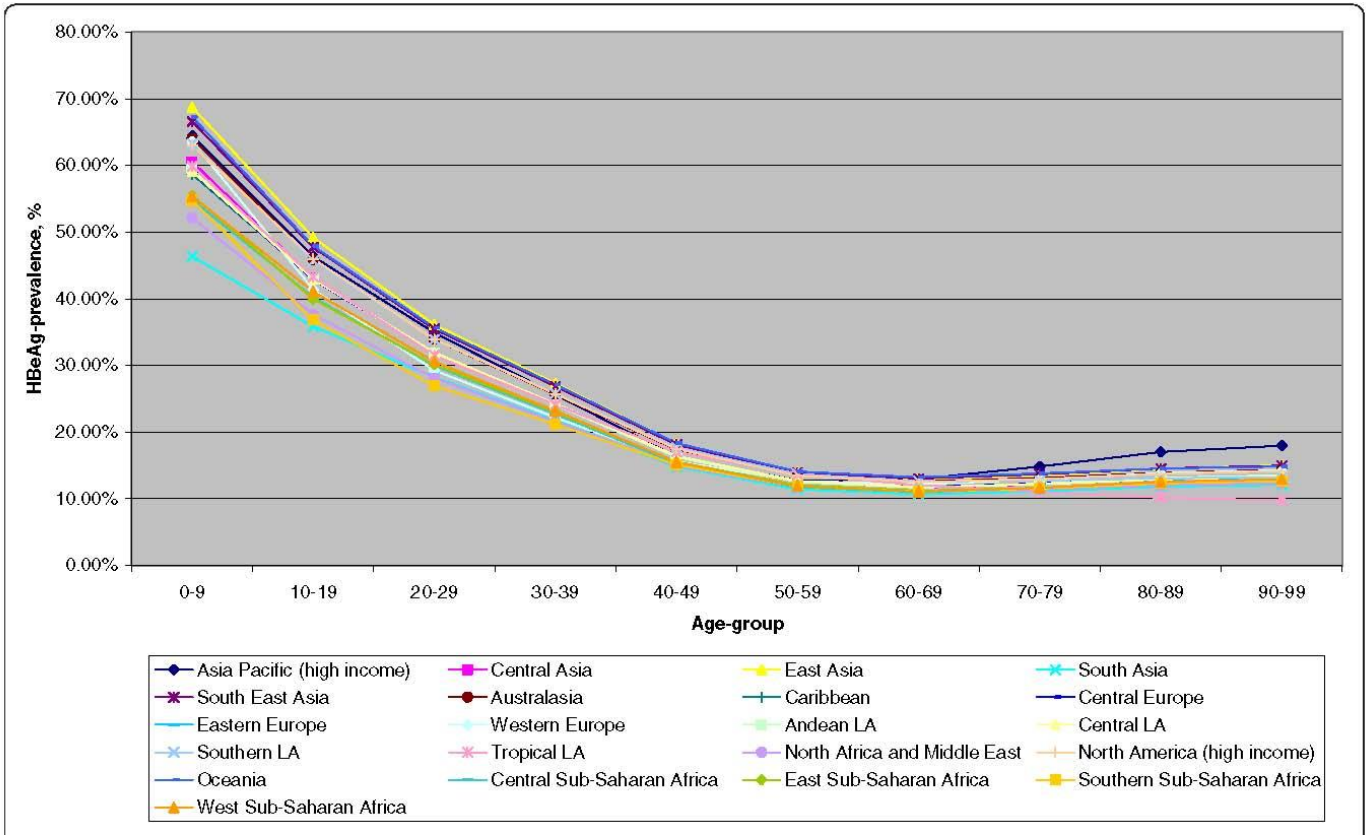
Kramvis 2016; Rev Med 2016 26(4):285-303

The Effect of Genotype/Subgenotype on HBeAg Expression



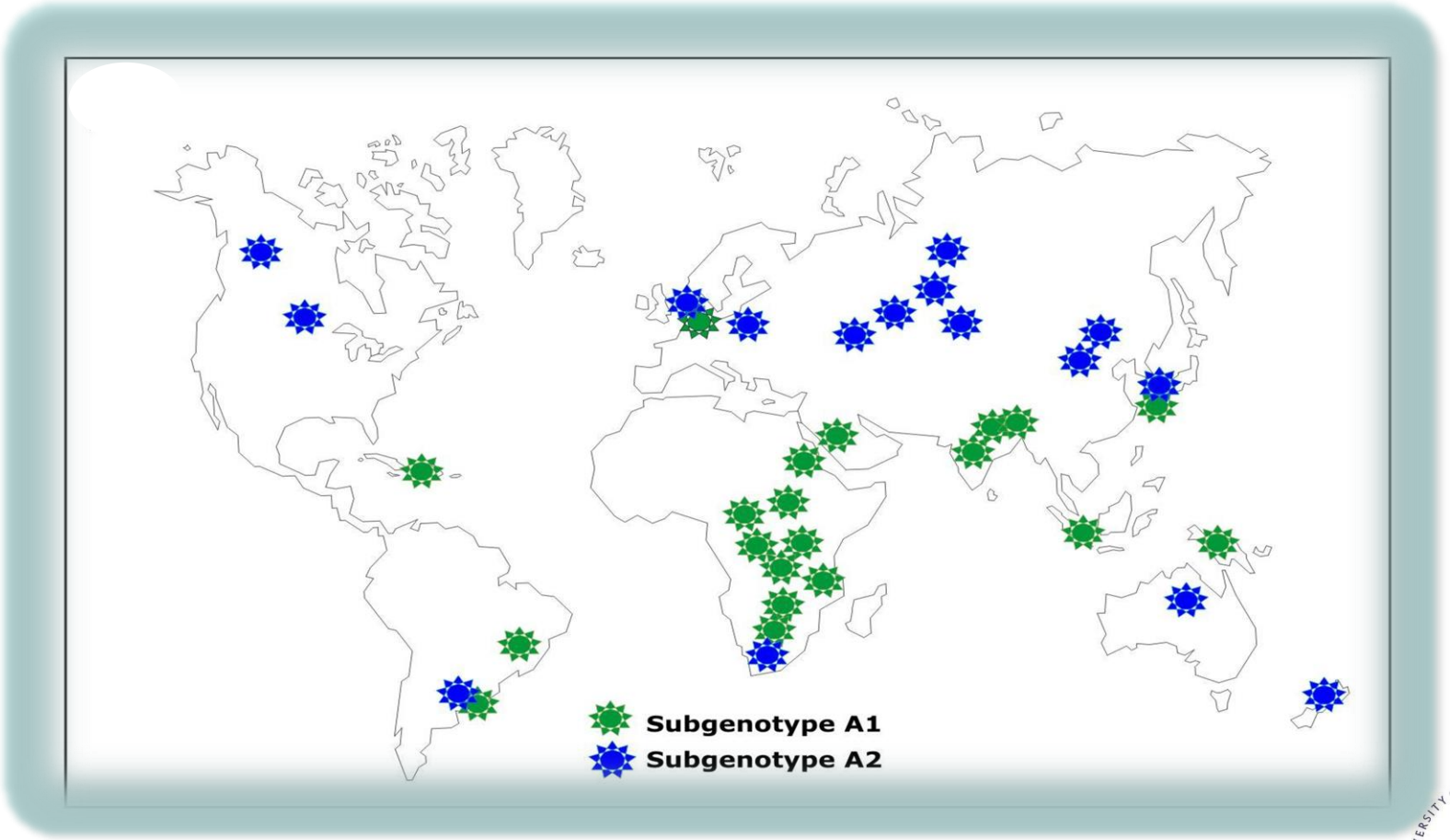
Tanaka et al Hepatology 2004; 40: 747-755

HBeAg Prevalence in HBsAg-positive Females: 2005

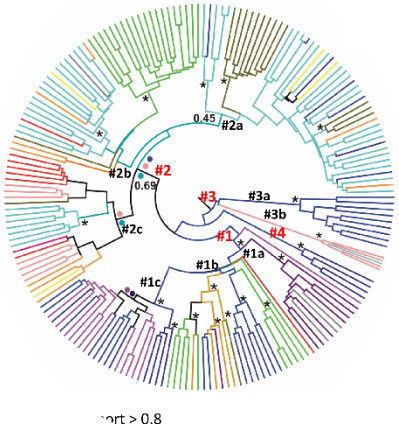


Ott et al BMV Infect Dis 2012; 12:131

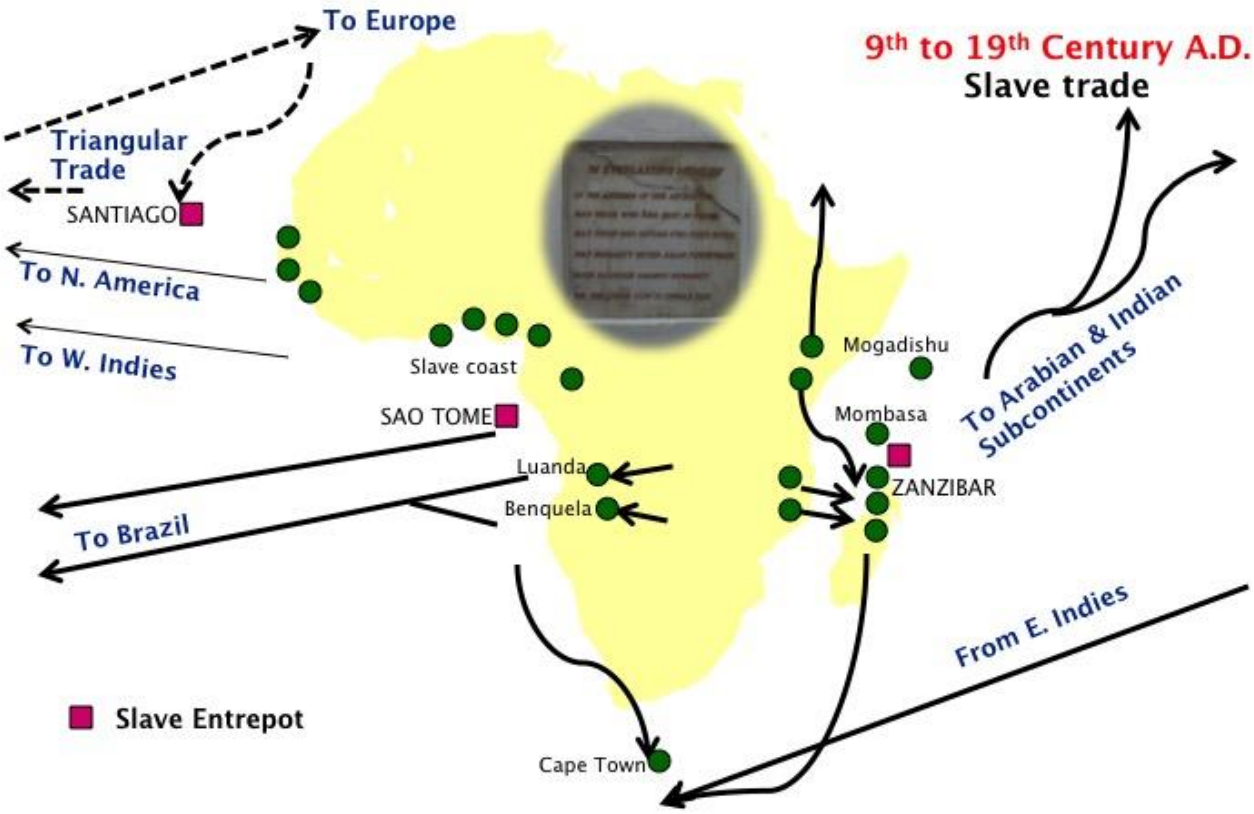
Geographic Distribution of Genotype A



Kramvis & Paraskevis Antiviral Ther 2013; 18:513



The Slave Trade

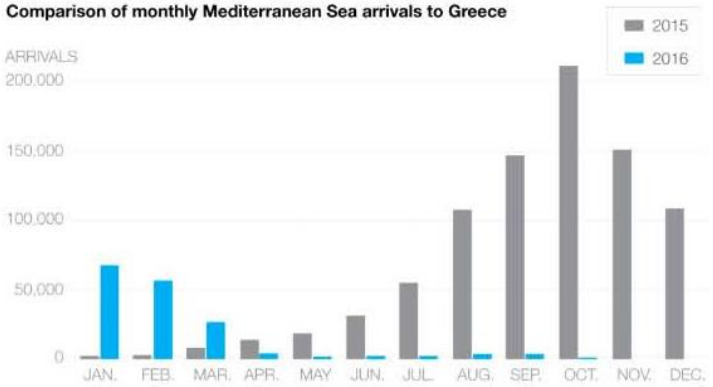


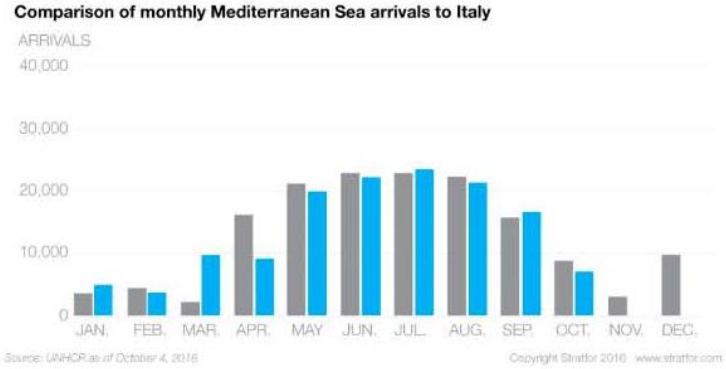
Kramvis & Paraskevis Antiviral Ther 2013; 18:513

Griffiths (1993) The Atlas of African Affairs

North Africa: The Other Side of Europe's Migrant Crisis

October 7, 2016 | 09:16 GMT





Changing HBV Genotype Distribution

Journal of Medical Virology 89:639–646 (2017)

First Epidemiological and Phylogenetic Analysis of Hepatitis B Virus Infection in Migrants From Mali

American Journal of Epidemiology

DOI: 10.1093/aje/kwx064

Original Contribution

Characteristics of US-Born Versus Foreign-Born Americans of African Descent With Chronic Hepatitis B

J Gastroenterol
DOI 10.1007/s00535-017-1315-4

The Japanese Society of Gastroenterology

CrossMark

ORIGINAL ARTICLE—LIVER, PANCREAS, AND BILIARY TRACT

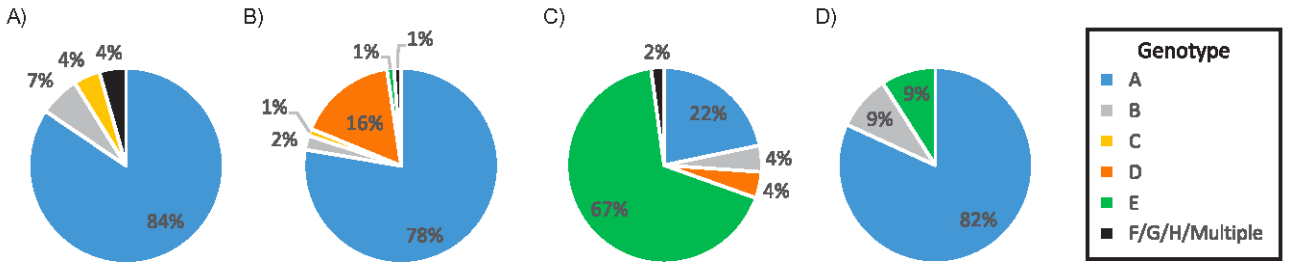
Natural history of chronic hepatitis B virus infection in children in Japan: a comparison of mother-to-child transmission with horizontal transmission

Celia et al J Med Virol 2017' 89:639-646
Hassan et al Am J Epidemiol 2017; DOI:10.1093/aje/kwx064
Takano et al J Gastroenterol 2017; DOI:10.1007/s00535-017-1315-4

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

Comparison of US versus Foreign Born African Americans with Chronic Hepatitis

	USAA	FBAA
Age*	47 years	40 years
Sexual transmission*	59%	3%
HBeAg-positivity*	19%	9%
Phase	CH	IC
Genotype	A2	A1/E



USA | East Africa | West Africa | Other

Hassan et al Am J Epidemiol 2017; DOI:10.1093/aje/kwx064

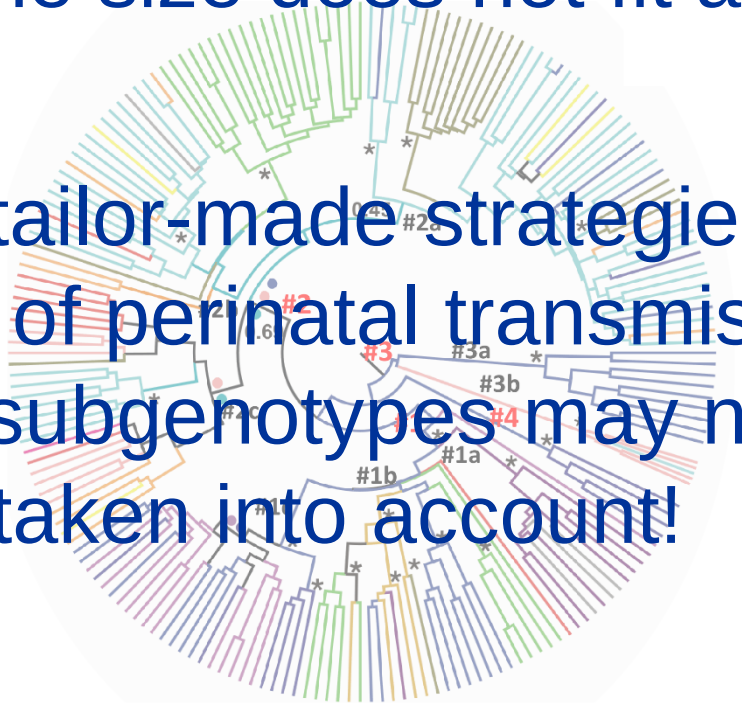
Comparison of MTCT *versus* Horizontal in Japanese Children

	MTCT	Horizontal
Genotype*	C	A or B
HBeAg-negativity at 15 years of age*	33%	45%
Hepatitis < 4 years*	lower	higher
HCC at 30 years	6%	11%

Takano et al J Gastroenterol 2017; DOI:10.1007/s00535-017-1315-4

Take Home Message

One size does not fit all!



We need tailor-made strategies for the prevention of perinatal transmission and genotypes/subgenotypes may need to be taken into account!

BWTS Programme "Bilateral (International) scientific and technologica cooperation (BSTC)"