MOLECULAR BIOLOGY AND EPIDEMIOLOGY OF HEPATITIS B AND C VIRUSES

By

Petros Karayiannis

Imperial College
London

Family: HEPADNAVIRIDAE

Primate HBV

Ground squirrel hepatitis B

Hepatitis B virus (HBV)

Duck hepatitis B virus

Woodchuck hepatitis Virus

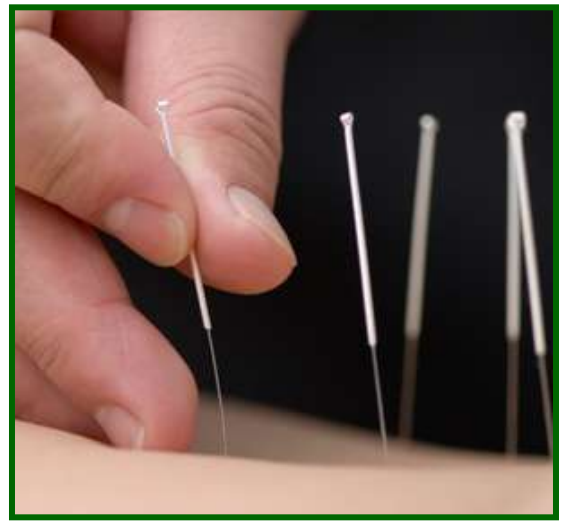
MAIN ROUTES OF HBV TRANSMISSION

DRUG ADDICTION

VERTICAL

SEX

TATTOOS



ACUPUNCTURE

BLOOD TRANSFUSION

Concentration of HBV in body fluids

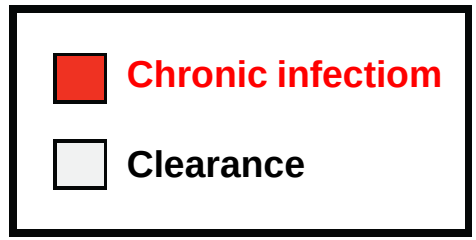
High	Moderate	Low/Not Detectable
blood	semen	urine
serum	vaginal fluid	feces
wound exudates	saliva	sweat
		tears
		breast milk

About 2 billion people worldwide have been infected with the virus.

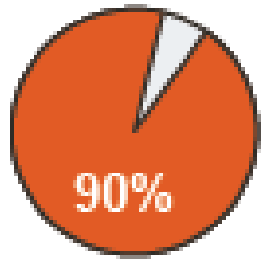
About 350 million live with chronic infection.

About 600,000 persons die each year due to the acute or chronic consequences of hepatitis B.

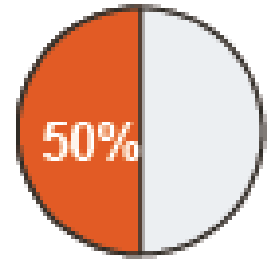
RISK OF CHRONIC HBV INFECTION



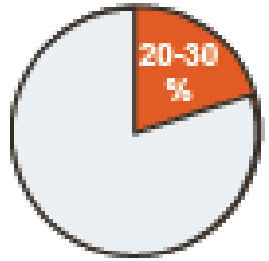
Time of infection:



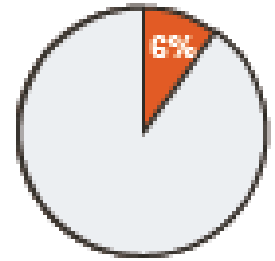
Neonates



Infants



Children



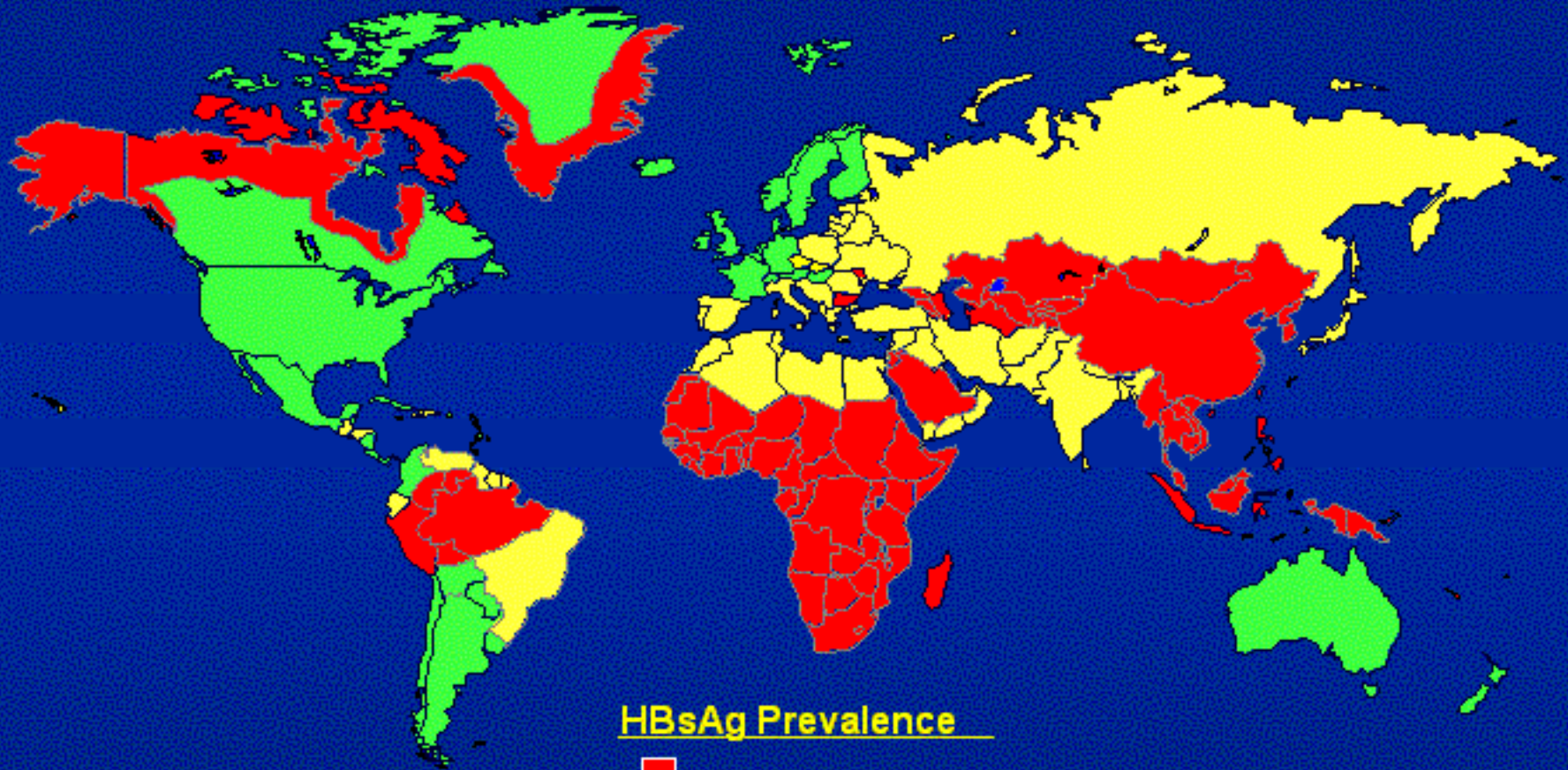
Adults – lasting immunity

Death from chronic liver disease occurs in:

15 – 25% of chronically infected persons

recovery generally within 6 mos

Geographic Distribution of Chronic HBV Infection

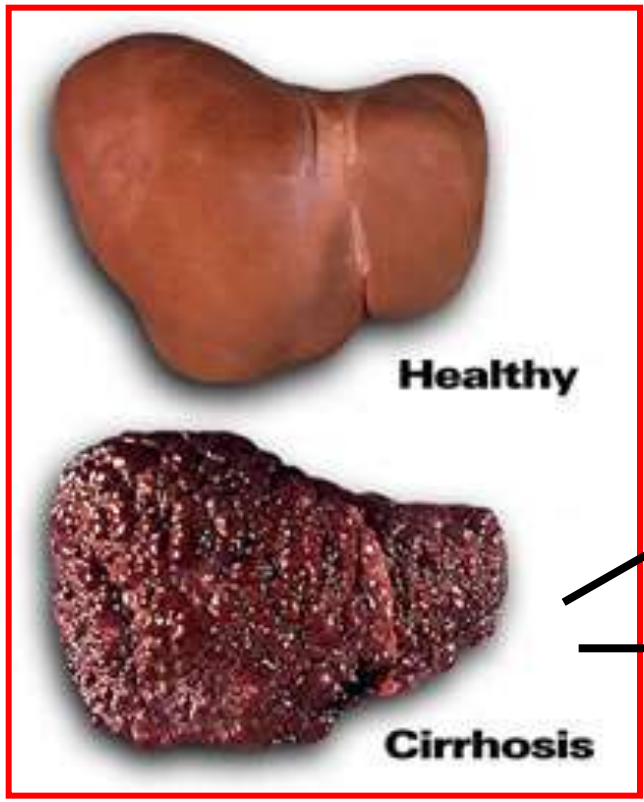


CDC
Centers for Disease Control and Prevention

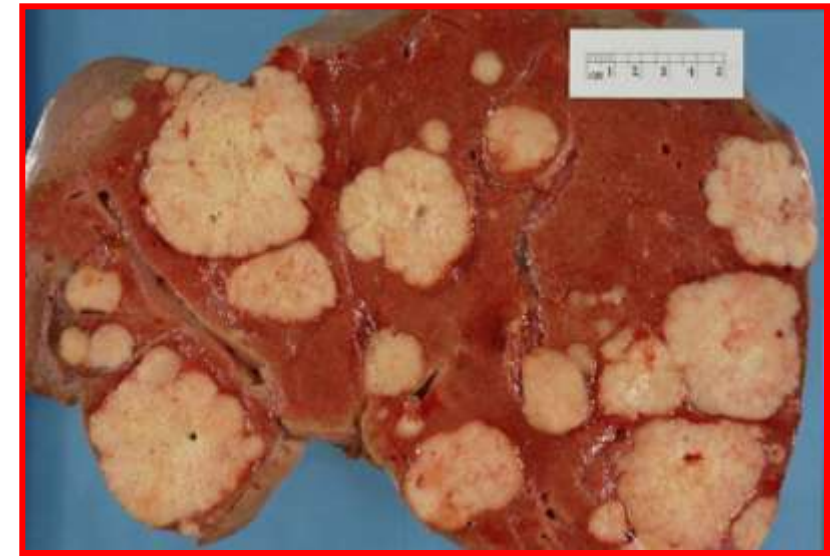
HBV

Incidence of Primary Hepatocellular Carcinoma

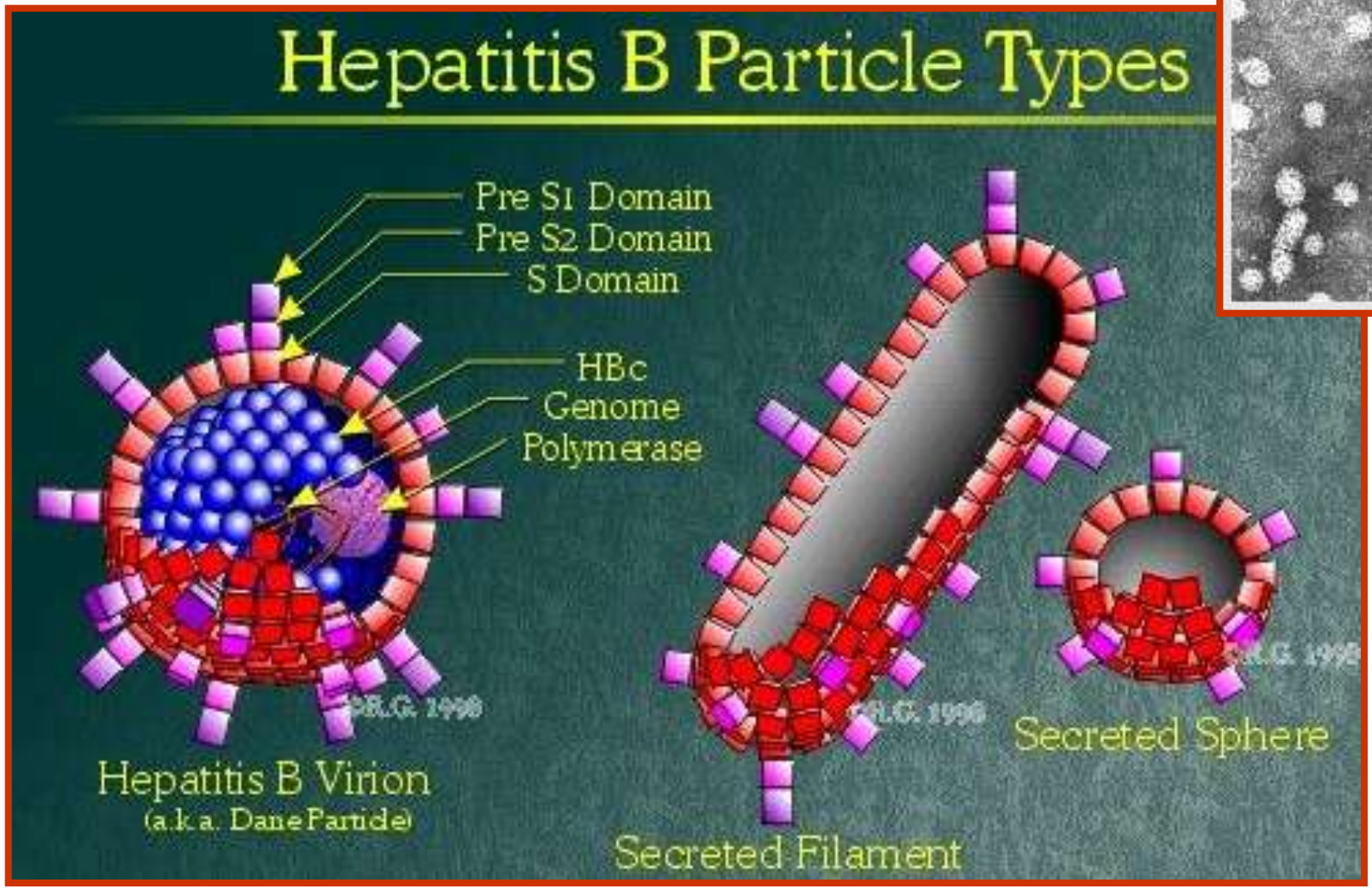
SEQUELAE OF CHRONIC HBV INFECTION

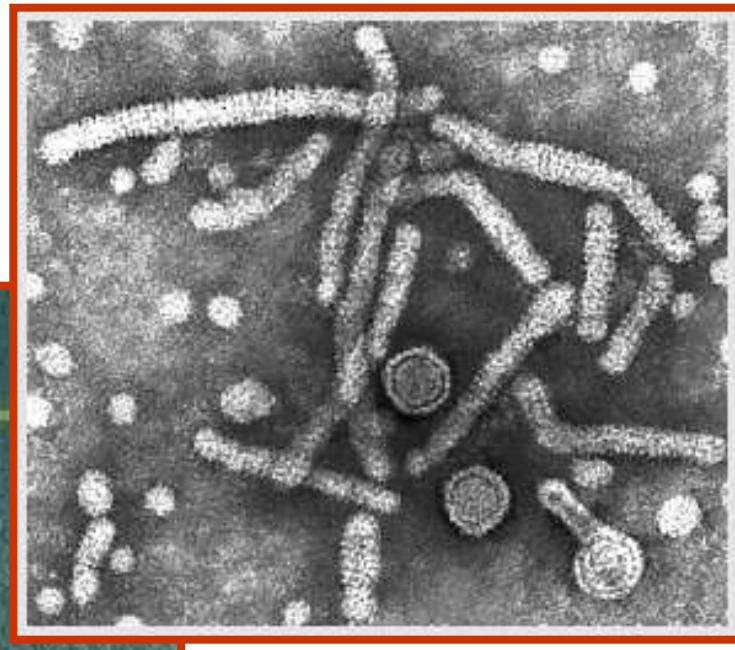


ASCITES



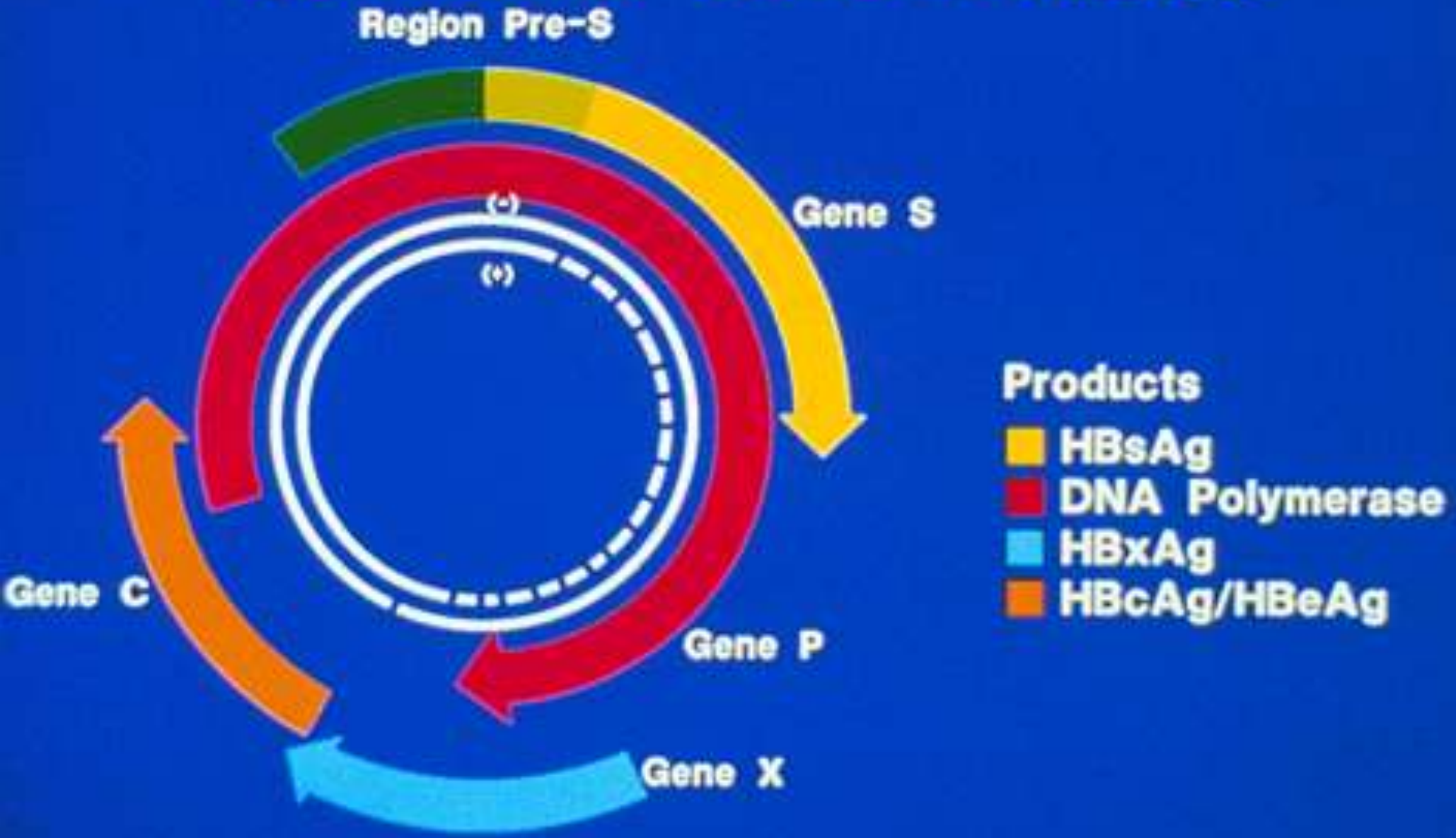
LIVER CANCER


Hepatitis B Particle Types
Pre S1 Domain
Pre S2 Domain
S Domain
HBc
Genome
Polymerase
Hepatitis B Virion
(a.k.a. Dane Particle)
Secreted Filament
Secreted Sphere

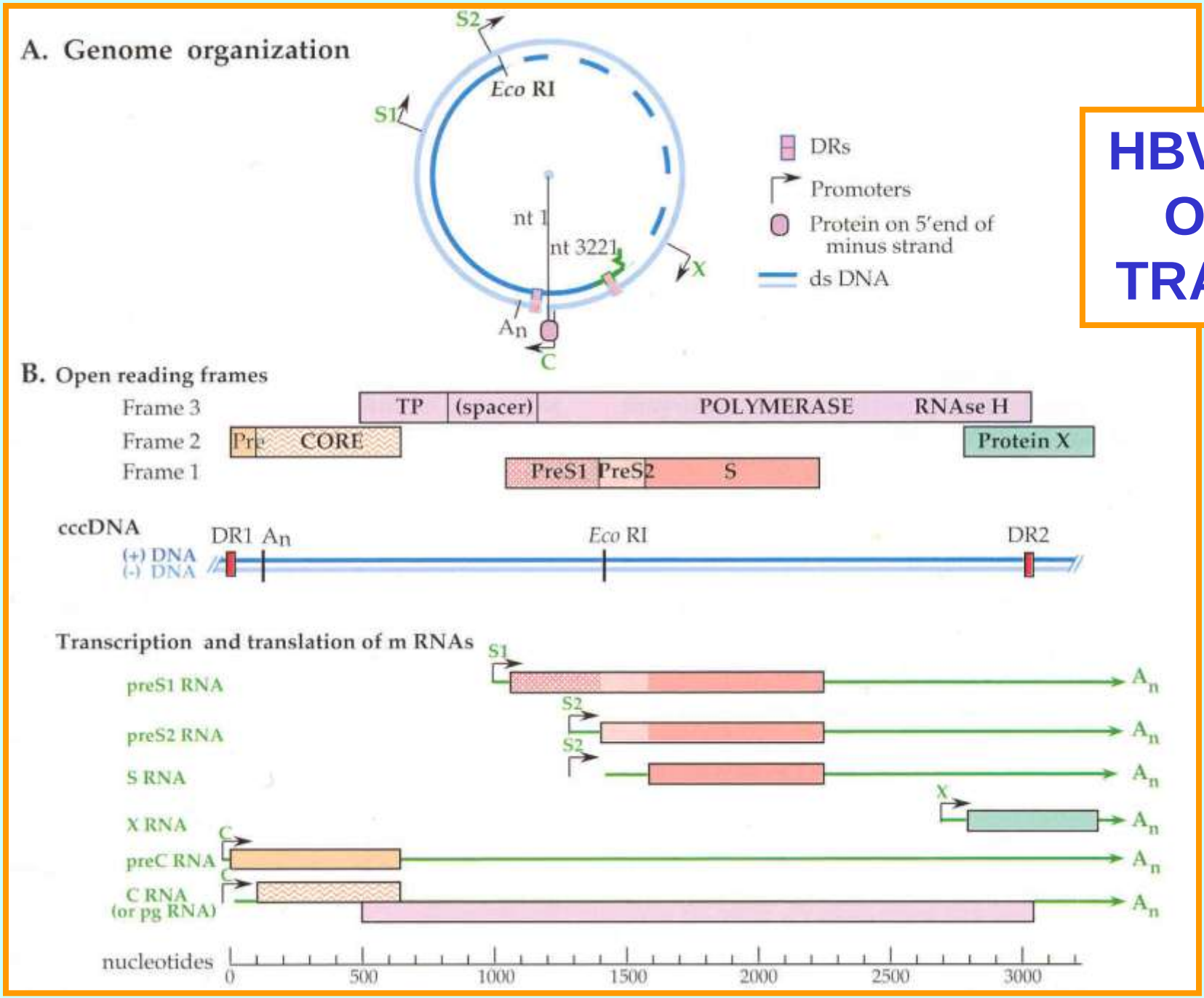


HBV

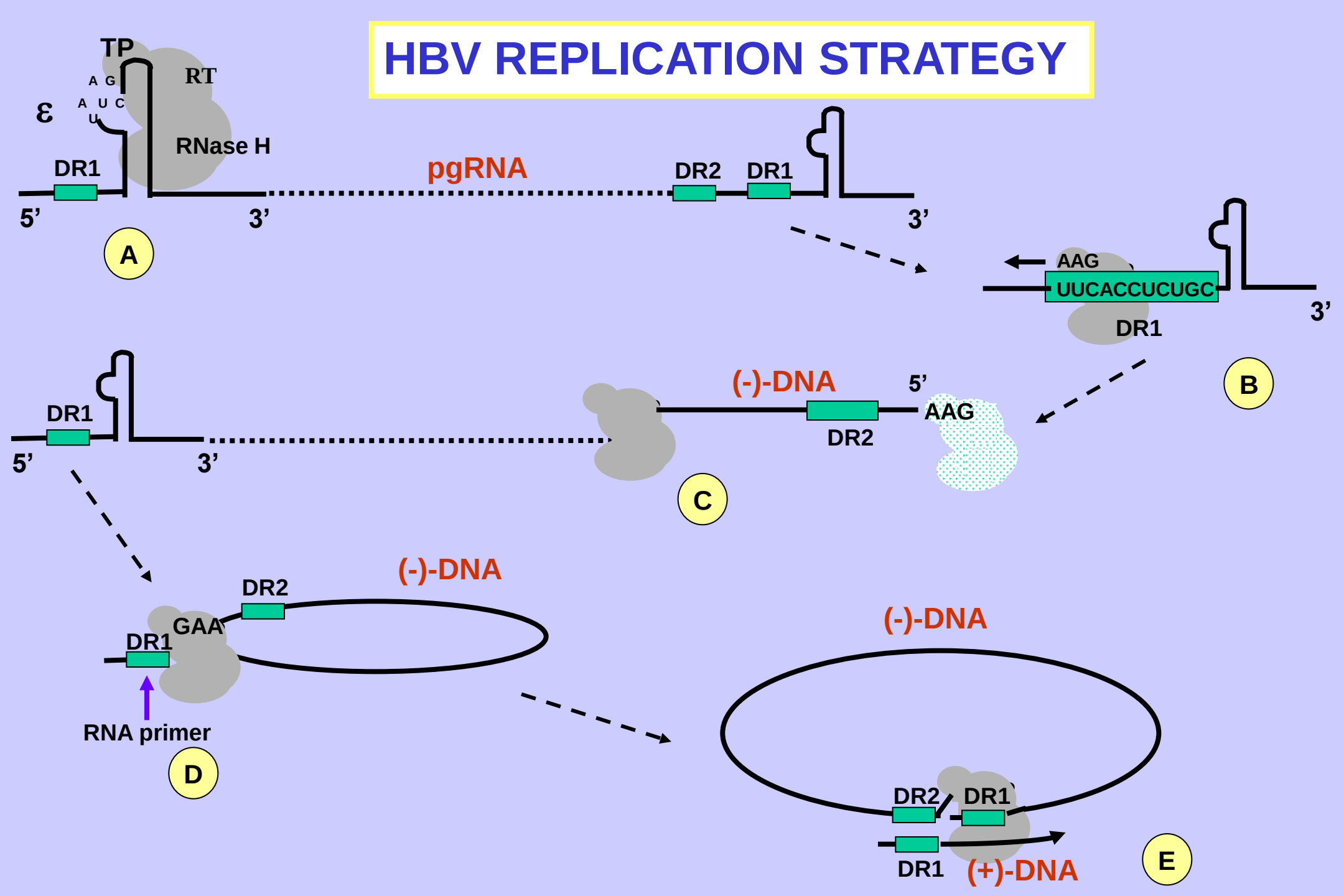
Genes and Gene Products



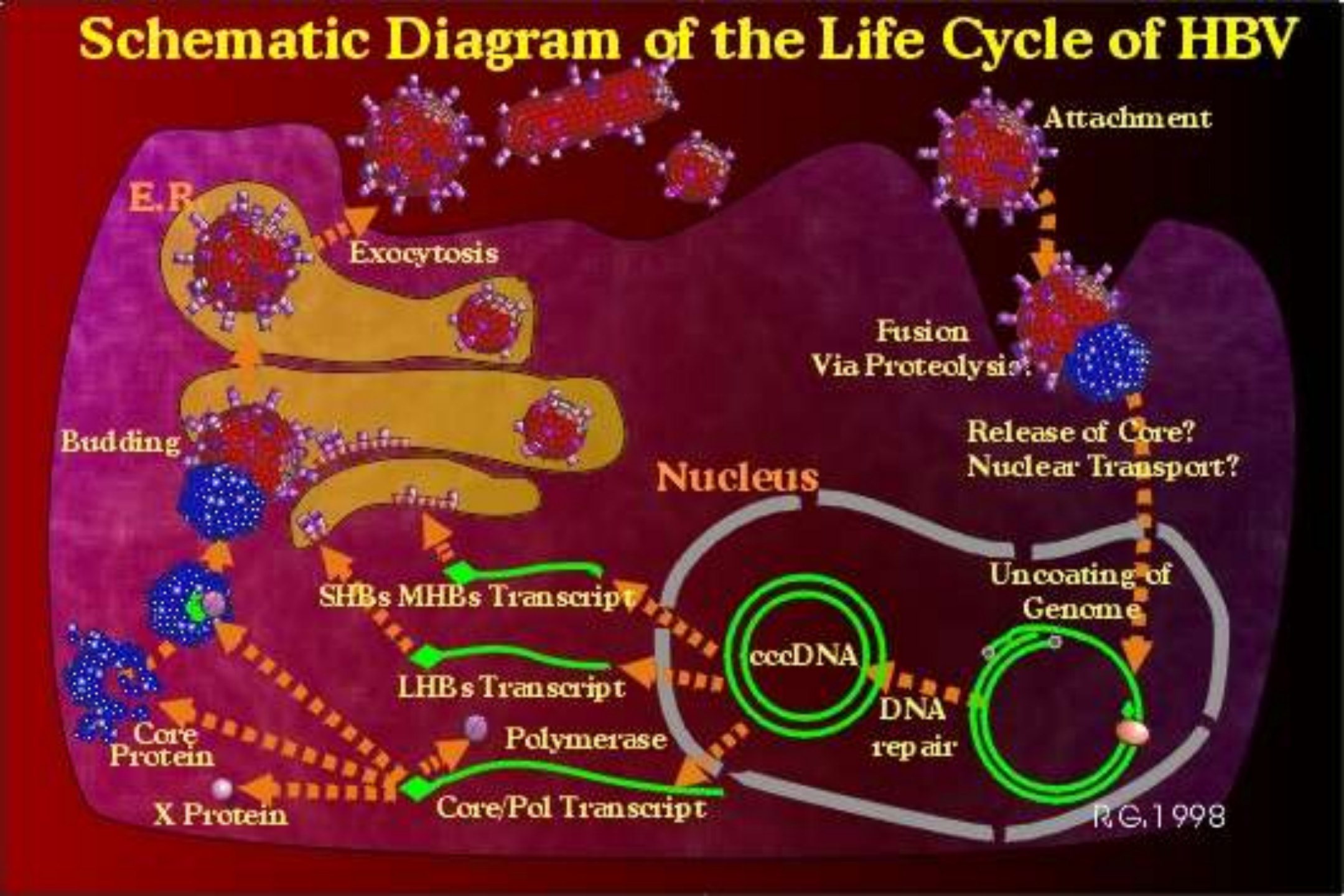
HBV GENOME, ORFs AND TRANSCRIPTS



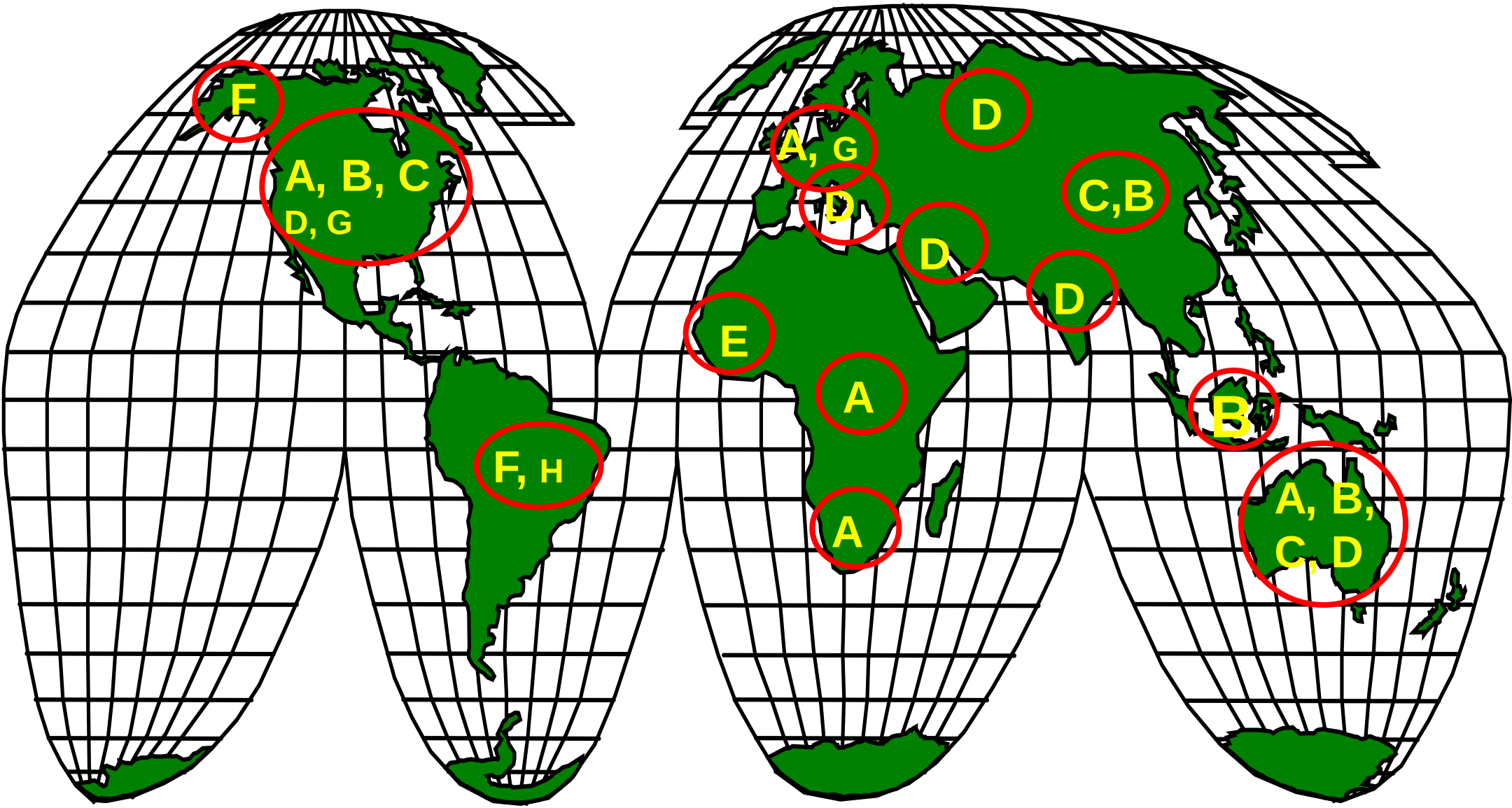
HBV REPLICATION STRATEGY



Schematic Diagram of the Life Cycle of HBV

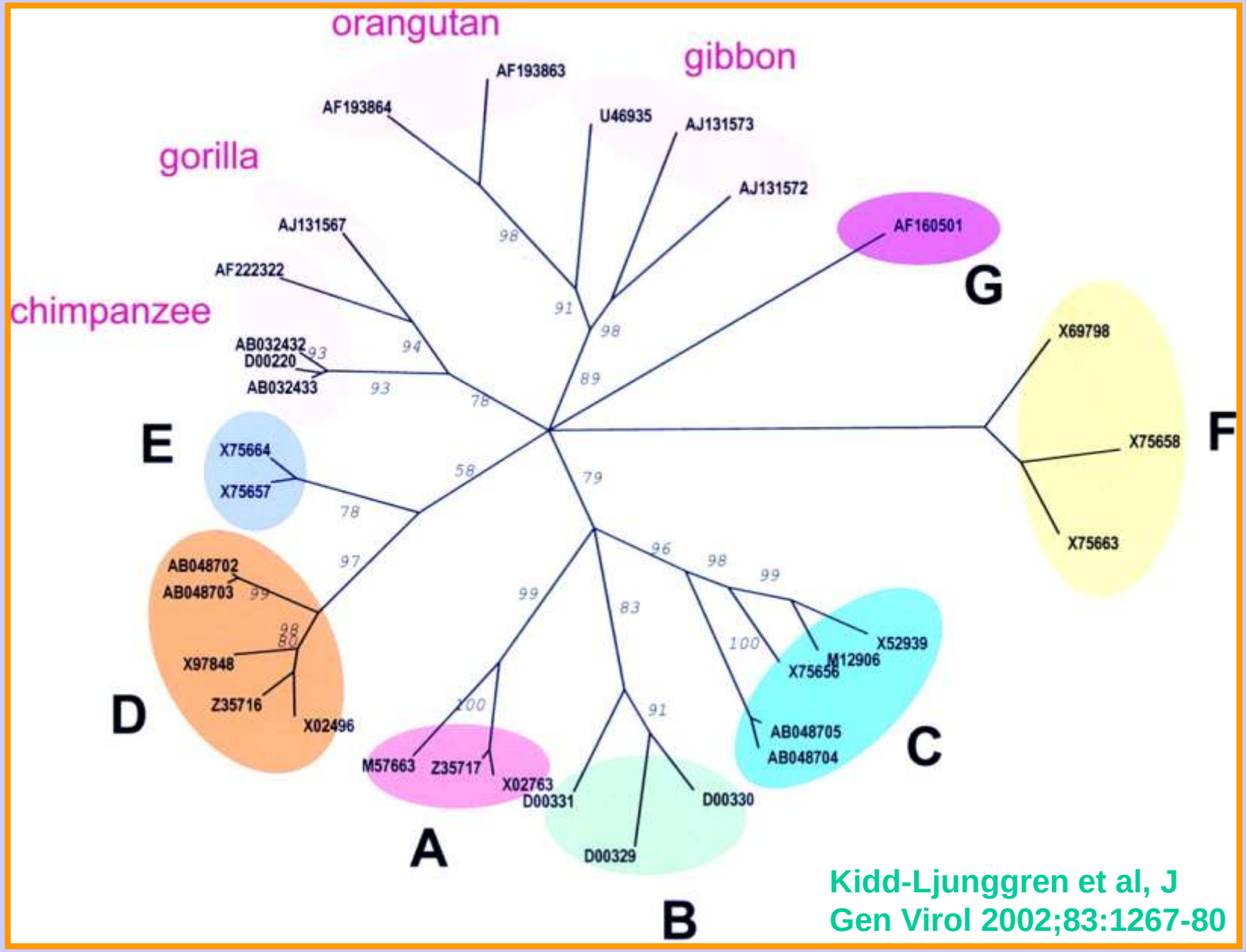


GEOGRAPHICAL DISTRIBUTION OF HEPATITIS B VIRUS GENOTYPES



Sub-genotypes: A1-3, B1-5, C1-5, D1-4, F1-4

UNROOTED PHYLOGENETIC TREE ANALYSIS OF SEQUENCES FROM HBV GENOTYPES AND HEPADNAVIRUSES FROM OTHER PRIMATES

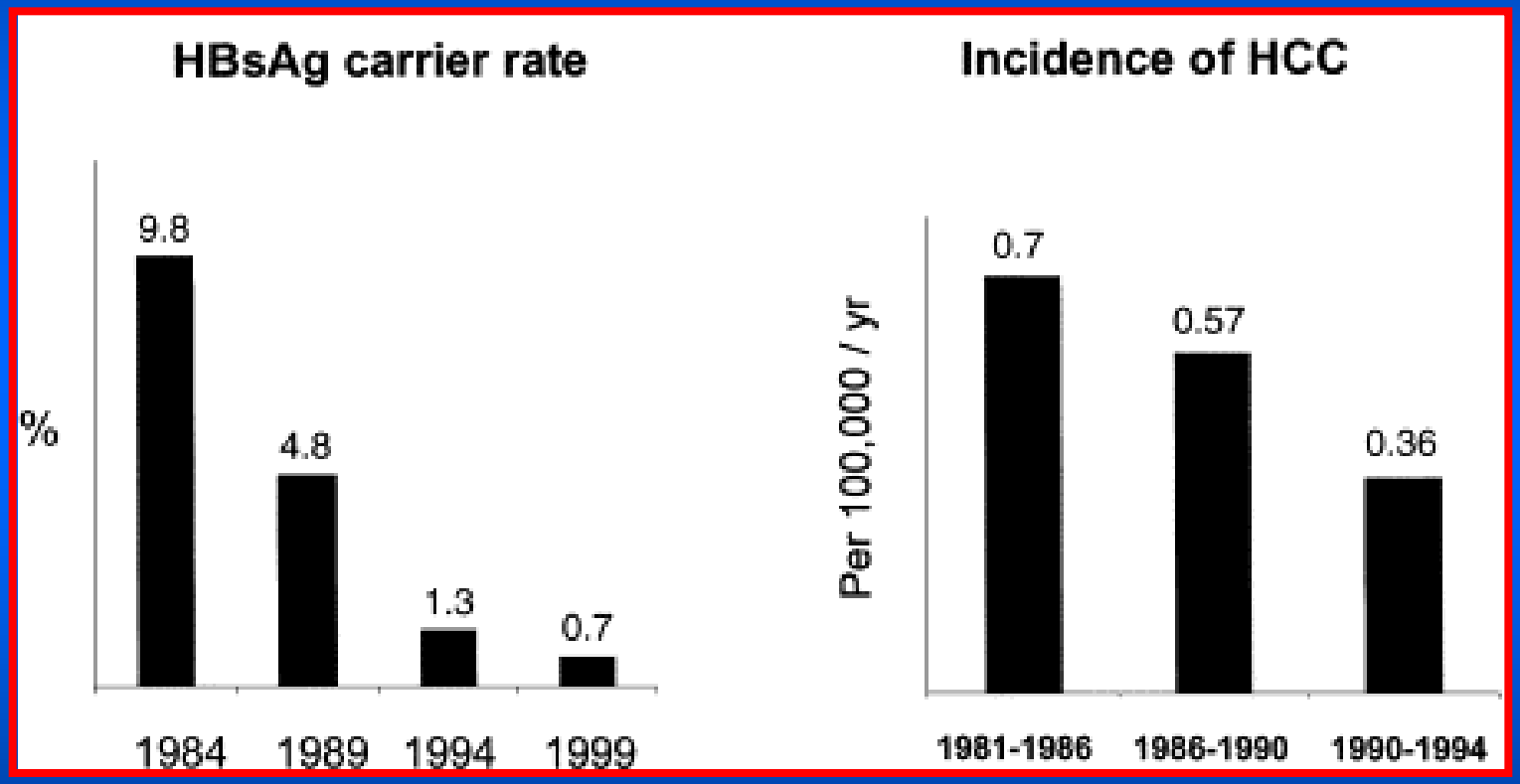


Kidd-Ljunggren et al, J Gen Virol 2002;83:1267-80

HEPATITIS B VIRUS VACCINE

- First introduced in 1982; plasma derived
- Subsequently produced in yeast by recombinant technology; HBsAg
- 3 Dose schedule: 0, 1 & 6 months
- Protection: 1st dose, ~30-50%, 2nd 75%, 3rd 95%
- 5% fail: risks are age, immunosuppression, obesity, smokers

Impact of Universal Vaccination on HBV Infection and HCC in Taiwanese Children

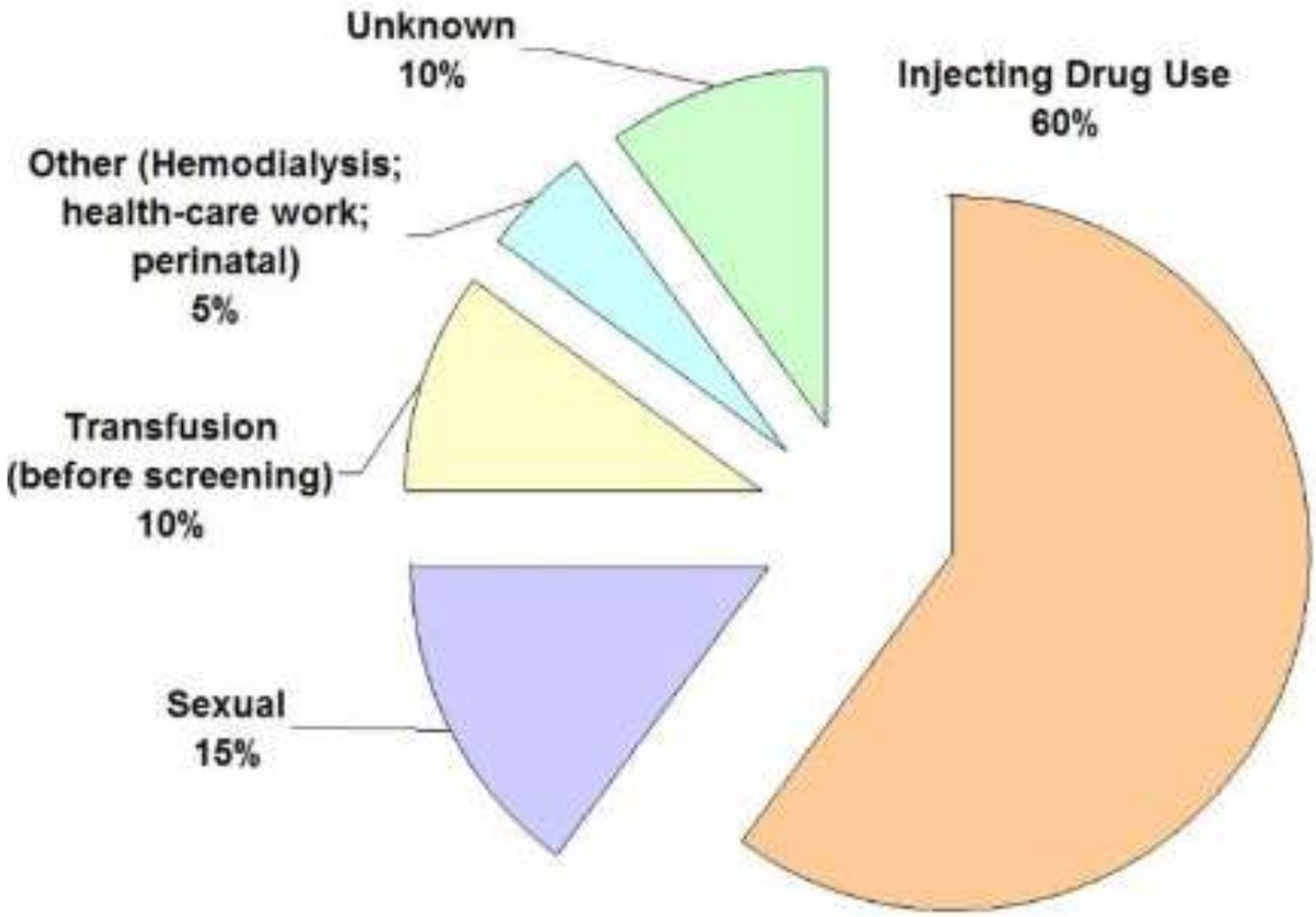


Ni et al, Ann Intern Med 2001;135:796-800

Hepatitis C Virus

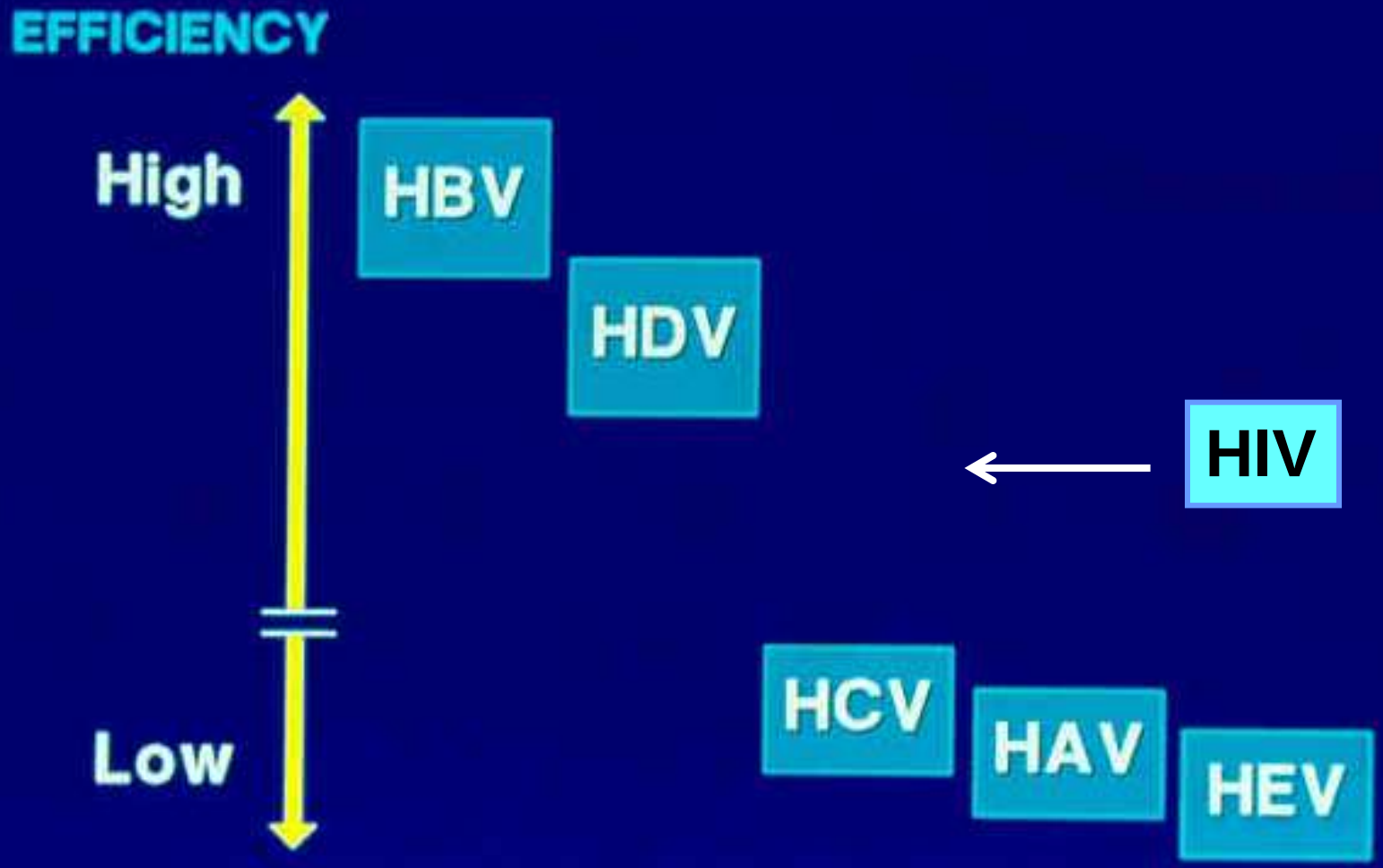
- 170 million HCV infected individuals worldwide
- Mostly subclinical
- High potential for chronic infection (> 70%)
- 50-70% of chronically infected individuals develop chronic liver disease
- Not a major cause of acute or Fulminant hepatitis
- Important cause for Primary Hepatocellular Carcinoma

Sources of Infection for Persons with Hepatitis C

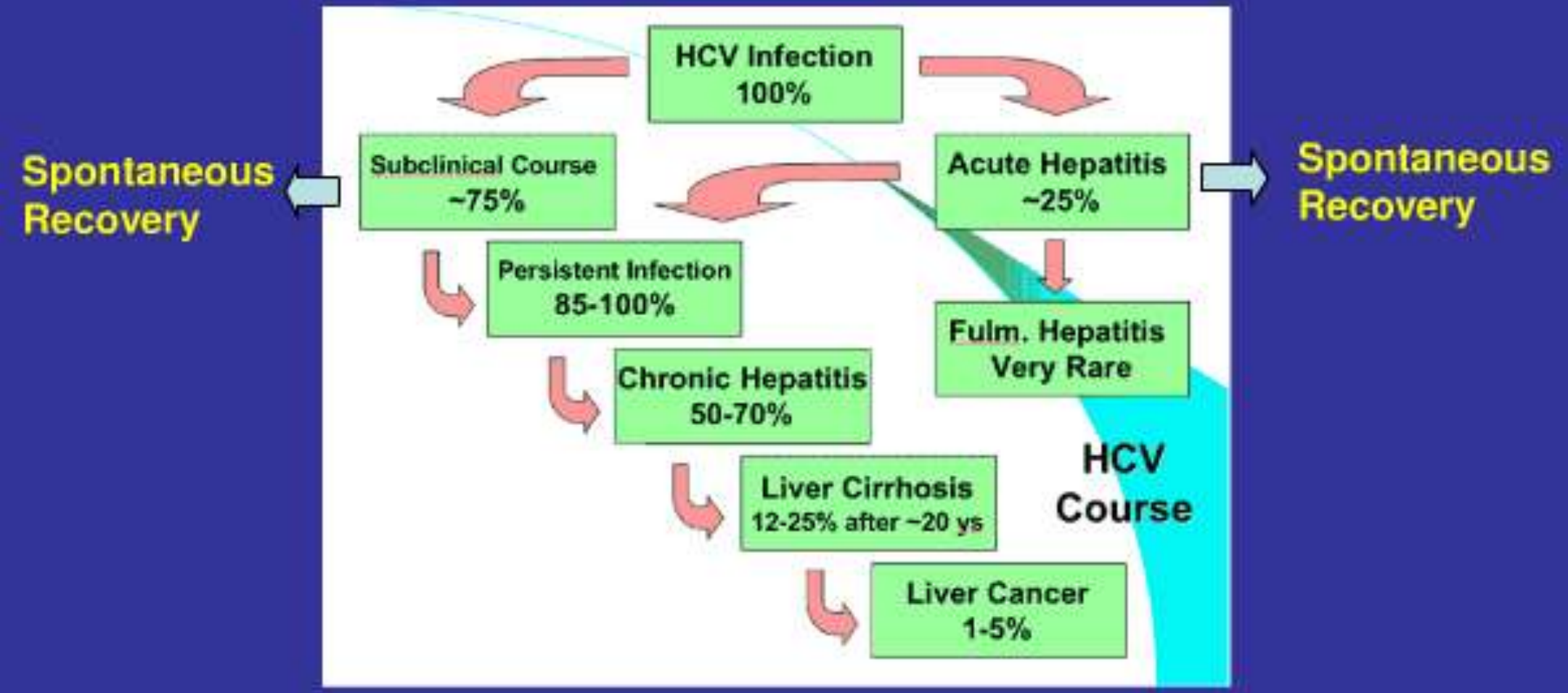


VIRAL HEPATITIS

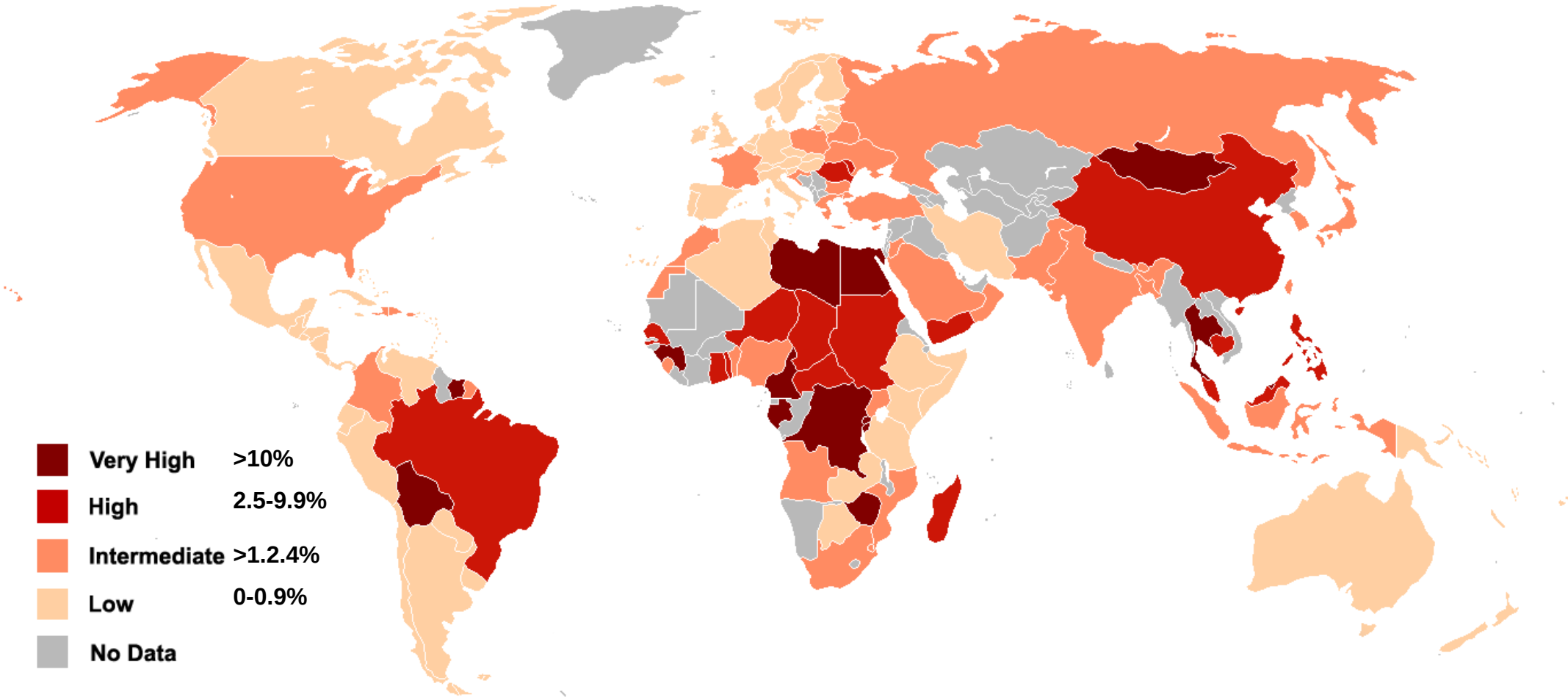
Sexual Transmission



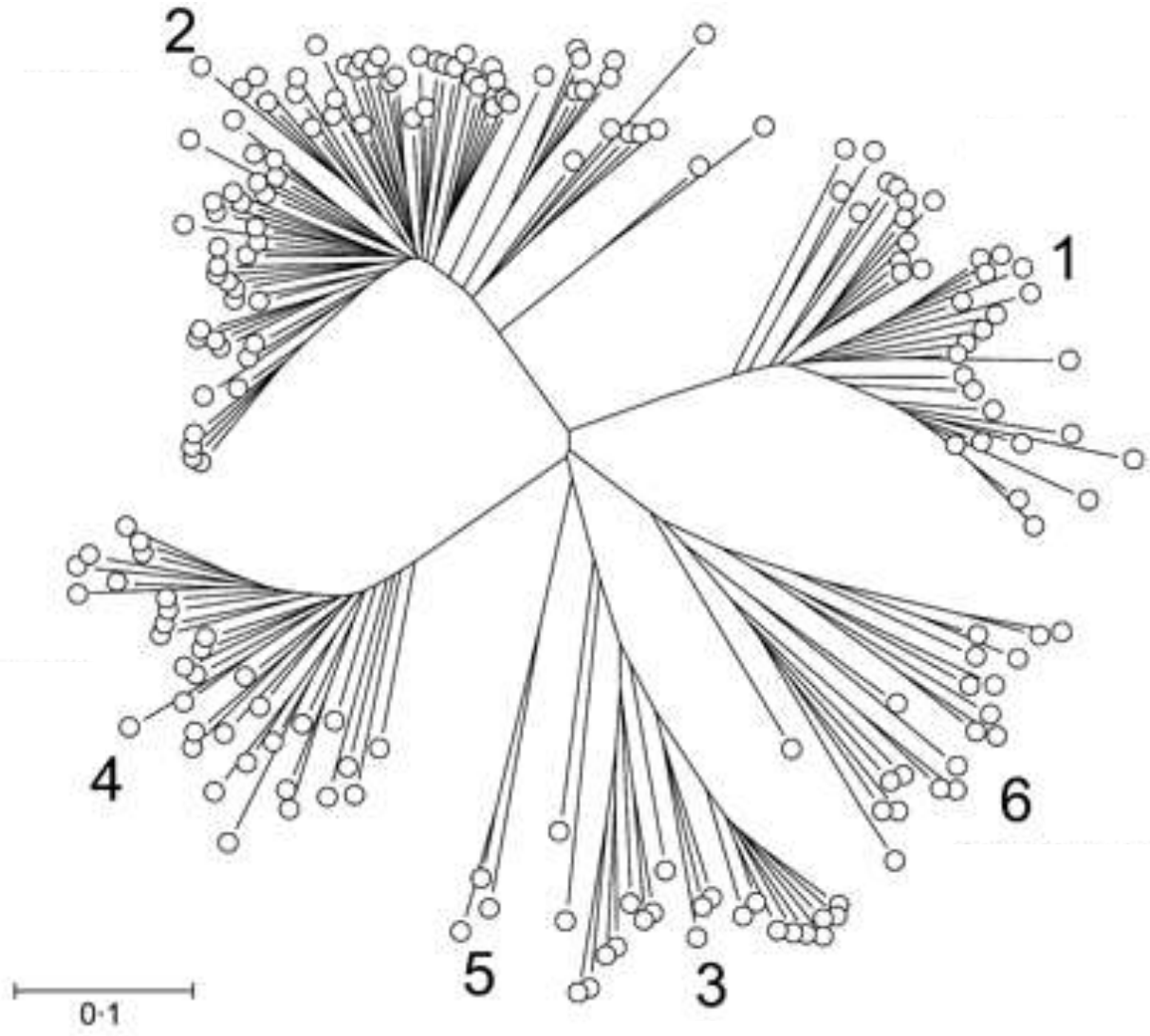
Clinical Course of HCV Infection



HEPATITIS C VIRUS PREVALENCE

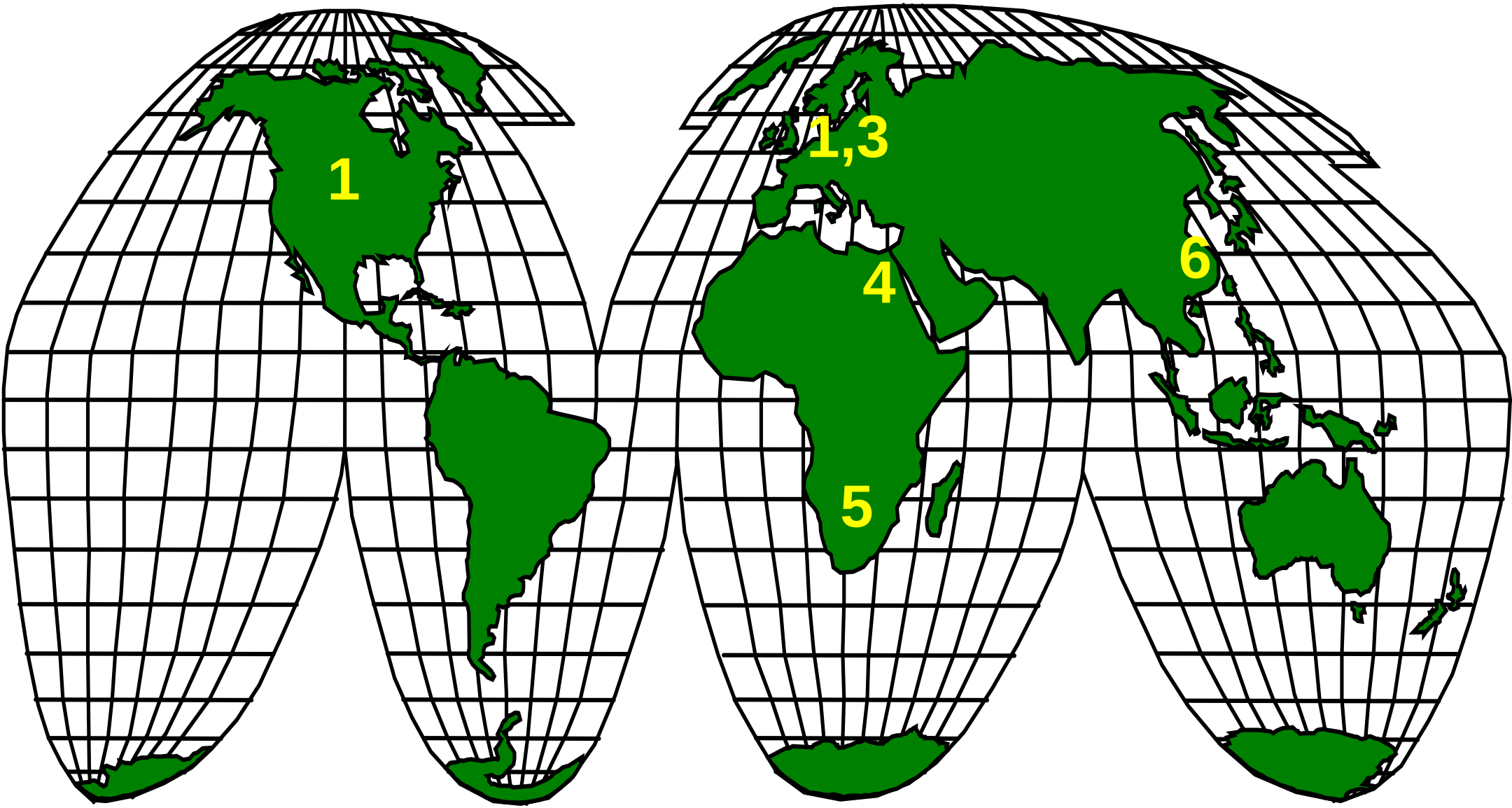


PHYLOGENETIC TREE OF HCV SHOWING GENOTYPES AND SUBTYPES

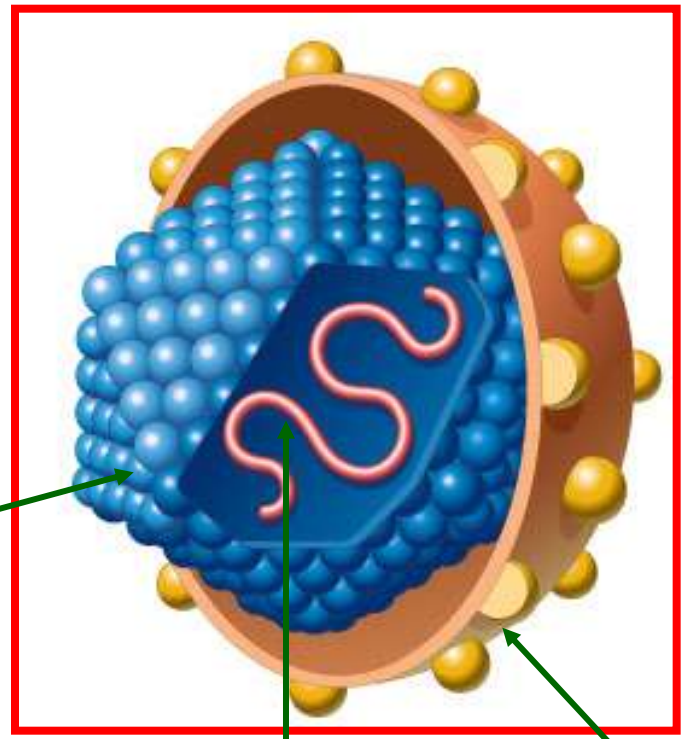


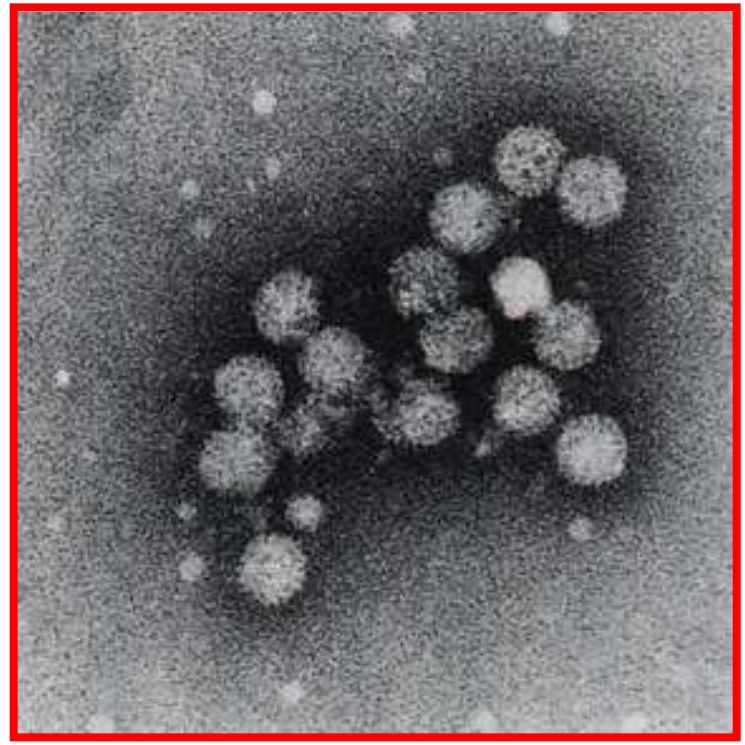
Simmonds, J Gen Virol 2004

GEOGRAPHICAL DISTRIBUTION OF HEPATITIS C VIRUS GENOTYPES



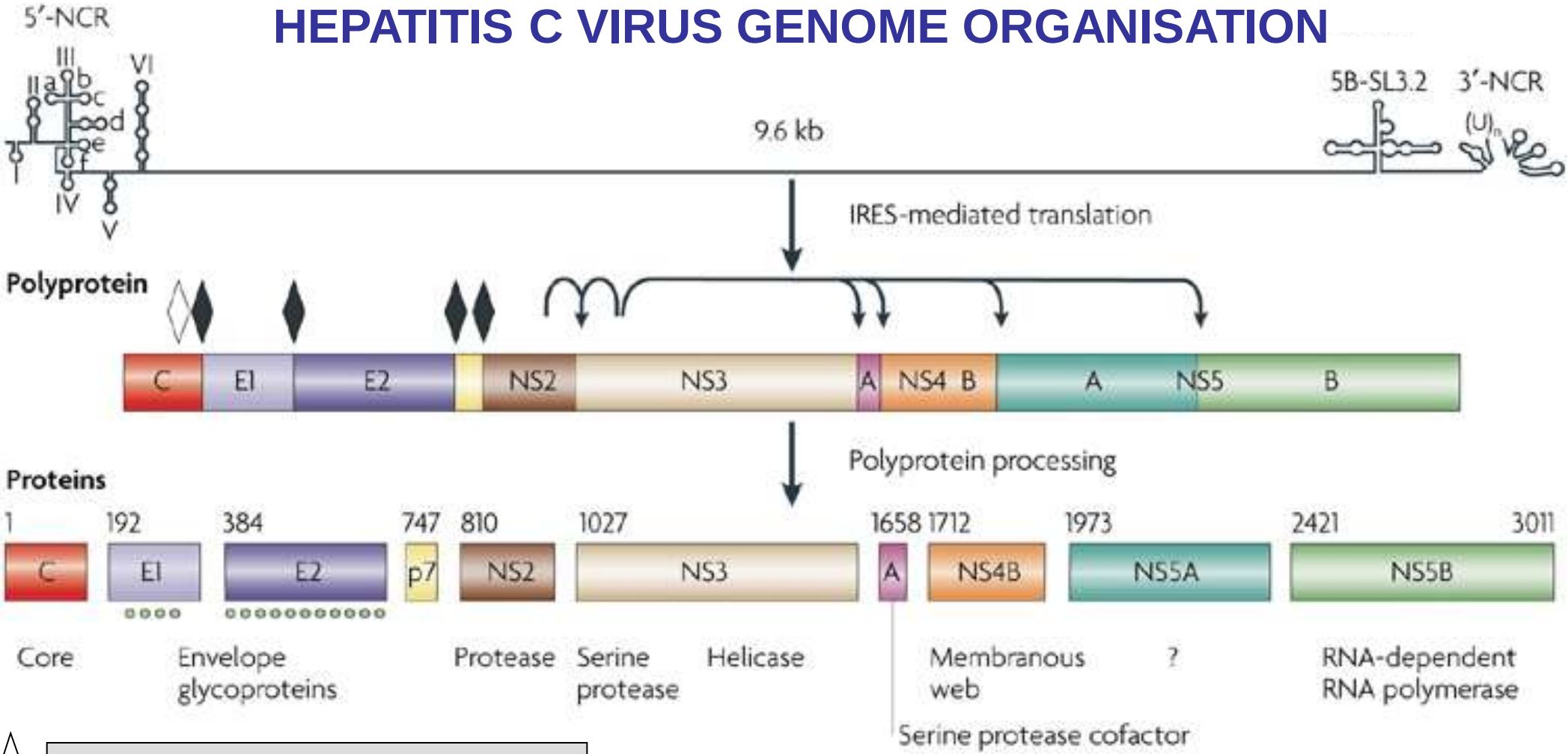
HEPATITIS C VIRION STRUCTURE





Electron micrograph

HEPATITIS C VIRUS GENOME ORGANISATION



SIGNAL PEPTIDE PEPTIDASE

SIGNAL PEPTIDASE

VIRALLY ENCODED PROTEASES

GLYCOSYLATION SITES

Nature Reviews | Microbiology

Moradpour et al, 2007;5:453-463

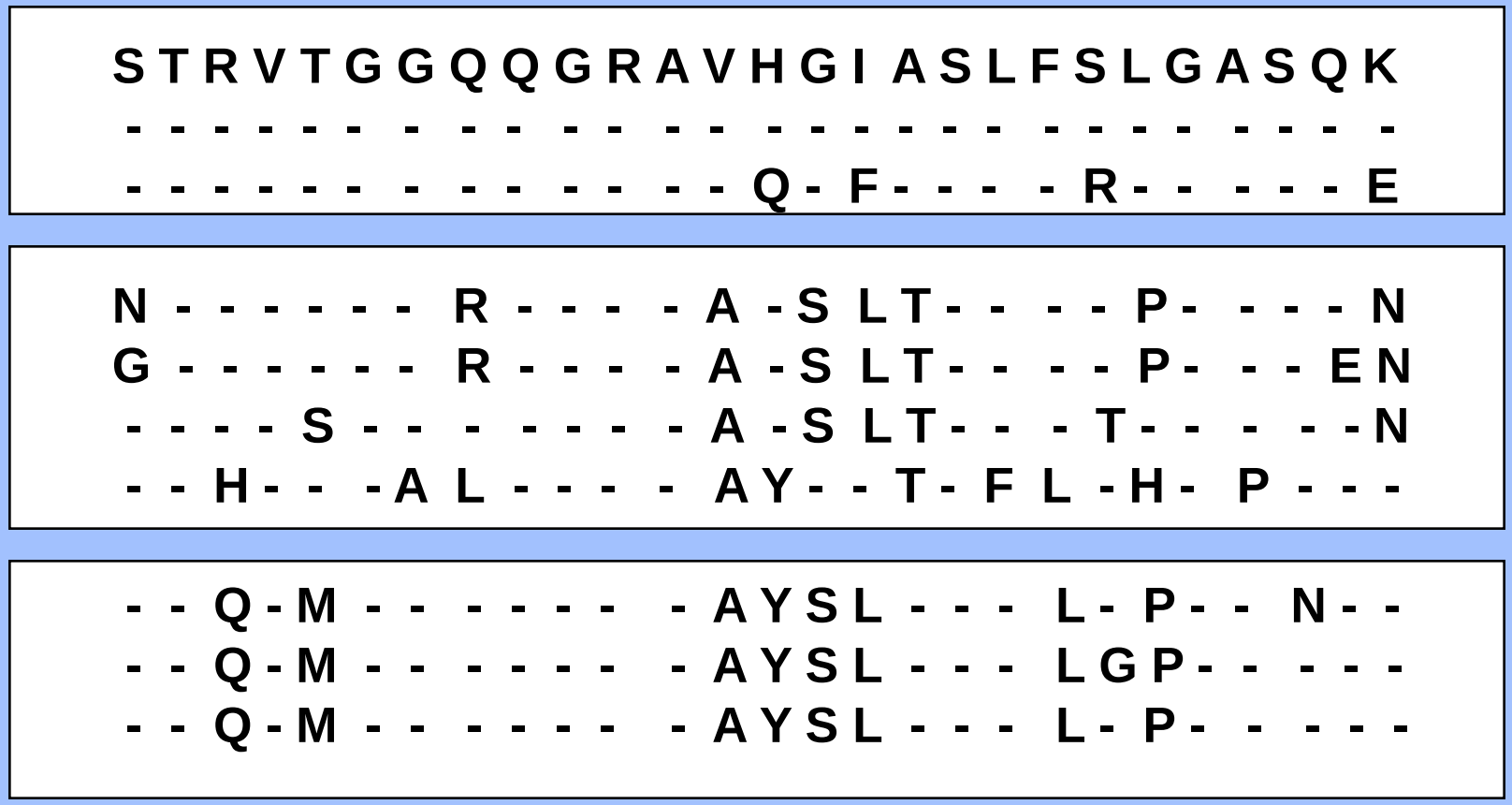
ANTIGENICALLY VARIABLE DOMAINS IN THE ENVELOPE GLYCOPROTEINS

VARIABLE REGION aa 246-275 386-411 456-482

		H V T G G S A G H T V S G F V S L L A P G A K Q N V
HCV-1	(1a)	
HCV-BK	(1b)	- - - - - A Q A K - T N R L - - M F - S - P S - K I
HCV-J1	(1a)	- - - - - Q - A R A M - - L - - - F T - - - - - - I
HCV-J	(1b)	- - - - - R V A S S T Q S L - W - S Q - - P S - K I
HCV-J4	(1b)	Y T S - - A - S - - T - T L A - - F S - - - S R - I
HCV-JH	(1b)	- - - - - V Q - - V T - T L T - - F R - - - S - K I
HCV-H	(1a)	- - - - - N - - R - T A - L - G - - T - - - - - - I
HCV-UK	(1a)	Y - - - - A - A K G T - T - A G - F - - - S R - - I

PK - 95

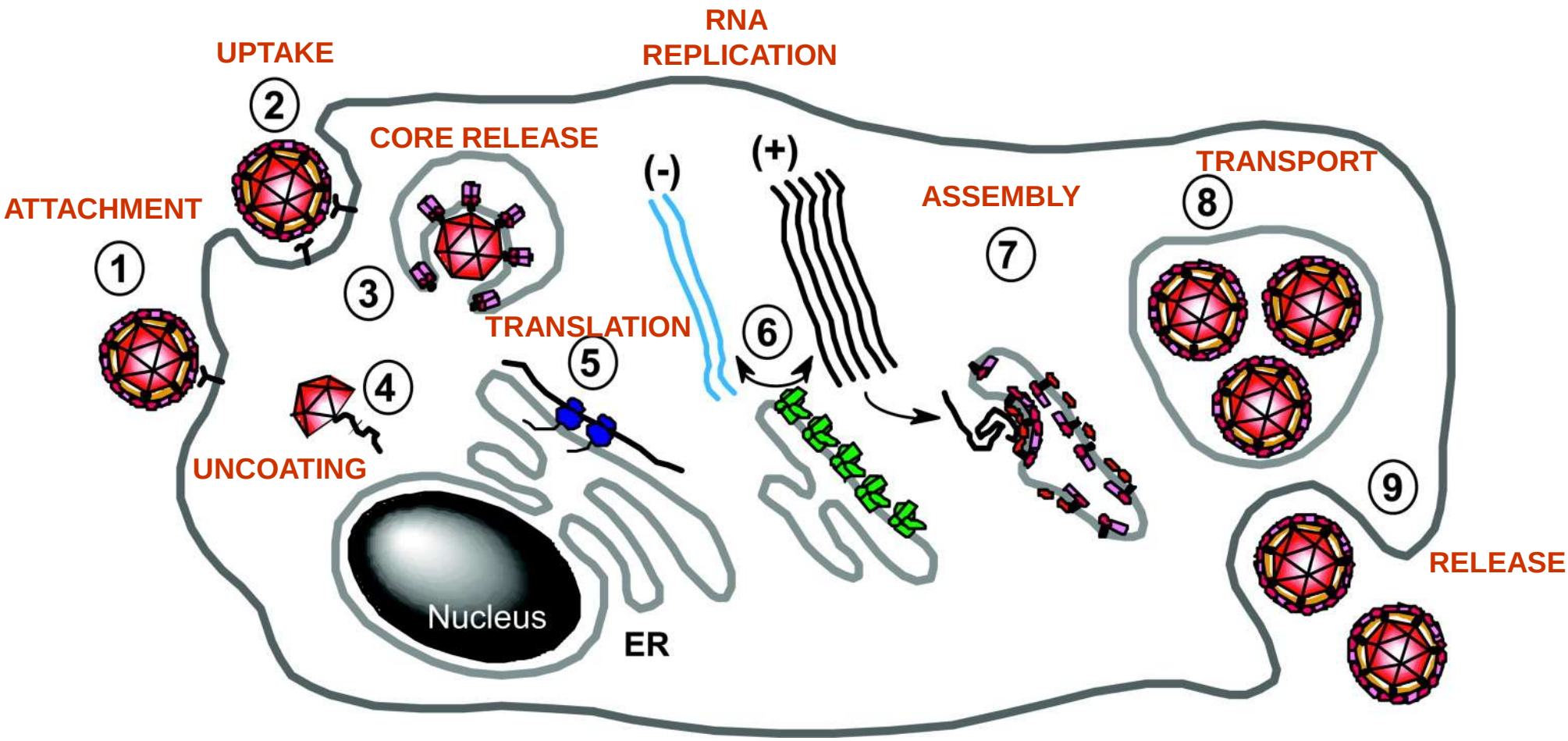
HCV QUASISPECIES: CHANGES IN THE HYPERVARIABLE REGION 1 OF THE E2/NS1 WITH TIME IN A CHRONIC CARRIER



Kato et al, 1992

PK - 95

LIFE CYCLE OF HEPATITIS C VIRUS: POTENTIAL TARGETS FOR THERAPEUTIC INTERVENTION



Pawlotsky, Hepatology 2006;43:S207-20

TREATMENT OF CHRONIC HEPATITIS CARRIERS

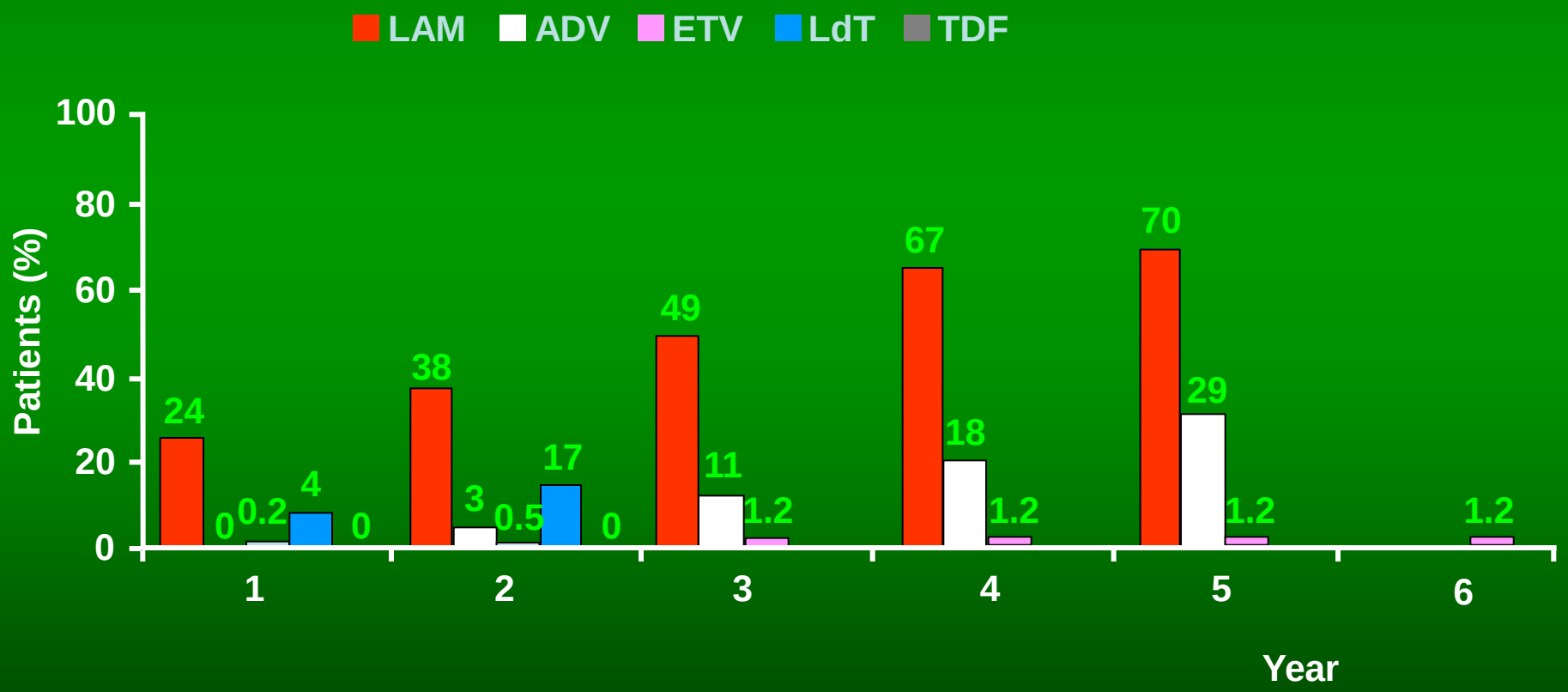
VIRUS	ANTIVIRAL AGENTS	LONG TERM RESPONSE
HBV		
- HBeAg	Peg-Interferon α*	40%
- anti-HBe	Peg-Interferon α	20%
HCV	Peg-Interferon + Ribavirin#	55-80%
HDV	Interferon α	Not sustained

* Peg = pegylated, addition of polyethylene glycol

Trials using protease and polymerase inhibitors are in progress

Cumulative Rates of Resistance With Oral Agents in Nucleos(t)ide-Naive Patients

Not head-to-head trials; different patient populations and trial designs



EASL HBV Guidelines. J Hepatol. 2009;50:227-242. Tenny DJ, et al. EASL 2009. Abstract 20.

- Από την παρουσίαση στο 6$_0$ συνέδριο του Συνδέσμου Βιολόγων Φυσιογνωστών (ΟΕΛΜΕΚ)
- Ινστιτούτο Νευρολογίας και Γενετικής Κύπρου

20 Μαρτίου 2010

- Δρ. Πέτρος Καραγιάννης,

  Καθηγητής Μοριακης Ιολογίας

  Τμήμα Ιατρικής στο Imperial College London