

DBS TESTING

what are we testing and why?

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SpR Virology/GU&HIV

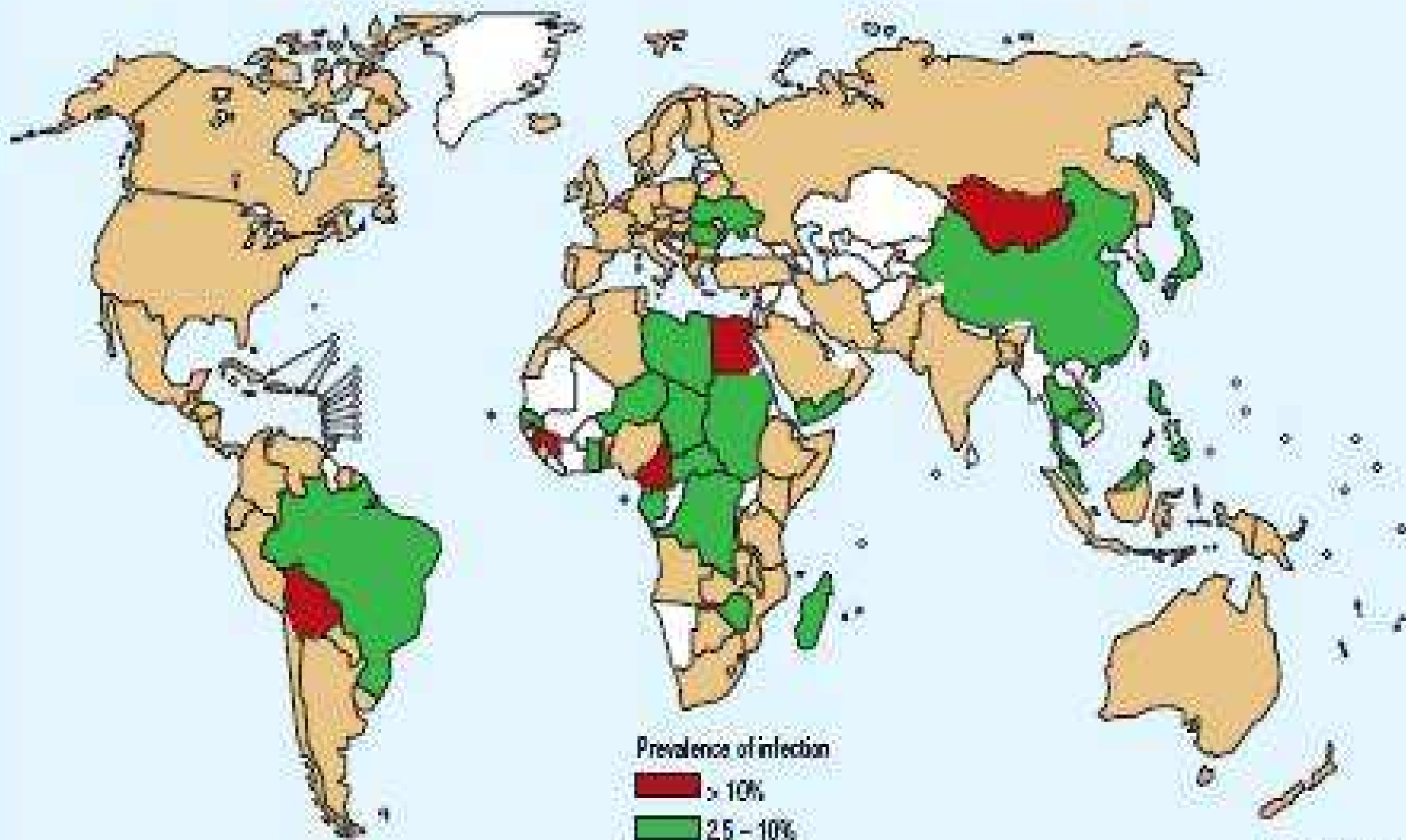
HPA Bristol

Plan

- Hepatitis C
 - Hepatitis B
 - HIV
-
- Why test?
 - What test?

What are we testing for ?

HCV



Prevalence of infection

> 10%

2.5 - 10%

1 - 2.5%

Source: WHO, 2001

Prevalence of HCV

- HPA Report 2007

231,000 15-59yr old HCV antibody positive

- Bristol IDU

53% HCV antibody positive

Hepatitis C Transmission

- Parenteral
- Sexual
 - Low efficiency – MSM
- Perinatal
- Occupational

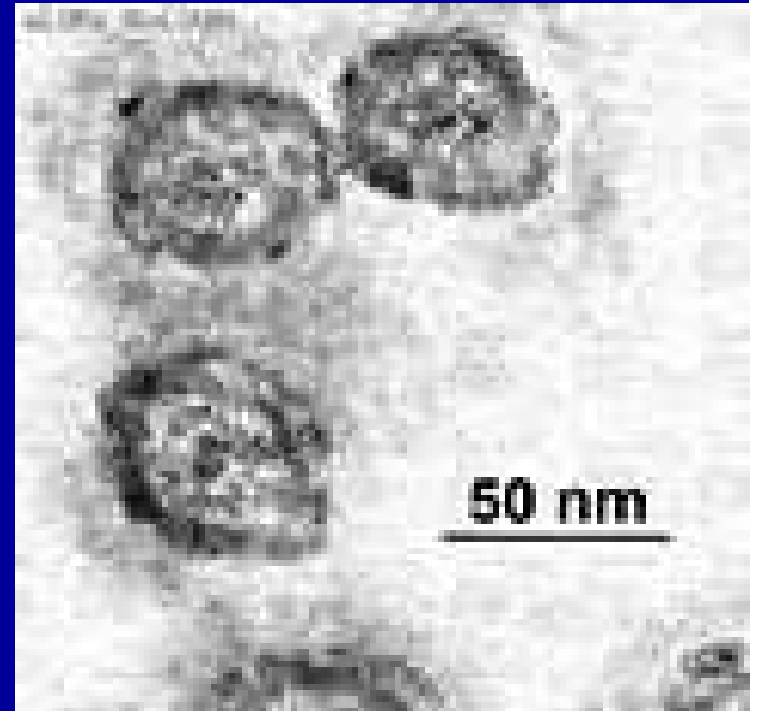
Risks of disease acquisition

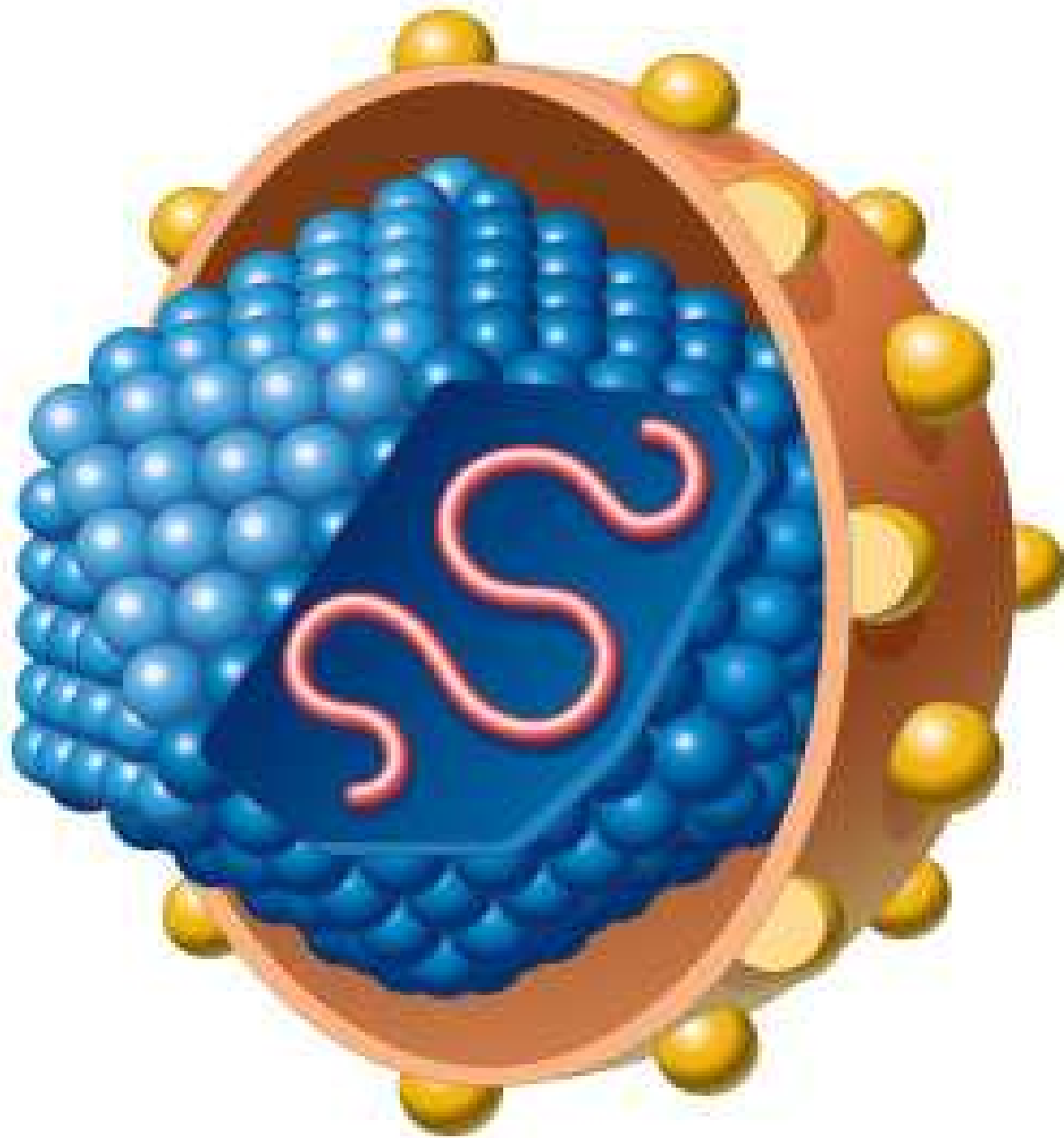
- 3-30% for HBV: 3/10 1 in 3
- 0.3-3% for HCV: 3/100 1 in 30
- 0.1-0.3% for HIV : 3/1000 or 1 in 300

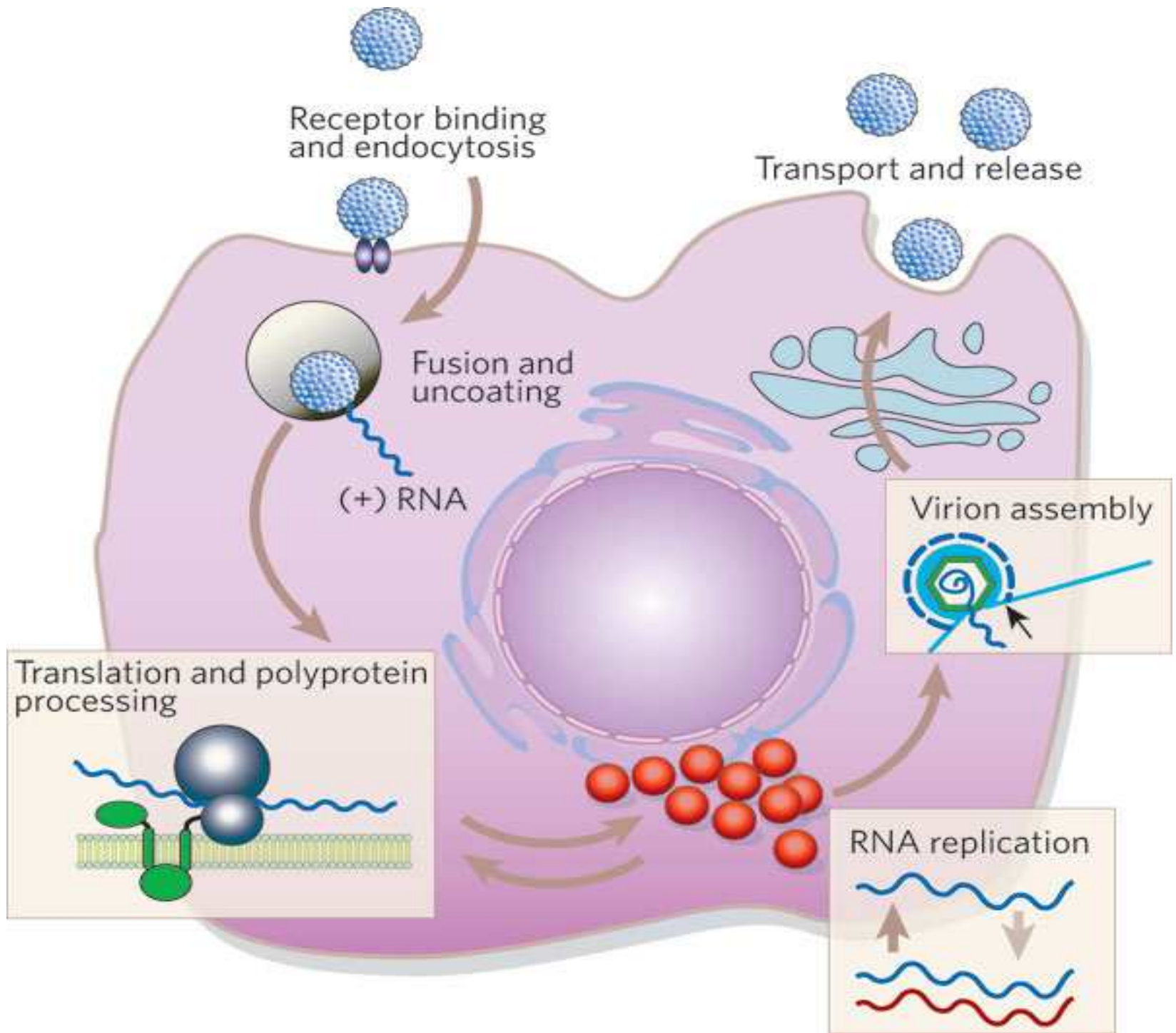
- for percutaneous exposure to infected blood
- the risk of mucocutaneous exposure is significantly less by 1/3.

Hepatitis C

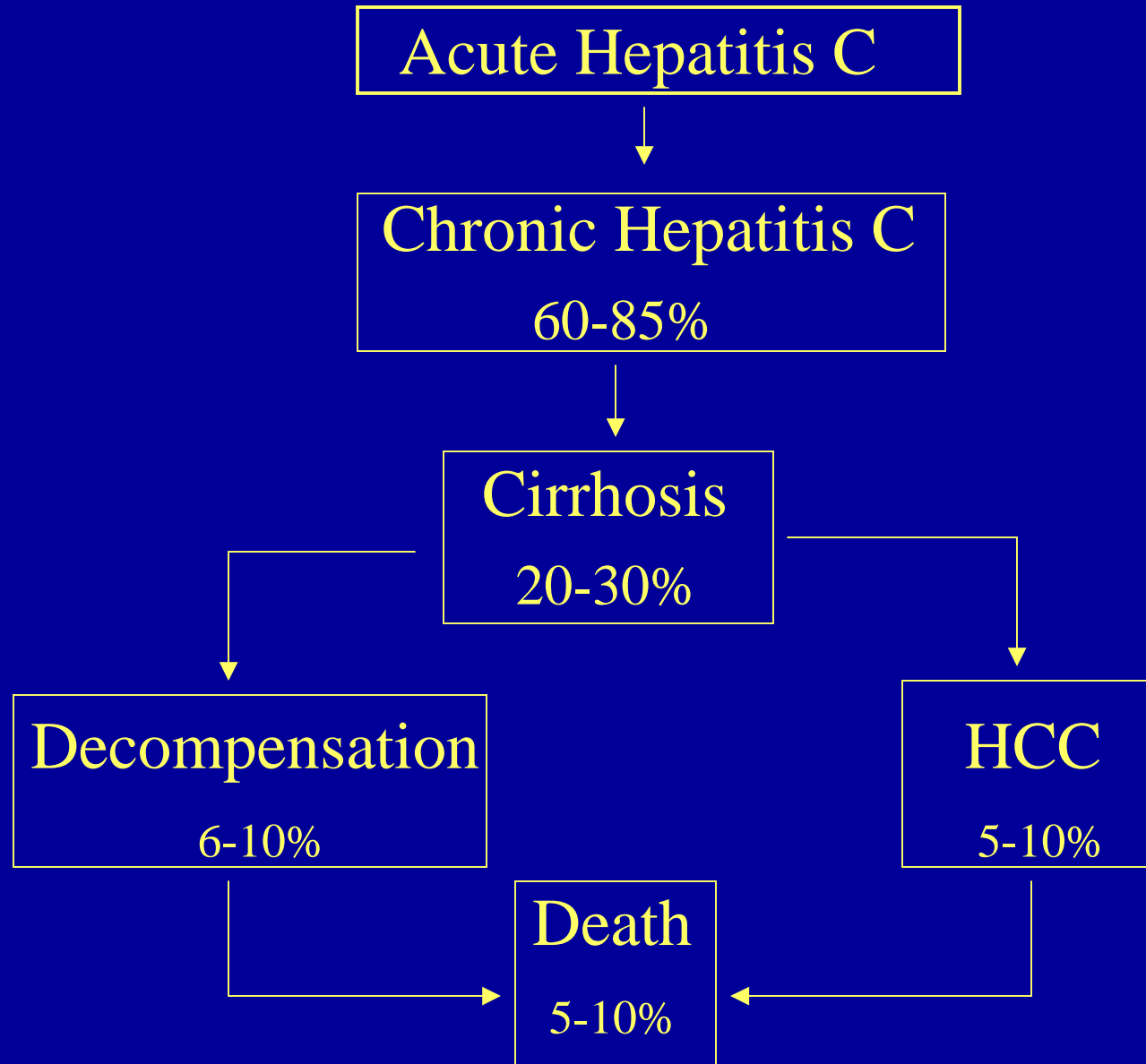
- Flavivirus family
- Enveloped
- Single stranded RNA virus
- Subdivided into 6 major genotypes







Natural history of Hepatitis C



Factors affecting outcome

- Gender
- Age at infection
- Inoculum
- Race
- Alcohol
- Immune status
- Co-infection
- Metabolic eg hepatic steatosis, type II DM

Features of Hepatitis C Virus Infection

Incubation period **Average 6-7 weeks**
Range 2-26 weeks

Acute illness (jaundice) **Mild ($\leq 20\%$)**

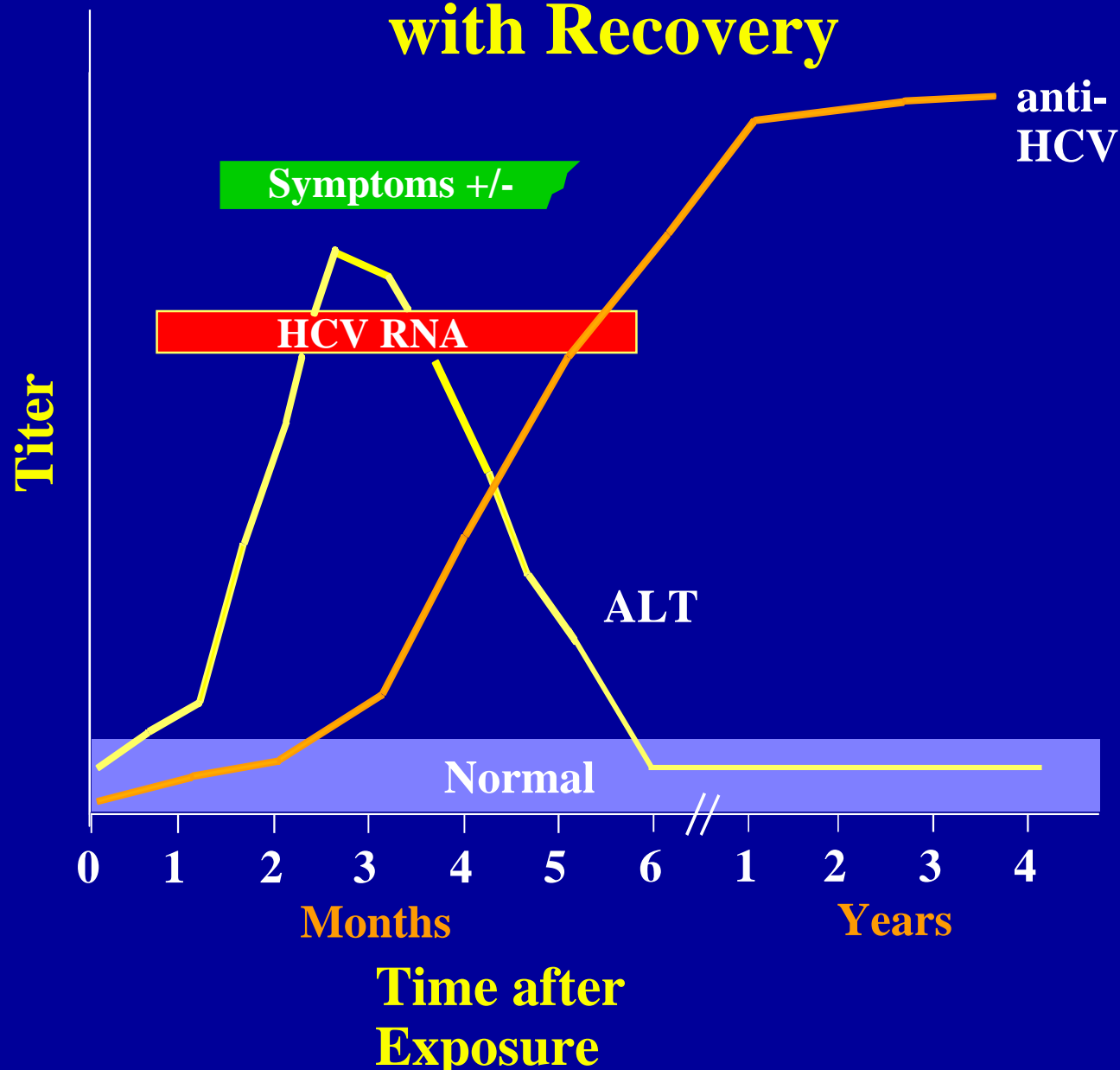
Case fatality rate **Low**

Chronic infection **60%-85%**

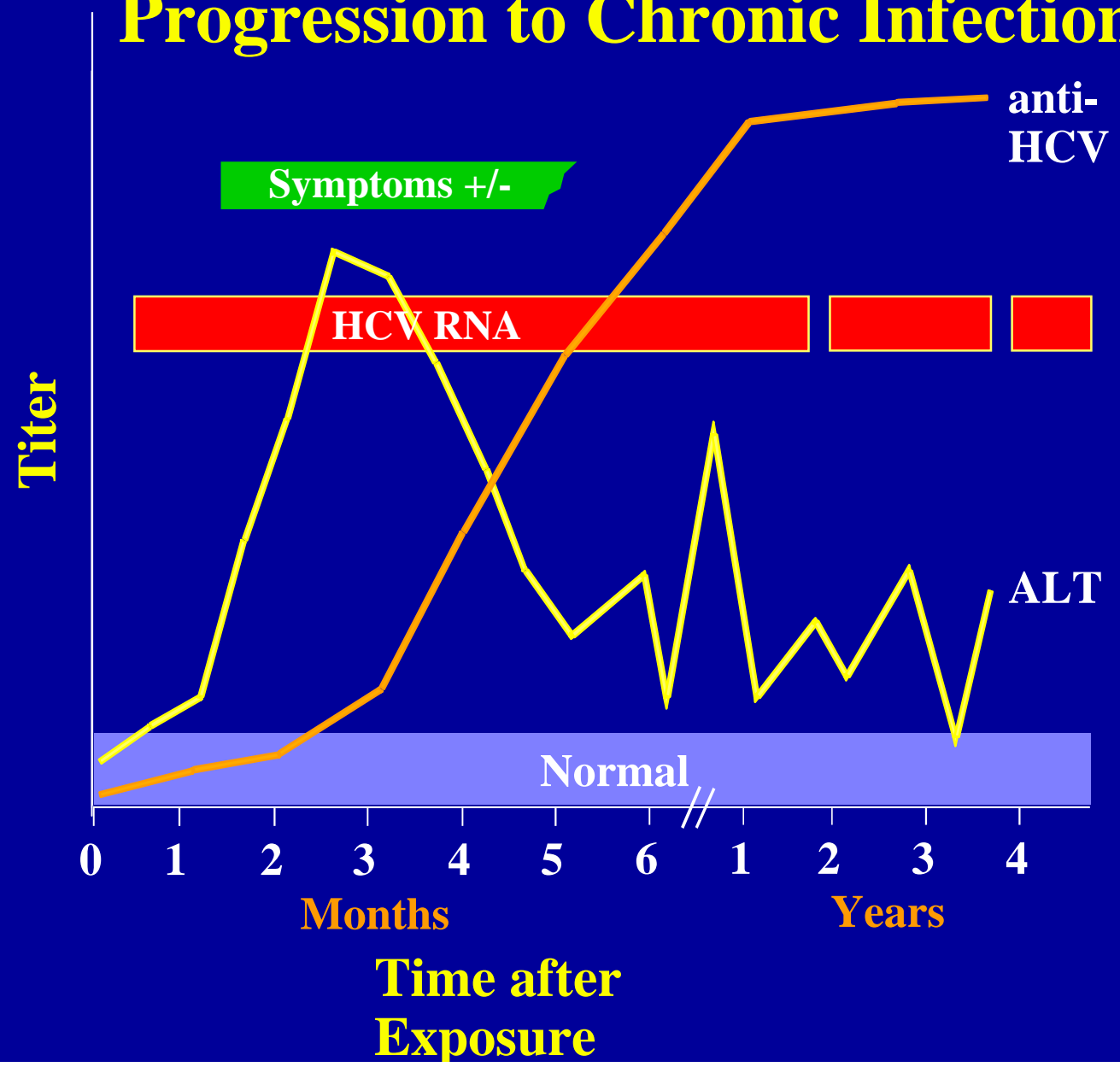
Cirrhosis **$< 5\%$ -20%**

Mortality from liver disease **1%-5%**

Serologic Pattern of Acute HCV Infection with Recovery

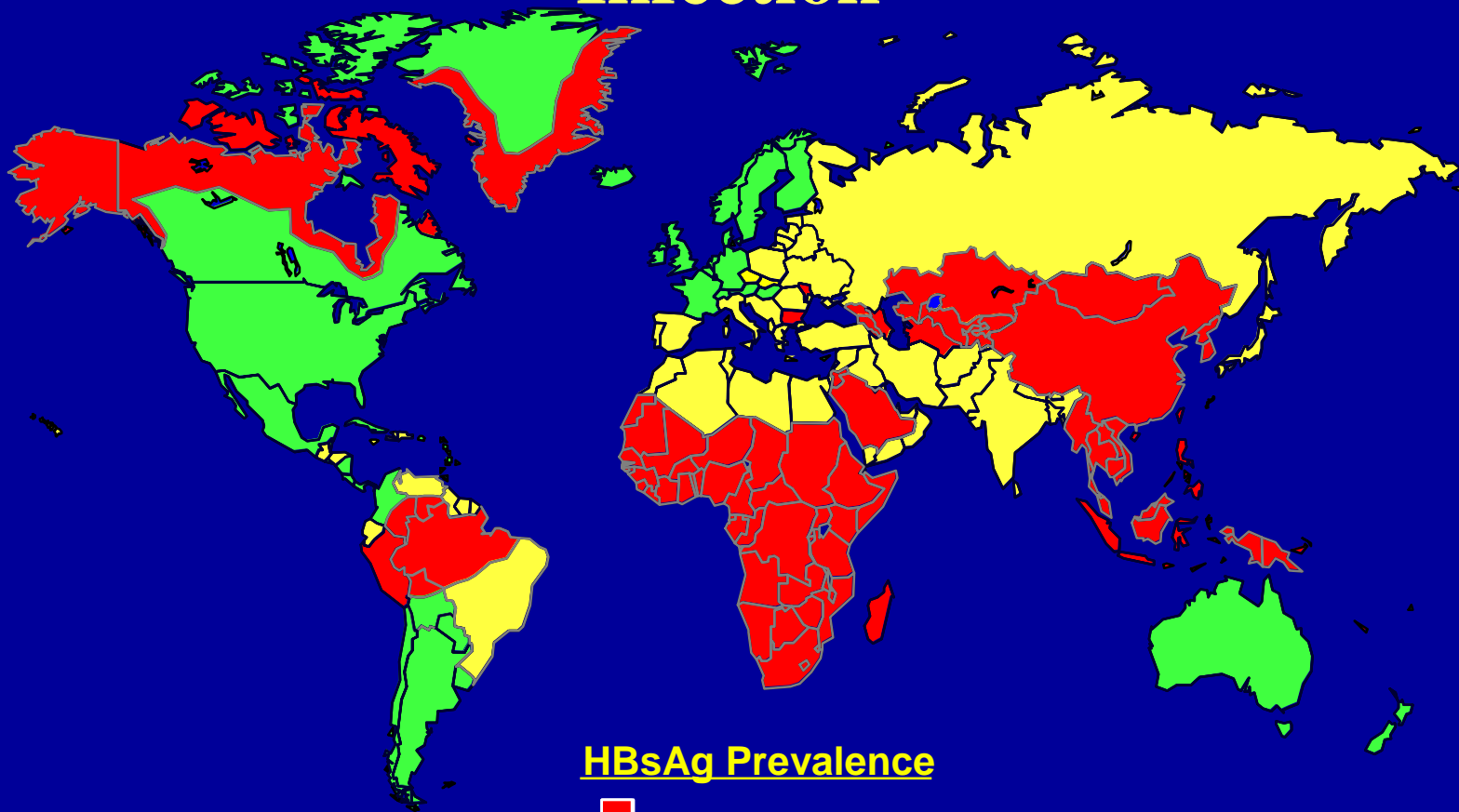


Serologic Pattern of Acute HCV Infection with Progression to Chronic Infection



HBV

Geographic Distribution of Chronic HBV Infection



HBsAg Prevalence

- $\geq 8\%$ - High
- 2-7% - Intermediate
- $< 2\%$ - Low

Prevalence of HBV infection

- Bristol IDU

32% are HBcAb positive

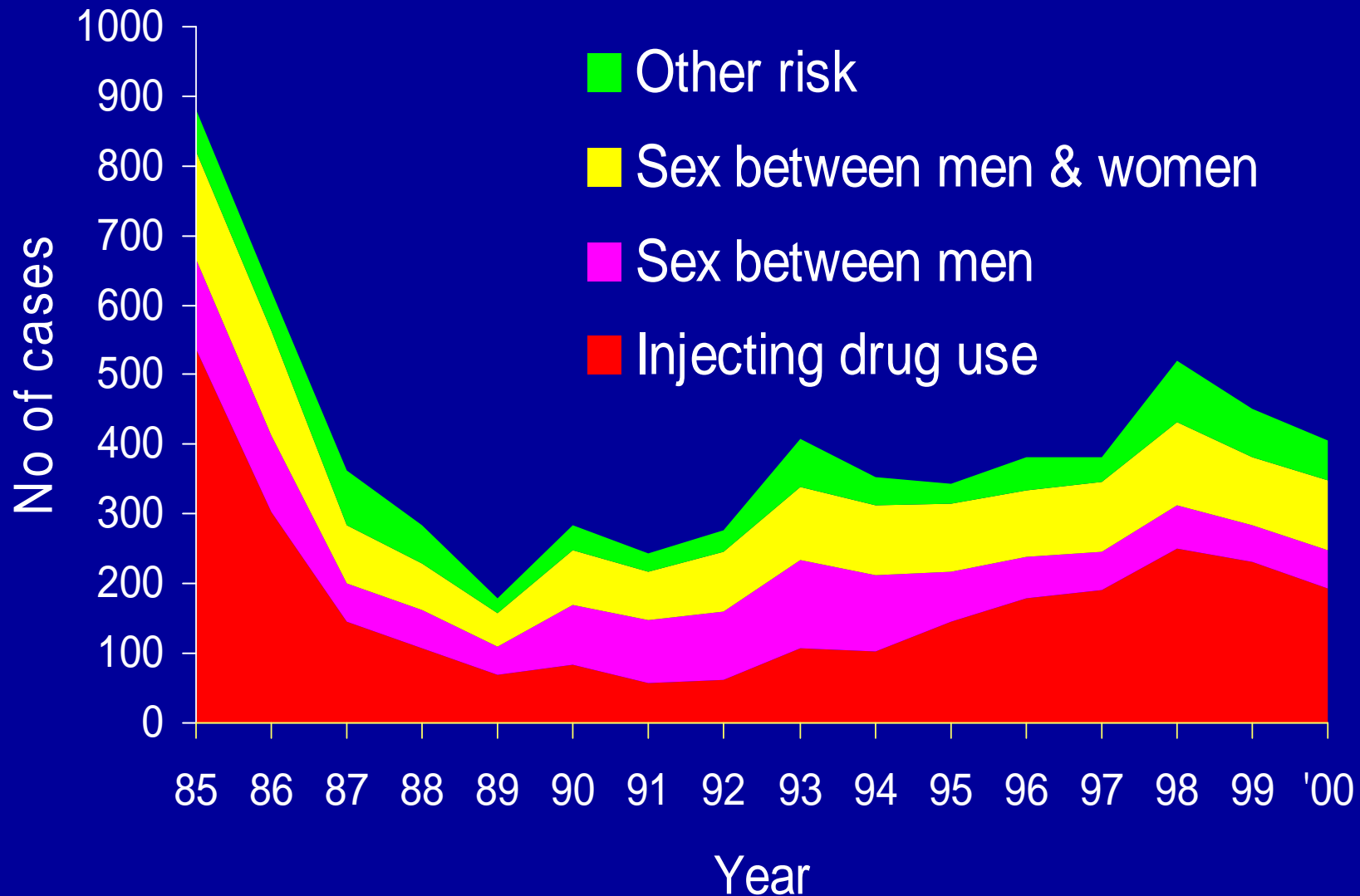
HBV is a bloodborne virus

Modes of Transmission

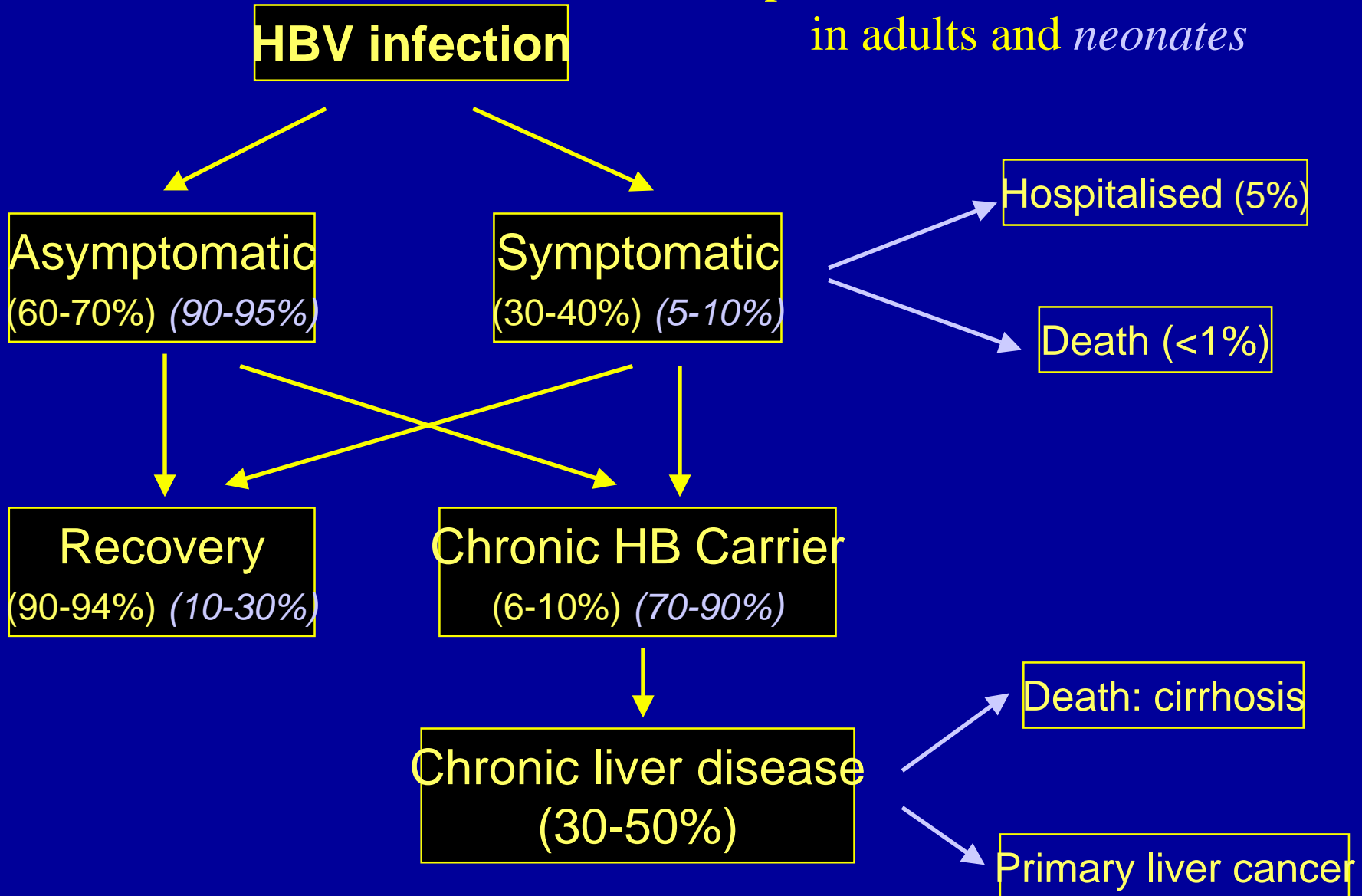
- Sexual
- Parenteral
- Perinatal

Acute HBV by major exposure categories

England and Wales, 1985-2000

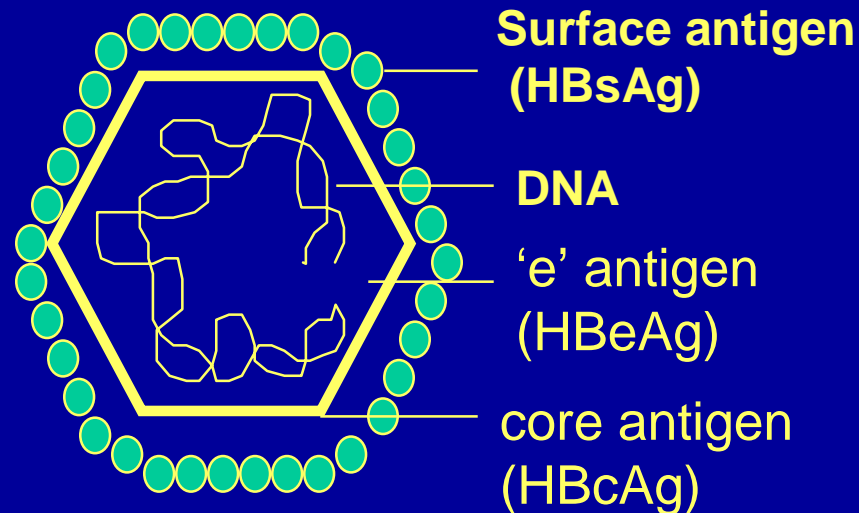


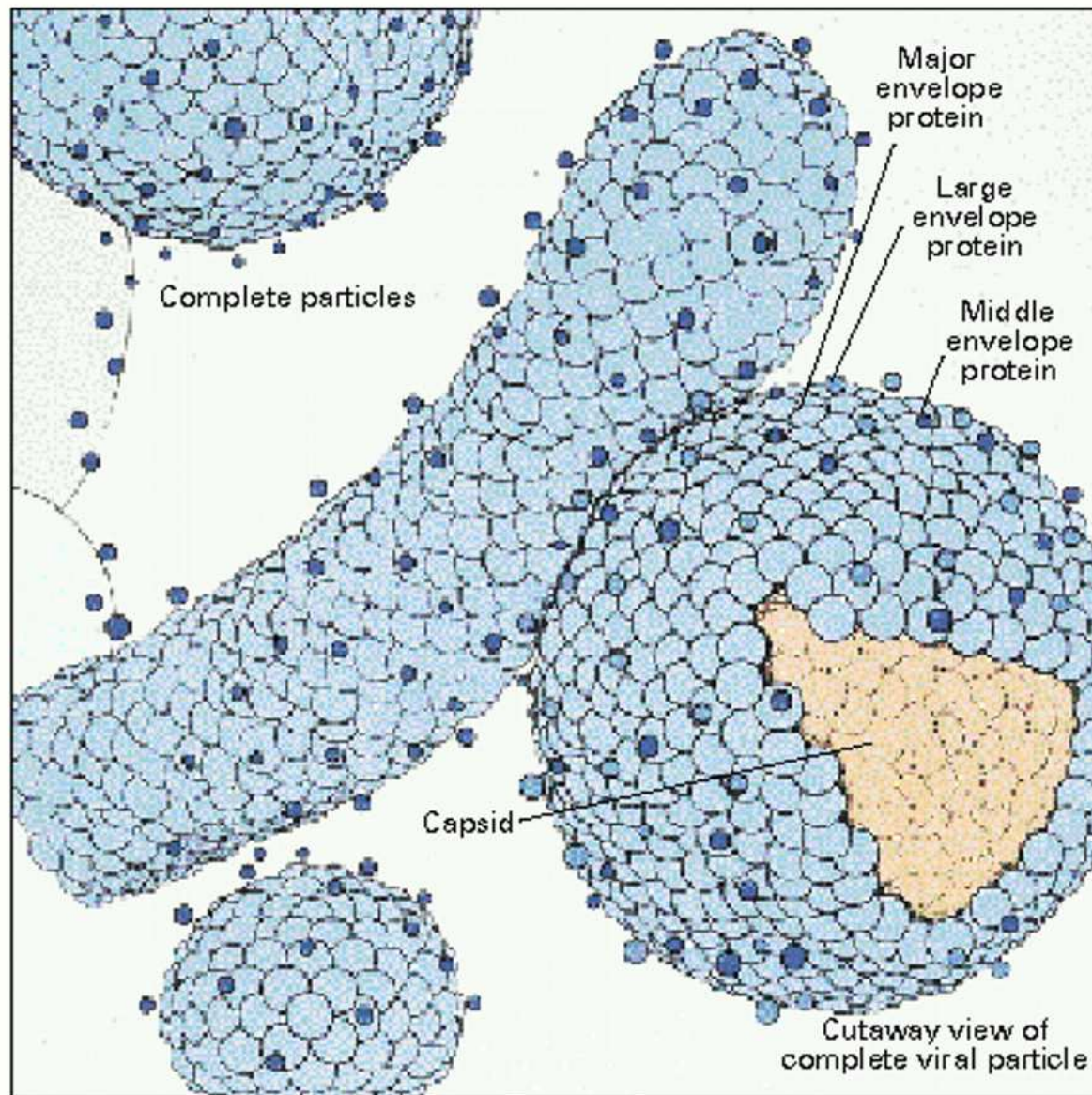
Hepatitis B: Estimated outcomes in adults and *neonates*



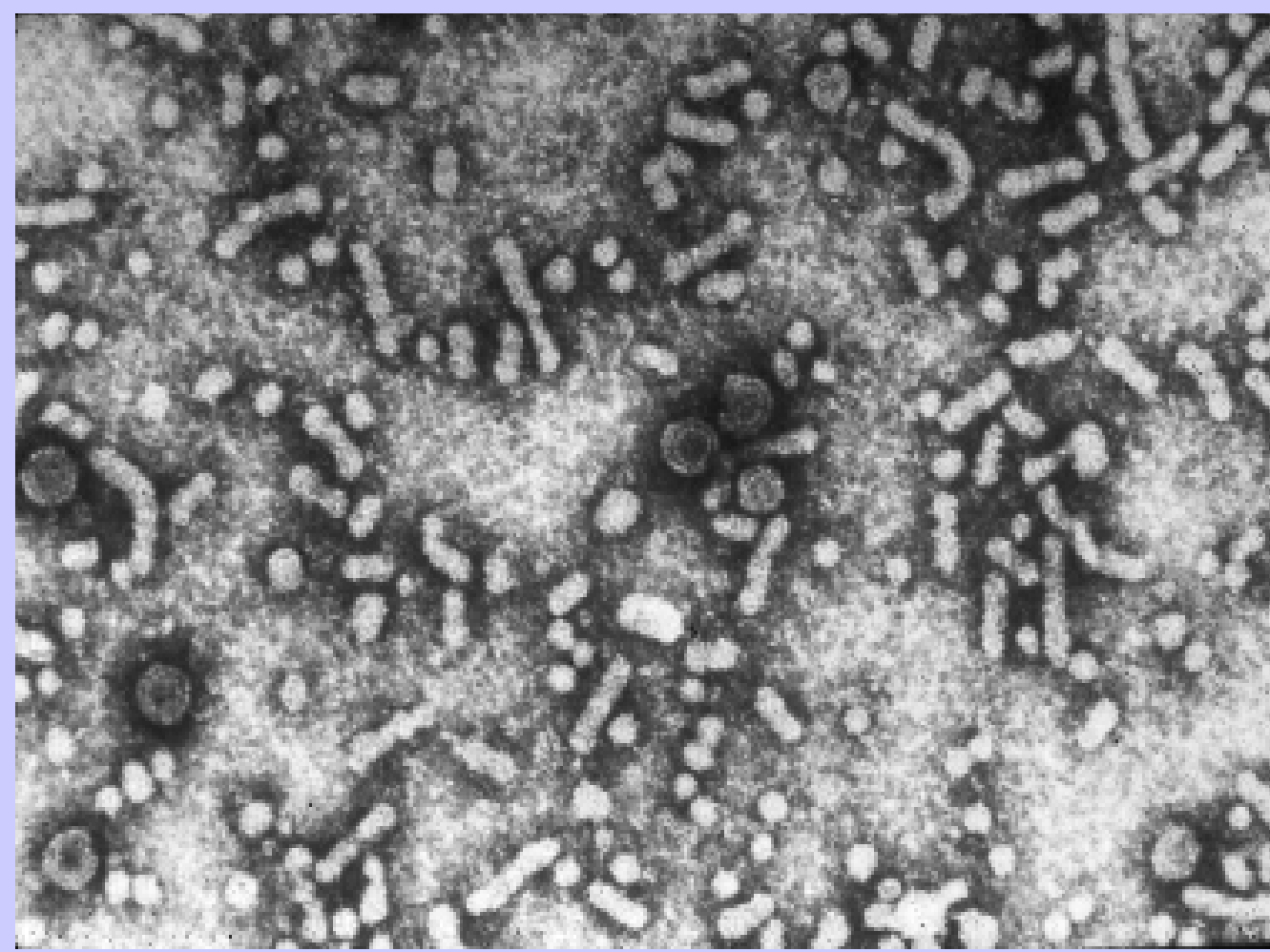
Hepatitis B virus: structure

- Dane particle (whole virion) 42nm
- Core enclosing the DNA
- Excess HBsAg in serum – rods and spheres



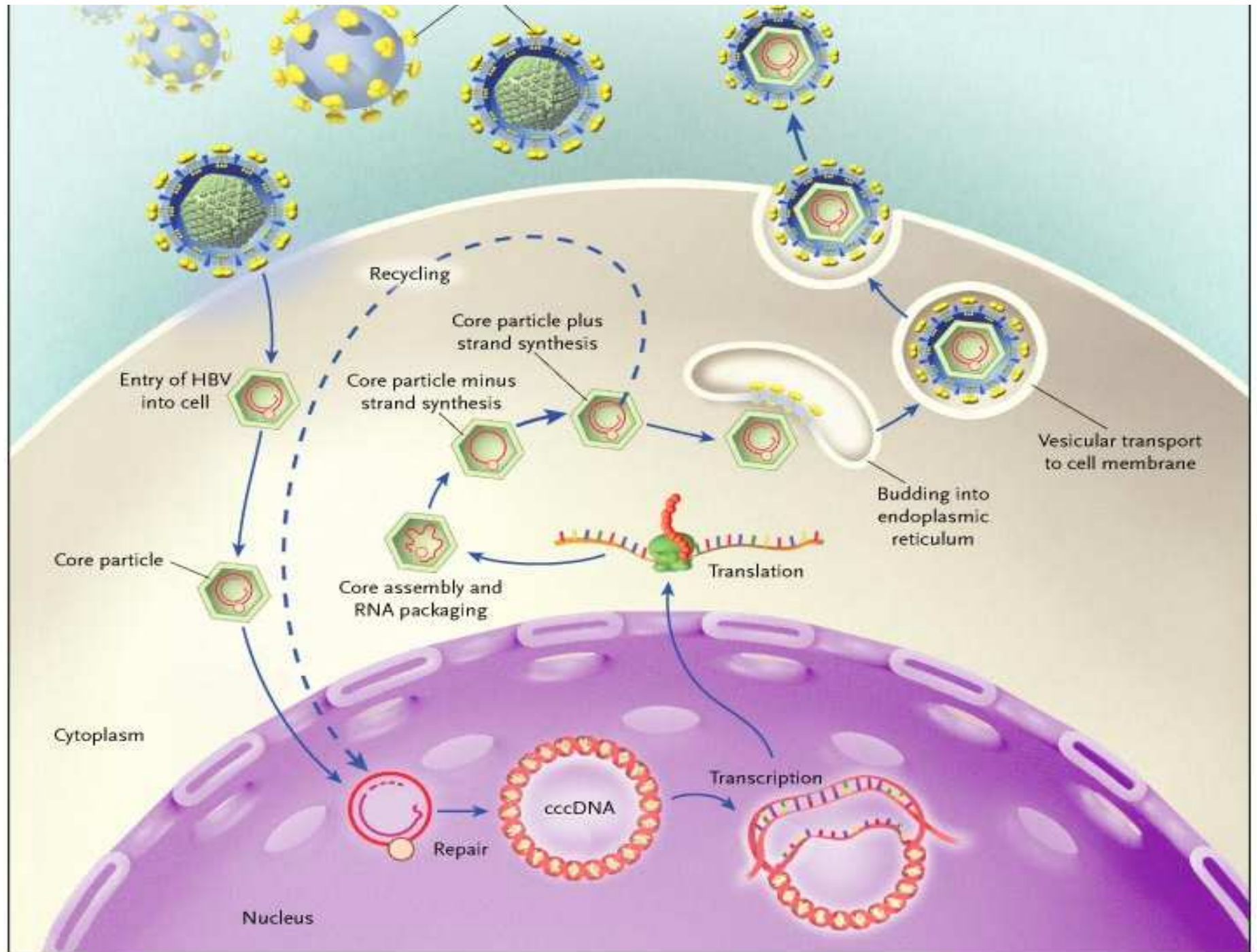


Hepatitis B Virology

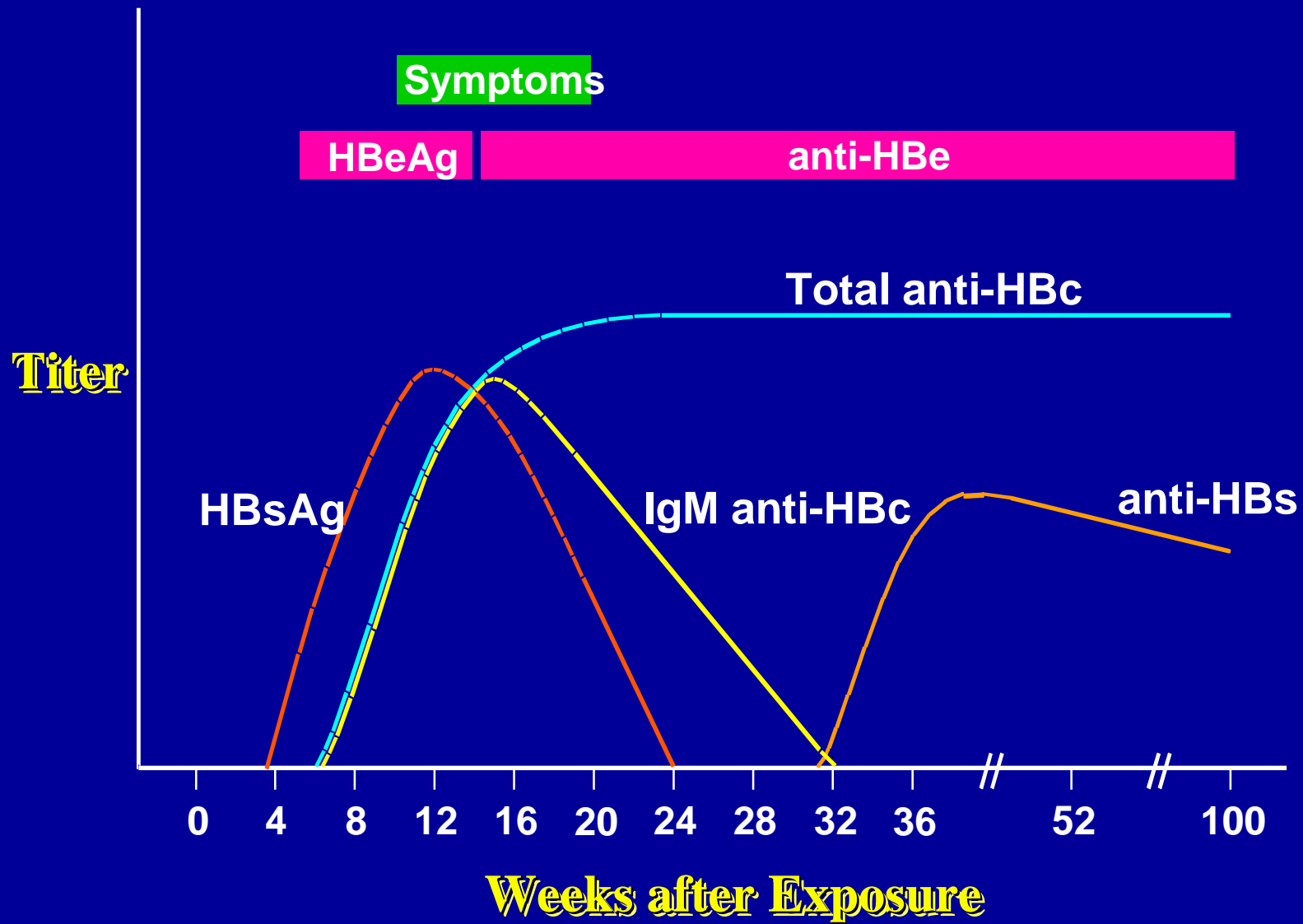


Hepatitis B - Clinical Features

- Incubation period: Average 60-90 days
Range 45-180 days
- Premature mortality from chronic liver disease (cirrhosis and HCC): 15%-25%



Acute HBV with Recovery



Hepatitis B Serological Markers

Stage of infection	HBsAg	Anti-HBc IgM	Anti-HBc IgG	HBeAg	Anti-HBe	Anti-HBs
Late incubation	+	-	-	+/-	-	-
Acute infection	+	+	+	+	-	-
Chronic infection	+	-	+	+/-	+/-	-
Recovery	-	-	+	-	+/-	+/-
Vaccine response	-	-	-	-	-	+

HBsAg- hepatitis B surface antigen, part of viral coat

Anti-HBc- antibody against core antigen (IgG or IgM)

HBeAg- hepatitis B e antigen, part of virus

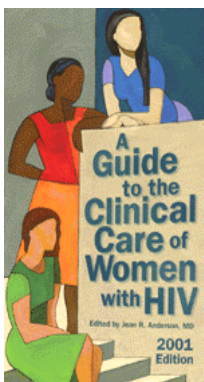
Anti-HBe- antibody against the e antigen

Anti-HBs- antibody against the surface antigen and a marker of clearance or immunisation

HIV

HIV in UK

- Adult prevalence 0.1%-0.2%
- IDU <1% (London 3-4%)
- IDU in Bristol 0.7%



Modes of Transmission

⌘ Parenteral

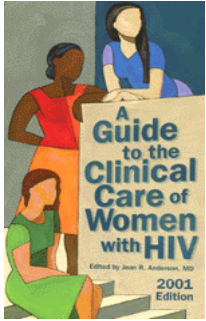
- ☒ Transfusion: 95% risk of infection with single unit of whole blood
- ☒ Injection drug use: 0.67% risk per exposure
- ☒ Healthcare workers (needlestick): 0.4% risk per exposure

⌘ Perinatal

- ☒ 25-30% risk of transmission without antiretroviral therapy or scheduled Cesarean section

⌘ Traditional practices

- ☒ Circumcision, ear piercing, tattooing with nonsterile instruments

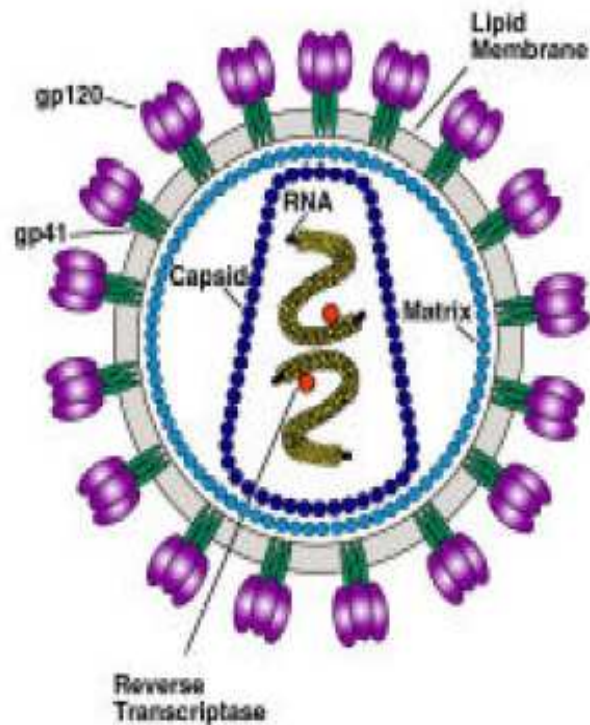


Modes of Transmission

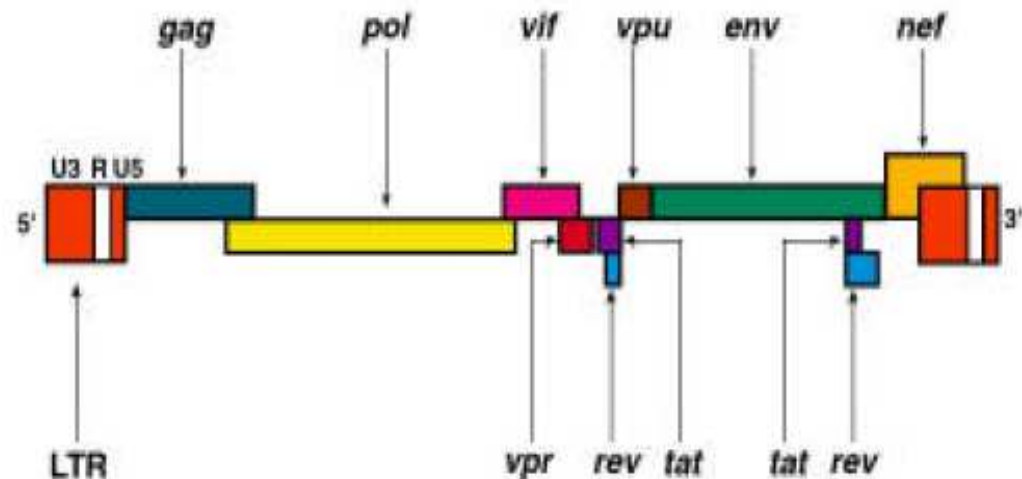
- ⌘ Sexual – predominant mode of transmission globally
- ⌘ Risk per episode
 - ☒ receptive vaginal intercourse: 0.1-0.2%
 - ☒ receptive anal intercourse: 0.1-3%
 - ☒ insertive vaginal intercourse: 0.1%
 - ☒ insertive anal intercourse: 0.06%
 - ☒ receptive oral intercourse: 0.04%

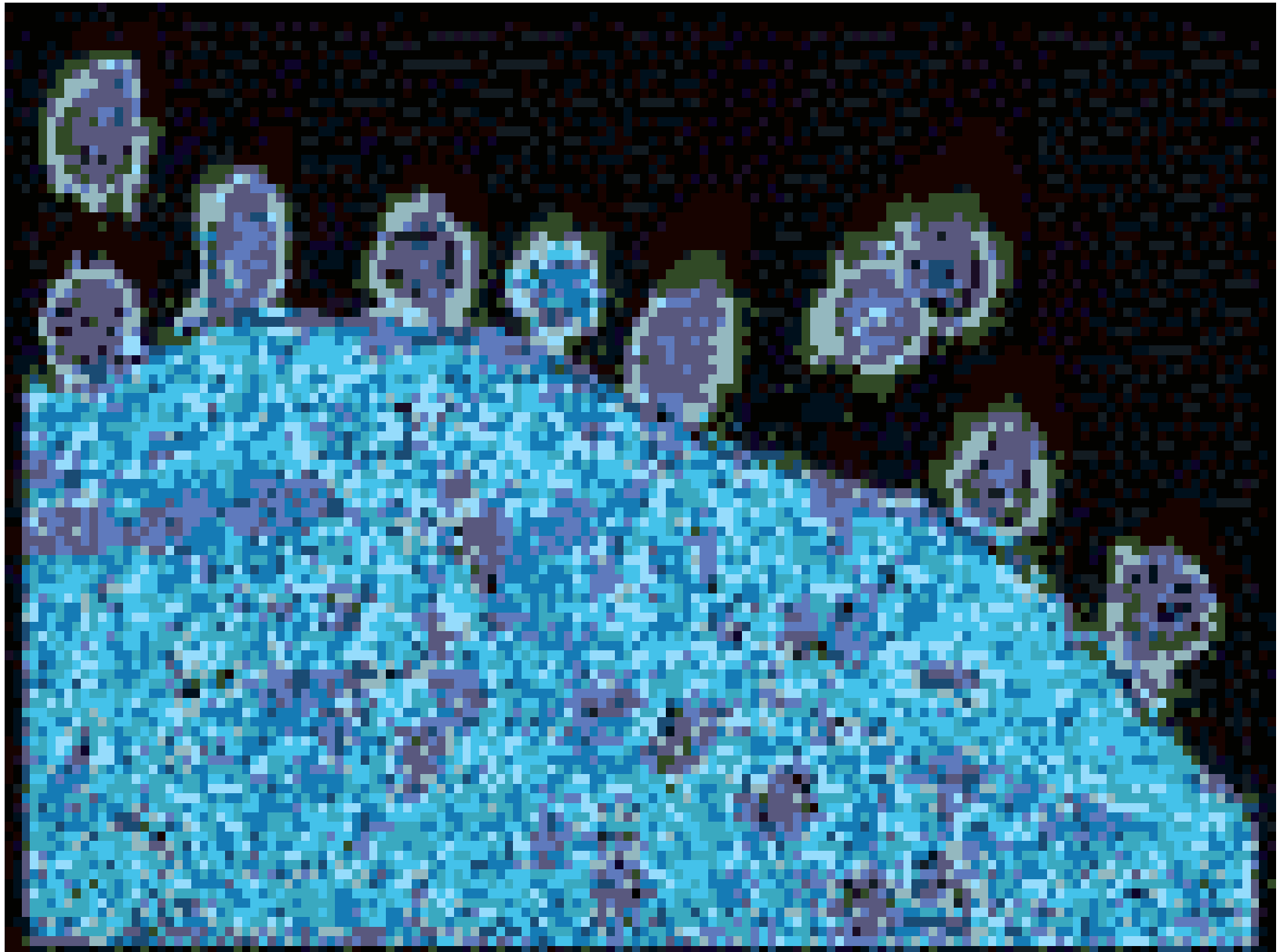
The Human Immunodeficiency Virus (HIV)

Organization of the HIV-1 Virion



HIV Genomic Map





HIV lifecycle

1. HIV attachment using CD4 and a coreceptor

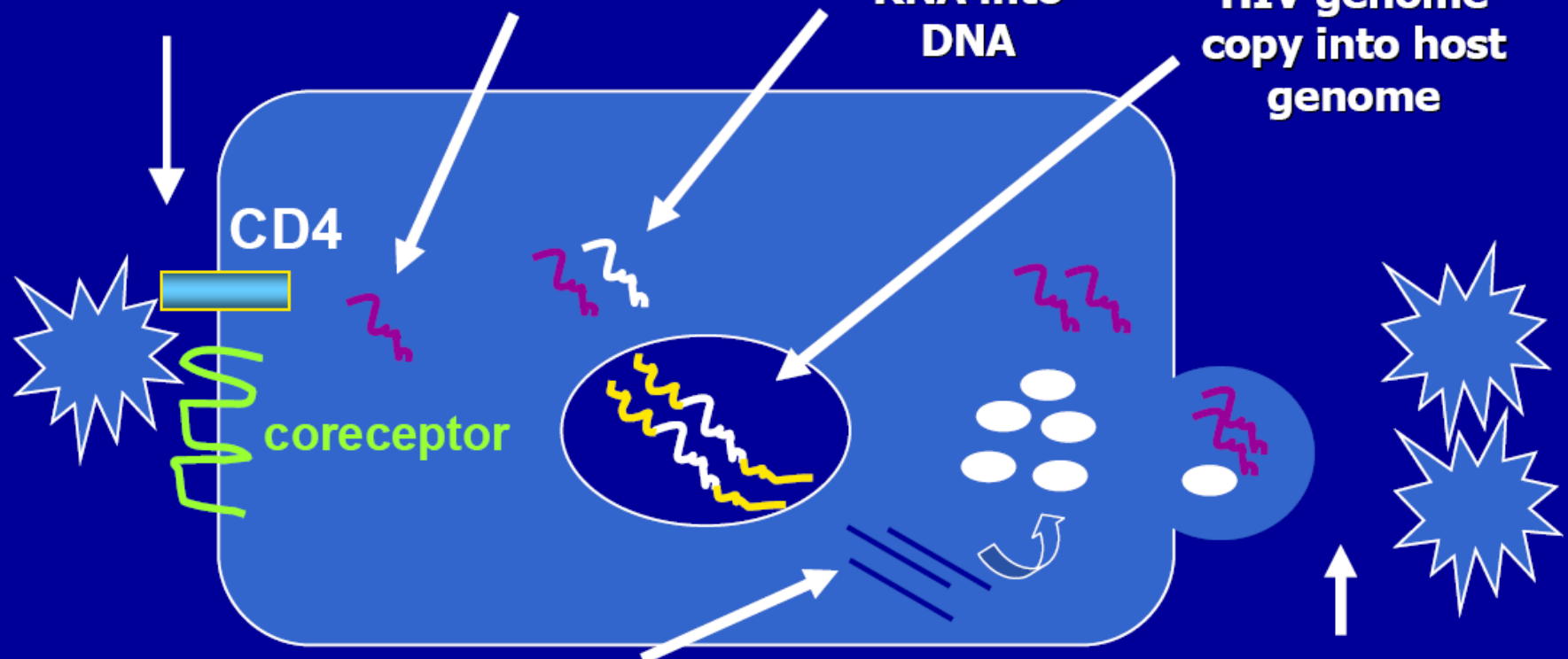
2. HIV fusion injects core with RNA genome

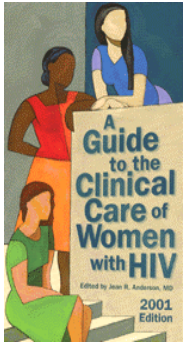
3. RT copies HIV RNA into DNA

4. Integrase incorporates HIV genome copy into host genome

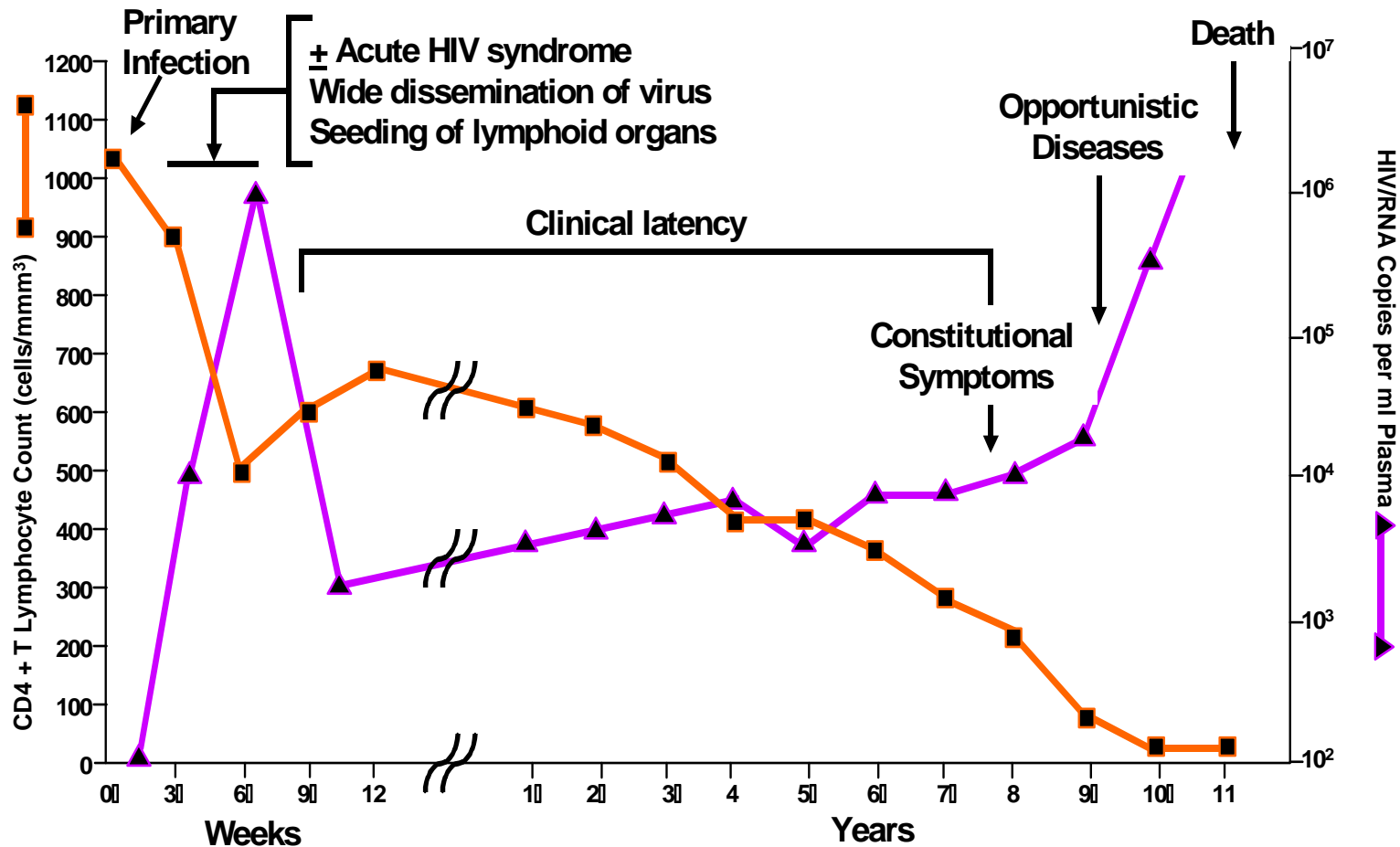
5. Protease processes immature proteins into mature HIV proteins

6. Virion release

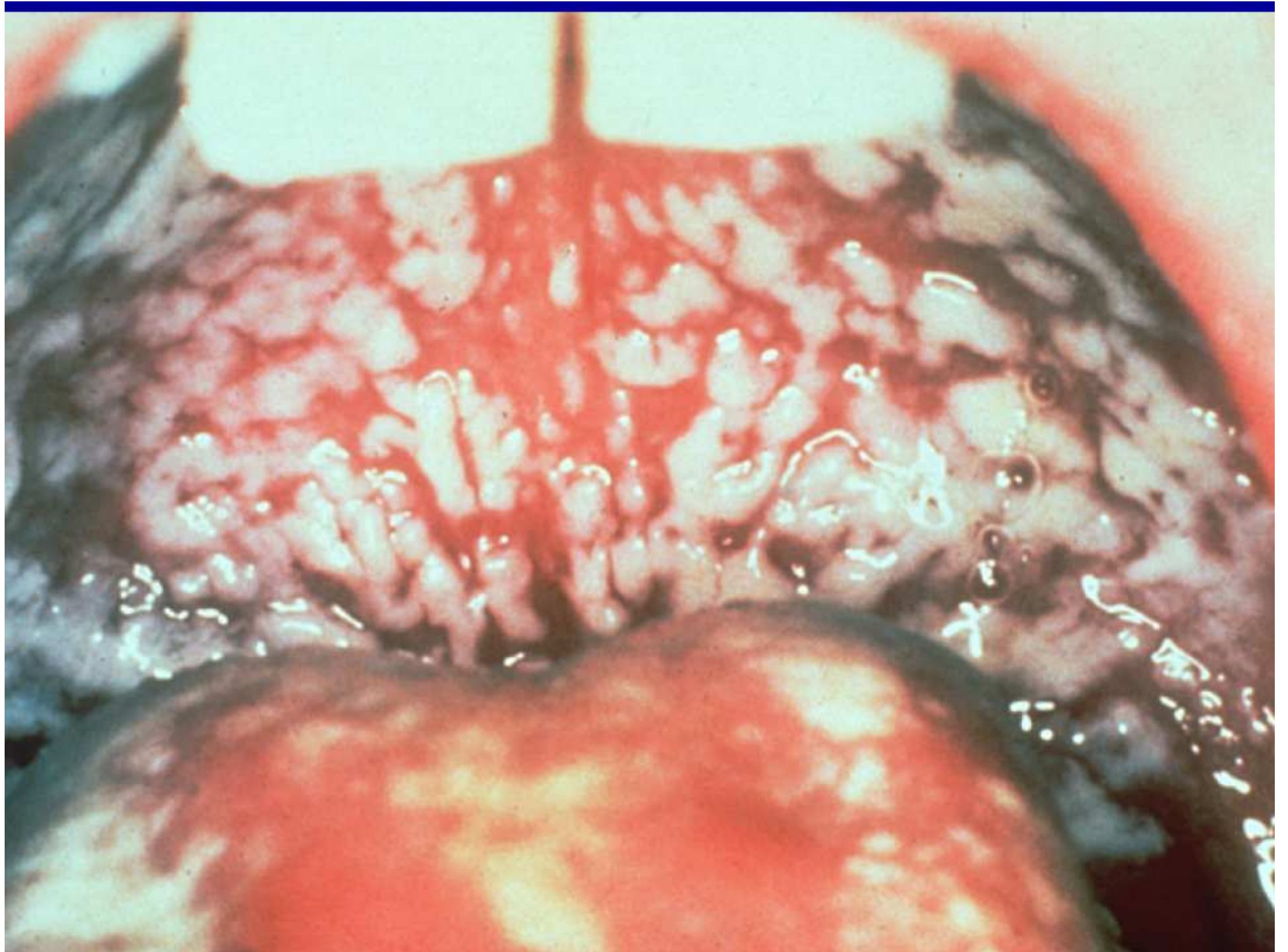




Natural History of HIV Infection Without the Use of Antiretroviral Therapy



Source: Fauci, A., Pantaleo, D., Stanley S., Weismann, D. *Annals of Internal Medicine* 124: 6754-3, 1996



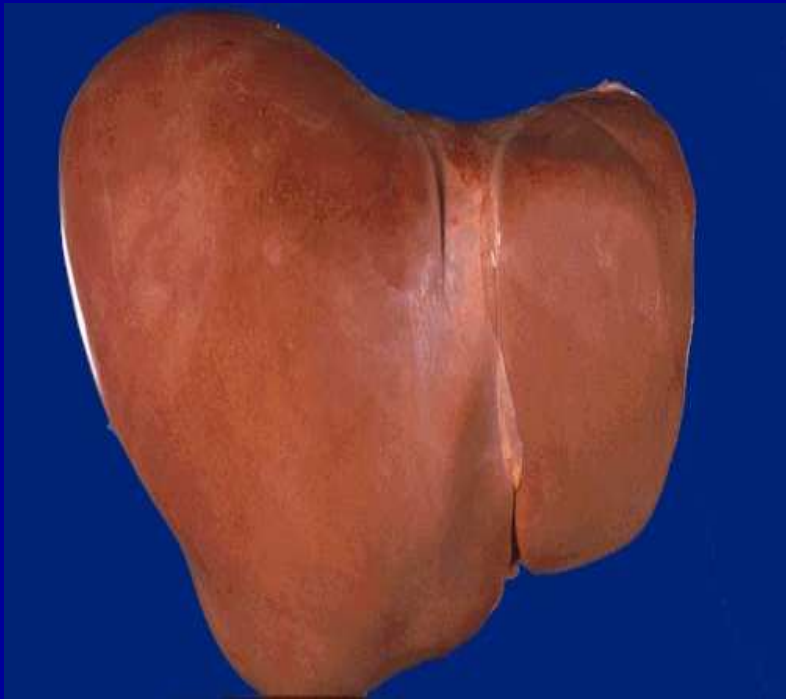


Why test?

1. Long term consequences of infection

Hepatitis B & C

Healthy Liver

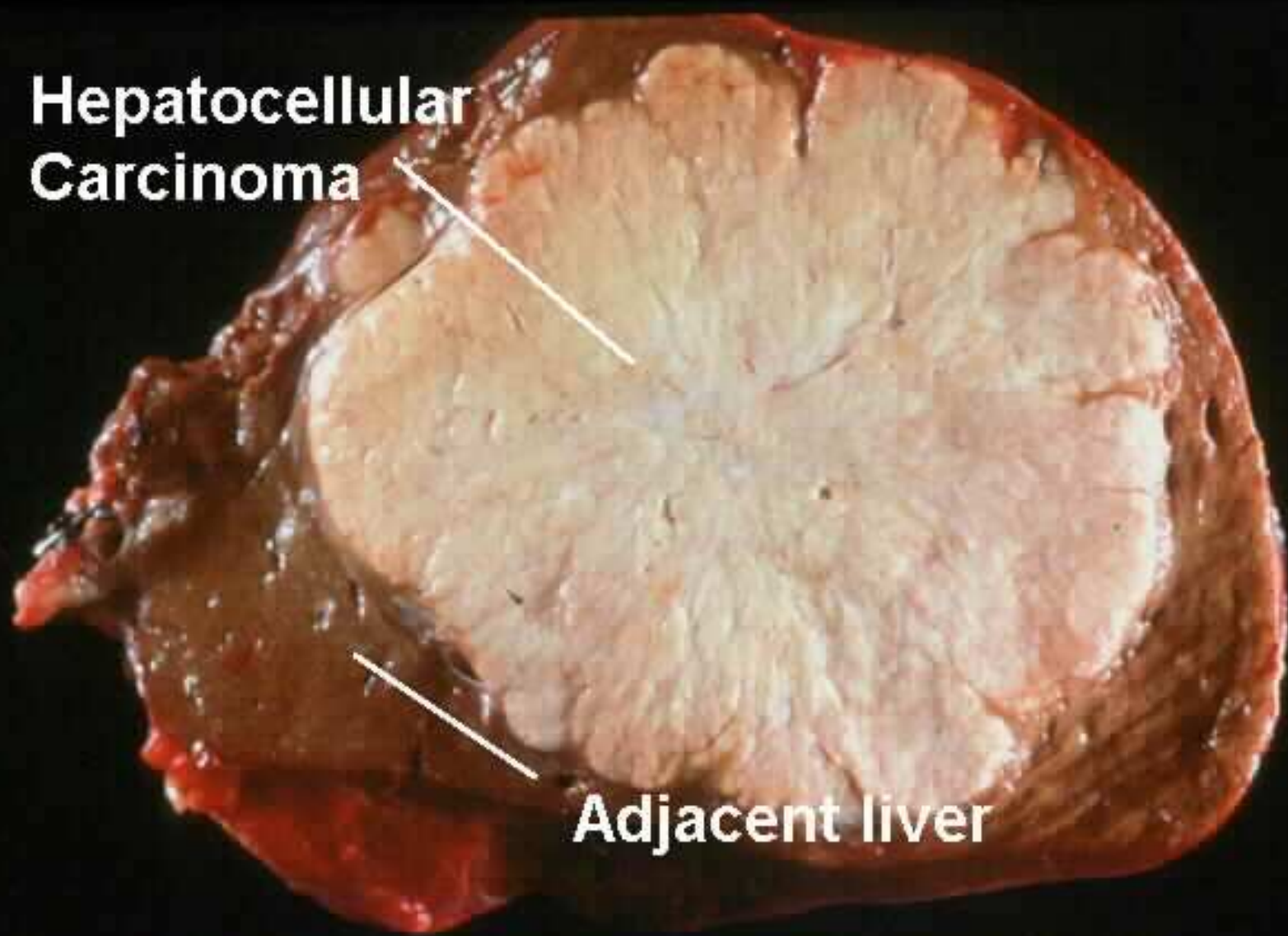


Cirrhosis





**Hepatocellular
Carcinoma**



Adjacent liver



HIV



Why test?

1. Long term consequences of infection
2. Prevalence of viral infections

Blood borne viruses in Intravenous Drug Users (IDUs)

High IDU prevalence: 3280-5540 (1.3-2%) aged
15-54

BBV prevalence

- 53% Hepatitis C virus (HCV)
- 32% Hepatitis B virus (HBV)
- 0.7% HIV

Low awareness/ uptake of HCV testing

- > 1/2 current IDU unaware that HCV positive

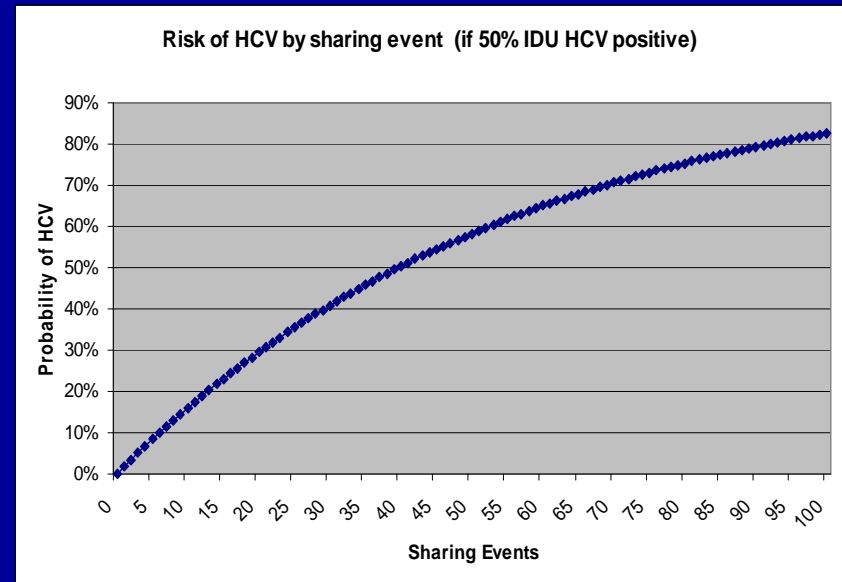
Blood borne viruses in Intravenous Drug Users (IDUs)

Ongoing high risk/
Incidence of HCV

- Evidence of recent infection (PCR+ve) in 9/114 HCV antibody-ve specimens

Likely to be high number of infections among current and ex-IDU in Bristol

- estimate 1,900 to 3,350



Why test?

1. Long term consequences of infection
2. Prevalence
3. Treatable/Preventable

HCV SVR

- Genotype 1 = 41-44%
- Genotype 2 & 3 = 66-75%





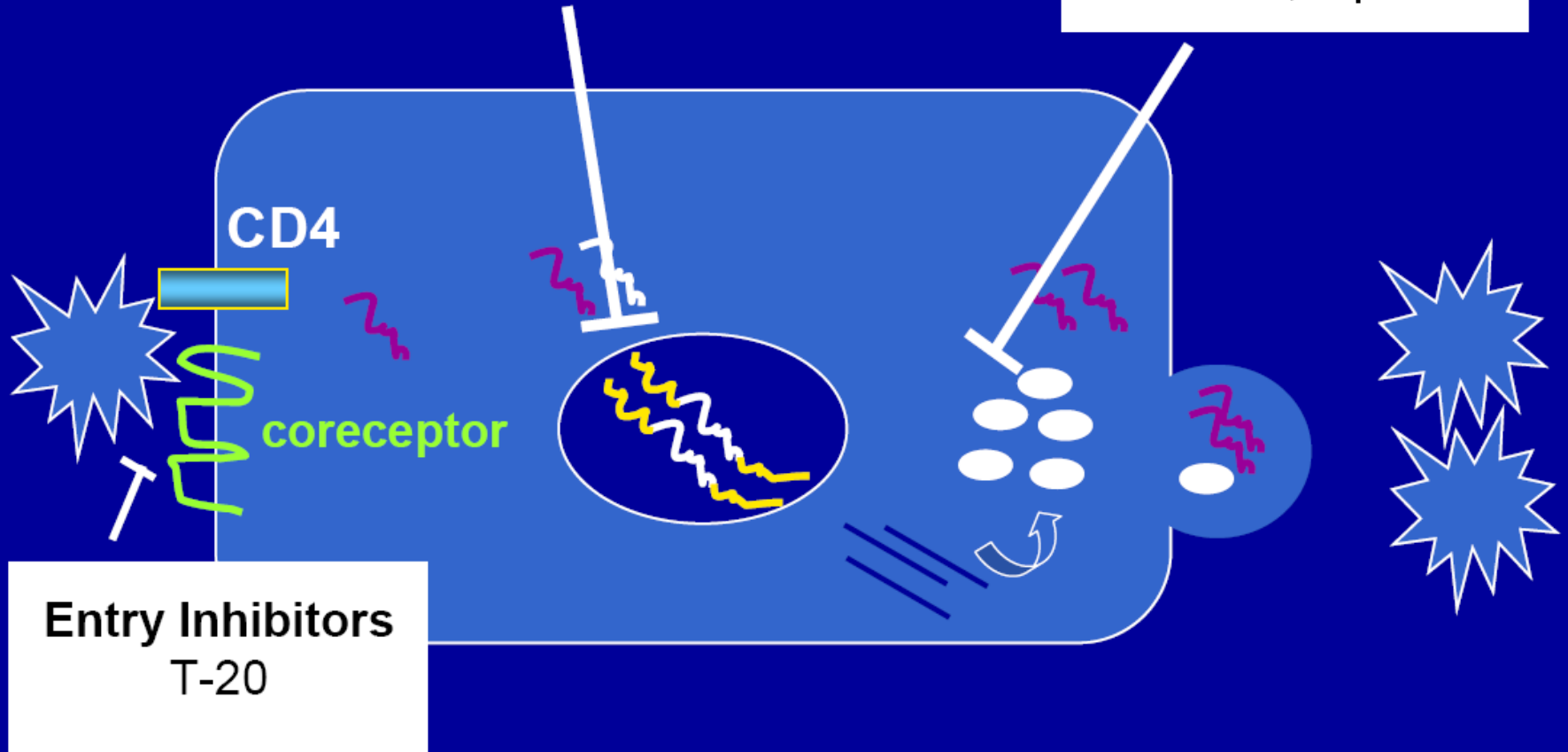
Characteristics of selective drugs for HBV

	1yr eAg s/c	Resistance 1 yr	Resistance 4 yr	Genotypic mutations	Cost/mth (US\$)
Lamivudine	12-18%	18-20%	70%	rtM204V, rtL80V, rtV173L, rtL180M	150
Adefovir	12-14%	2%	18%	rtN236T, rtA181T/V	525
Entecavir	21%	0%	?	rtT184G, rtS202I, rtM250V	600
Tenofovir	?	?	?	?	430
Emtricitabine	?	12%	?	rtM204I	290
Telbivudine	?	4.5%	?	rtM204I	?
PEG-IFN	25-32%	0%	0%	none	1300

Established Strategies of HIV Therapy

Reverse transcriptase inhibitors
NRTIs: zidovudine, lamivudine, tenofovir
NNRTIs: nevirapine, efavirenz

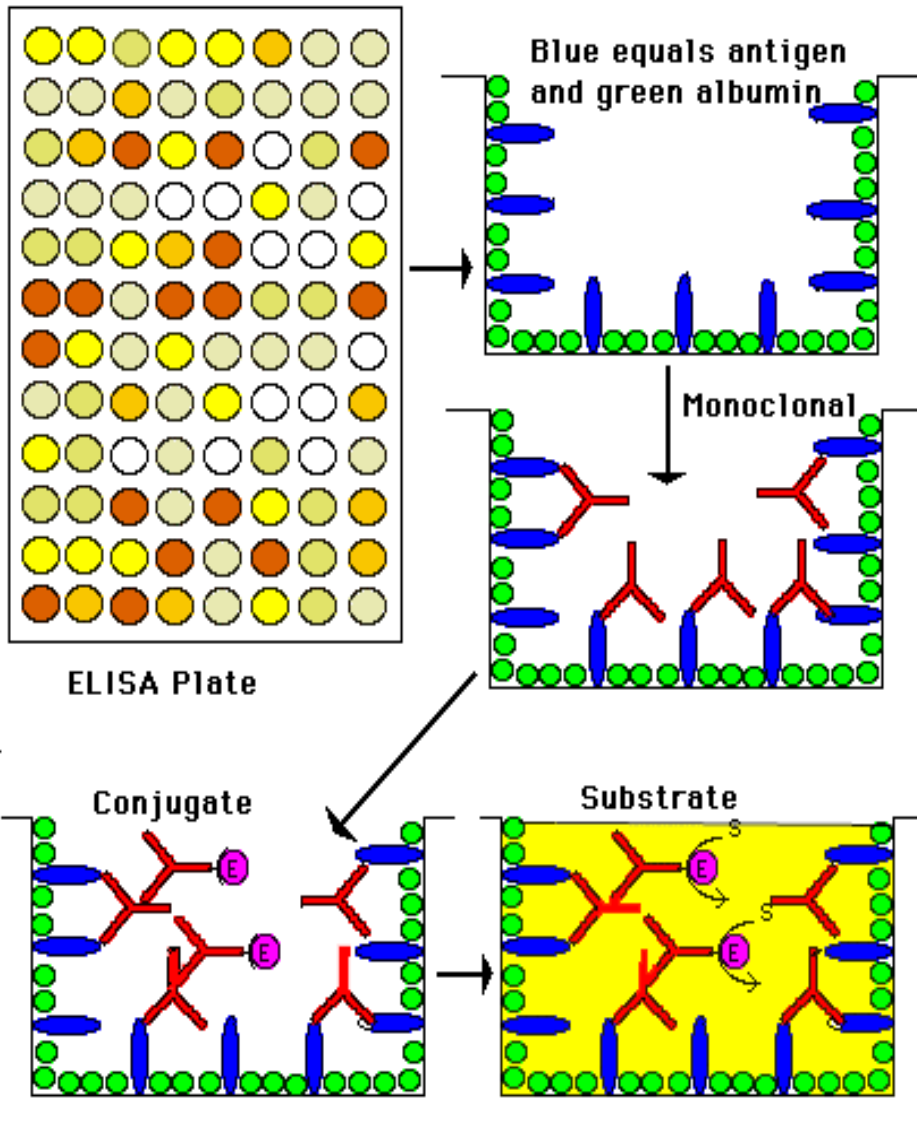
Protease Inhibitors
Ritonavir, Tipranavir



Why test?

1. Long term consequences of infection
2. Prevalence
3. Treatable/Preventable
4. Sensitive and specific tests available

Enzyme Linked Immunosorbent Assay (ELISA)



Microtitre plate
ELISA

Healthy Liver



Cirrhosis





Thank you

HCV – 1 (and 4)

(difficult-to-treat)

PEG – IFN- α 2a 180ug/week

+

Ribavirin 1000-1200mg od
(based on BW < or > 75kg)

FOR 48 WEEKS



HCV – 2 and 3

(easy-to-treat)

PEG – IFN- α 2a 180ug/week

+

Ribavirin 800 mg od

FOR 24 WEEKS



Burden of Hepatitis C Virus Infection

Estimated 200,000 people in England are chronically infected

HCV infection is now the major indication for liver transplant in USA and Europe

Prophylaxis-HBV

HBV status of exposed person	HBsAg positive source	Source unknown	HBsAg negative source
<= 1 dose HB vaccine	Accelerated course vaccine plus 1xHBIG	Accelerated course vaccine	Initiate course of vaccine
>= 2 doses HB vaccine (anti-HBs unknown)	1 dose of vaccine followed by a second one month later	1 dose of vaccine	Finish course of vaccine
Known responder (anti-HBs >10)	Consider booster dose	Consider booster dose	Consider booster dose
Known non-responder (<10)	HBIG x1 then repeat Consider booster dose vaccine	HBIG x1 then repeat Consider booster dose vaccine	No HBIG Consider booster dose

Table relates to significant exposures only

Know your status!

HIV Risks

- Receptive anal 0.1-3%
- Insertive anal 0.006%
- Fellatio 0-0.04%
- Mucous membrane exposure 0.09%

- risk of HIV transmission per exposure from a known HIV positive individual