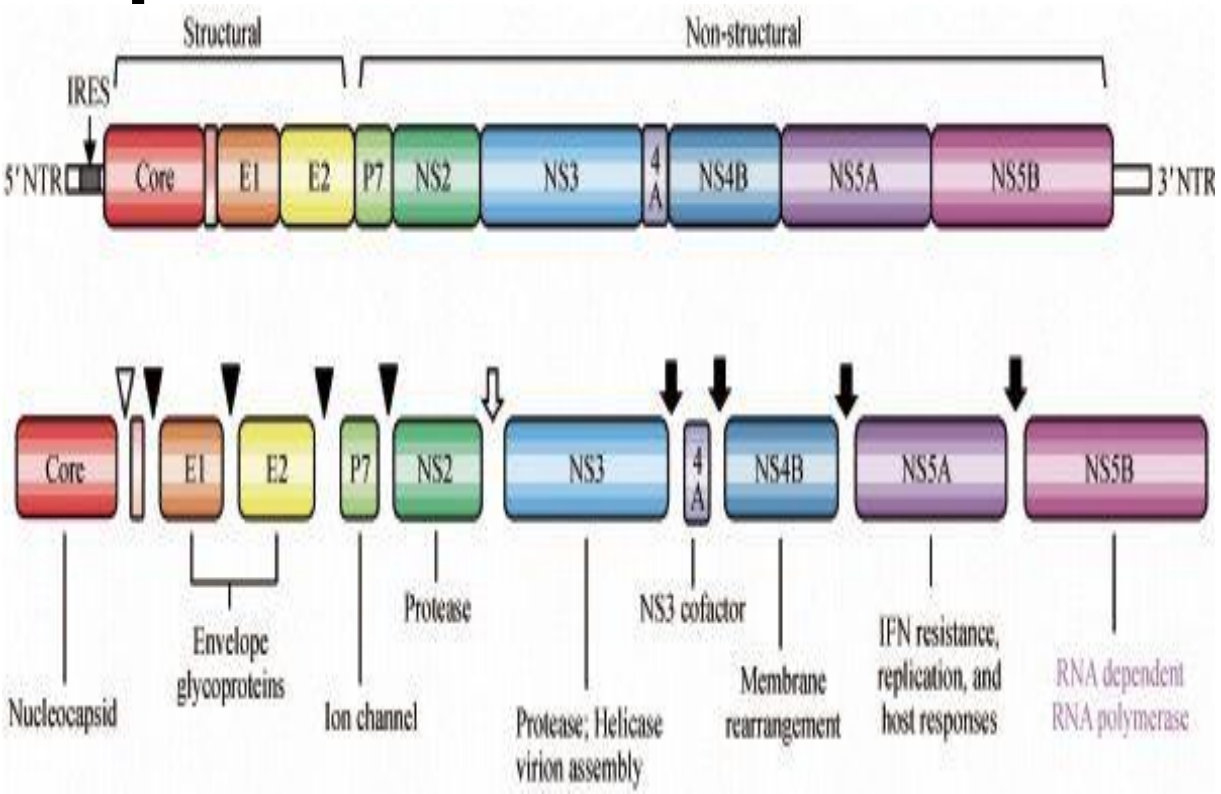
Hepatitis B and C

11.6.2018

Hepatitis C Virus

- RNA Virus
- Replicates prolifically and without proofreading
- No immunization currently available
- Conservative estimates: 3-4 million Americans are viremic



Adapted from Fronteirs Journals

How does (or can) one acquire HCV?

- Blood
  - Intravenous drug use (IVDU) is the leading cause in the United States
    - Snorting instruments
  - Skin exposures e.g. needle sticks
  - Dental Work
  - Unprofessional tattooing
  - Blood Transfusion (before 1992)

- Sexual Contact
  - Rare

- Mother to Child
  - Rate is 1.7 to 4.3%

Platt et. al. Cochrane Database Syst Rev. 2017

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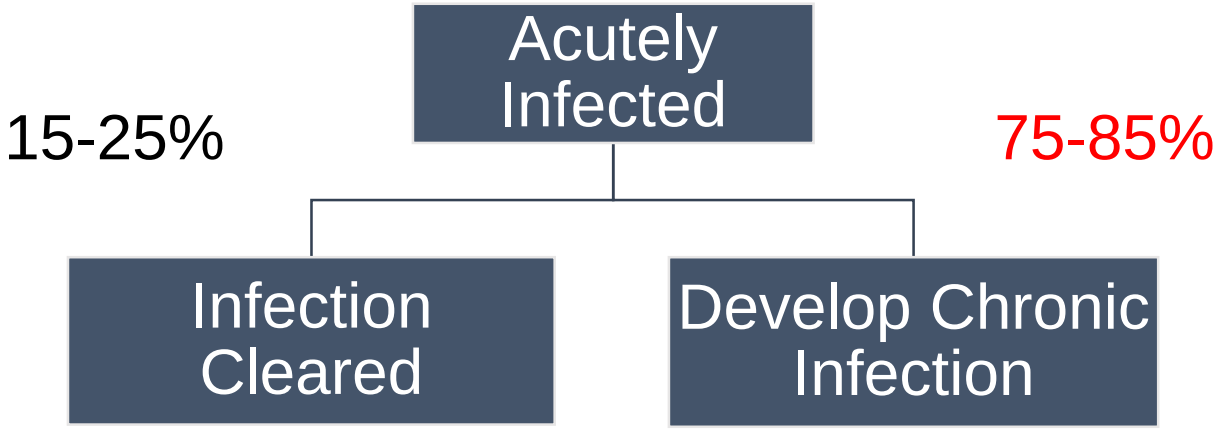
What happens when someone acquires HCV?



Thrift AP et. al. Nat Rev Gastroenterol Hepatol. 2017

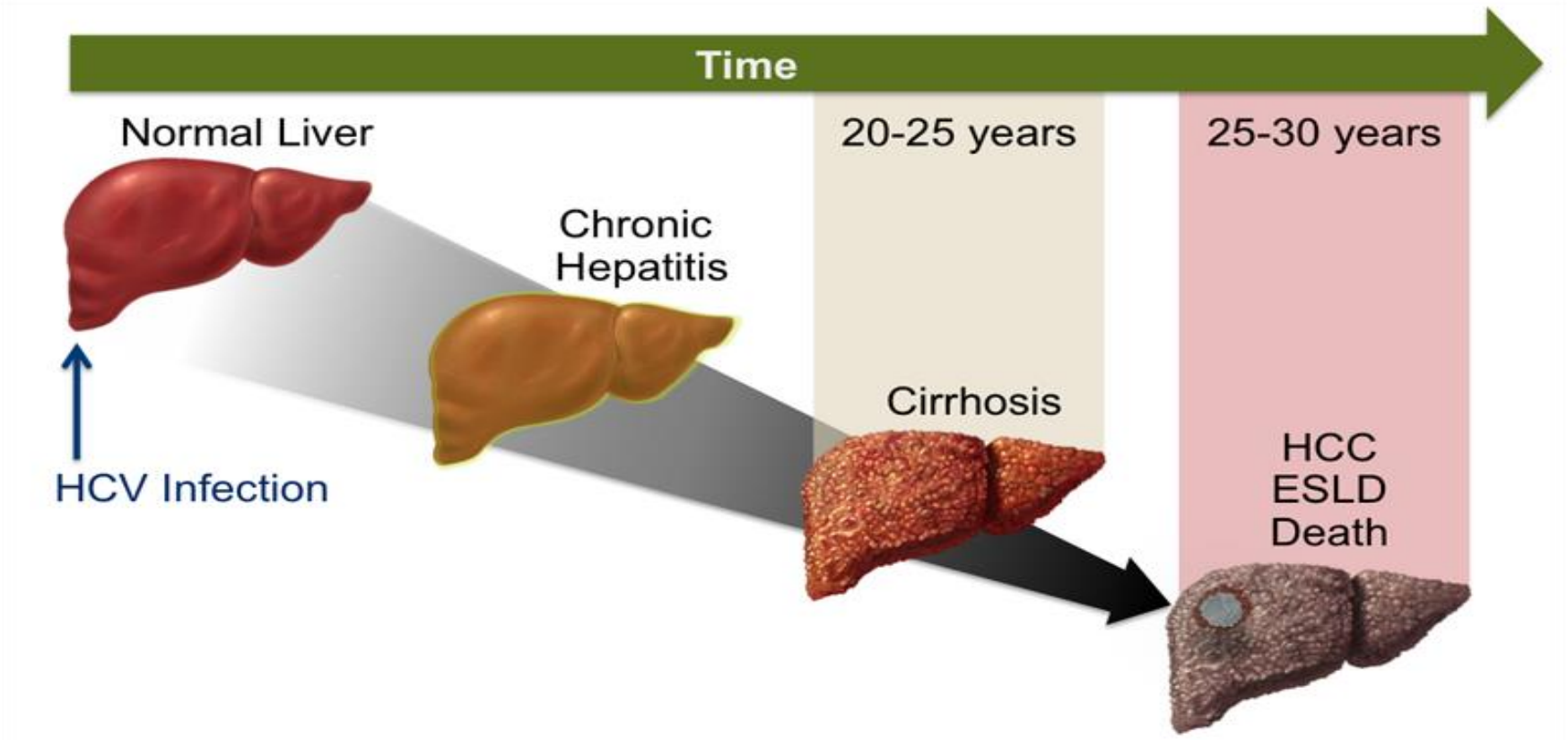
What happens when HCV establishes chronicity?

- Acquisition is usually CLINICALLY SILENT
  - Jaundice, severe acute liver injury is rare

- Symptoms are OFTEN GENERAL and NON SPECIFIC
  - Fatigue
  - Migratory joint aches
  - “Brain fog”

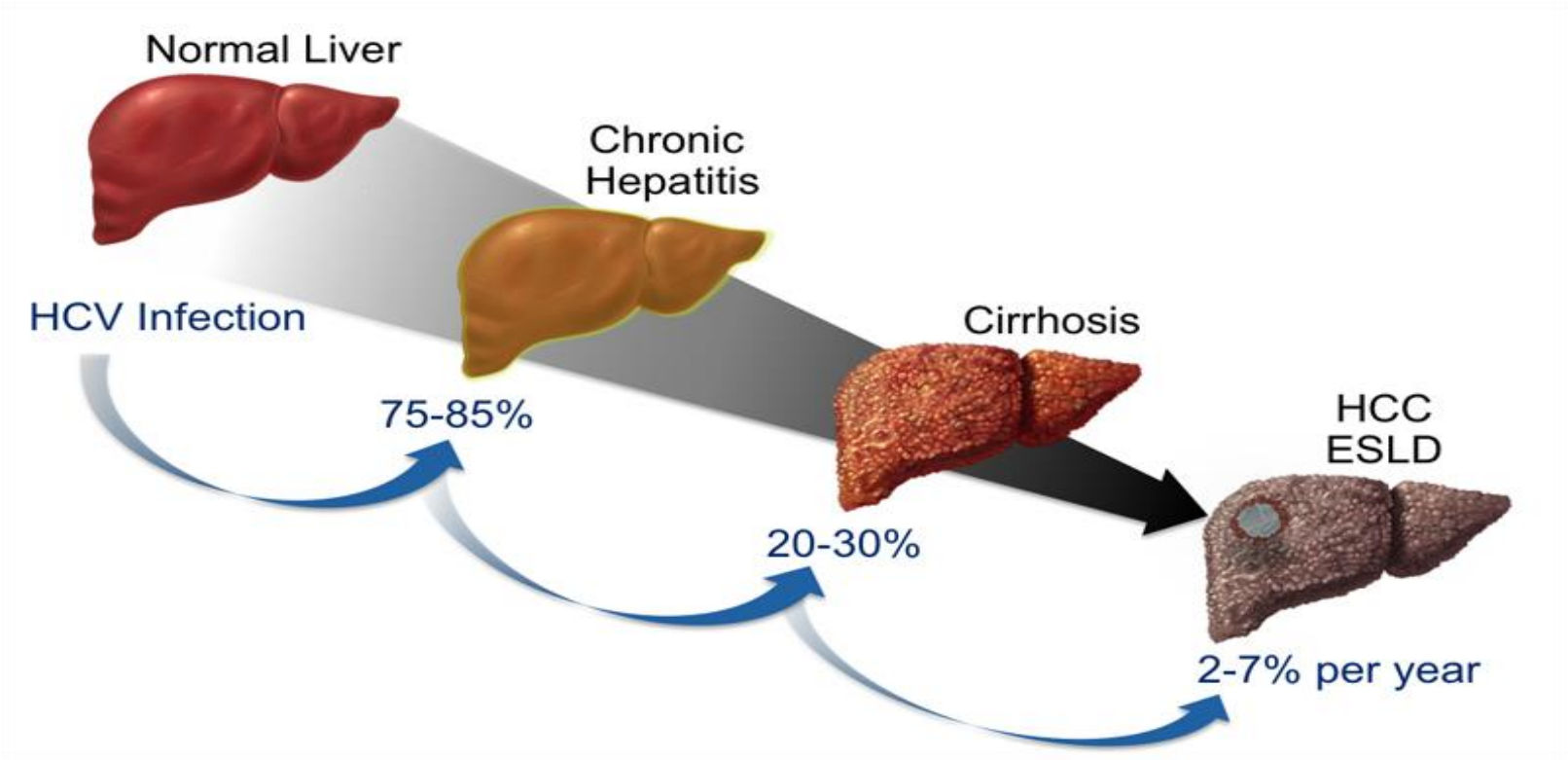
Debes JD et. al. Transplantation. 2017

Natural History of Chronic HCV Infection



Adapted from https://www.hepatitisc.uw.edu

Progression to Cirrhosis and End Stage Liver Disease



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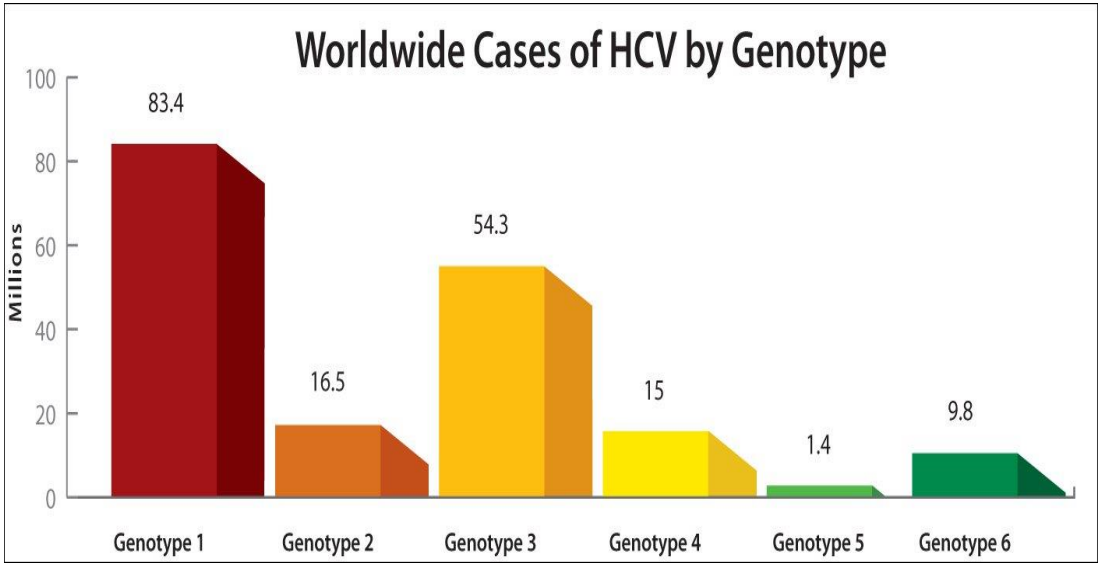
Summary

- Acquisition of HCV is often silent, without many symptoms
- Progression to chronicity is common
- Liver damage can continue “under the radar” for decades
- Unrecognized and untreated infection can lead to cirrhosis
- Cirrhosis and associated complications are deadly

Highly tolerable therapy can cure HCV and halt disease progression and….
may stabilize or potentially reverse damage already done

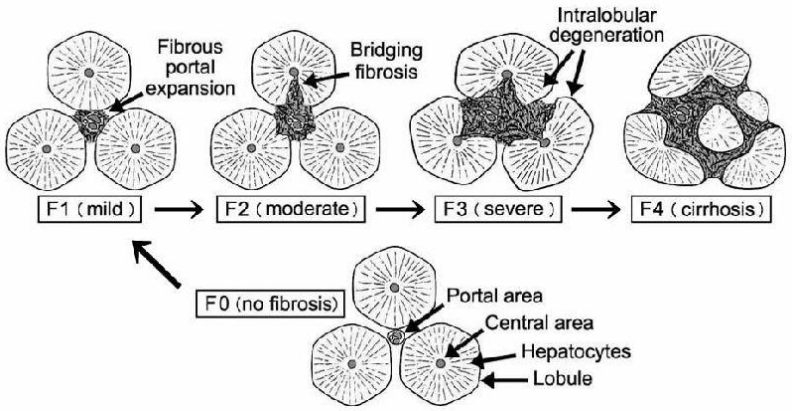
Hepatitis C Genotypes

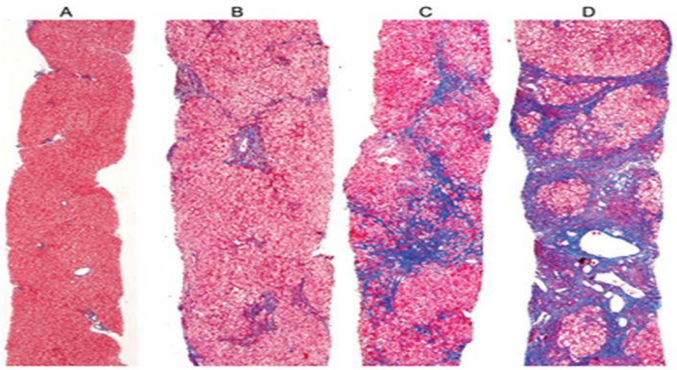
- **Hepatitis C**
  - RNA virus with high mutation rate
- **6 known genotypes**
  - Type 1 most common in US
  - Type 3 associated with liver fat deposition and now considered the hardest to treat
  - Antivirals may be most effective in a certain genotype

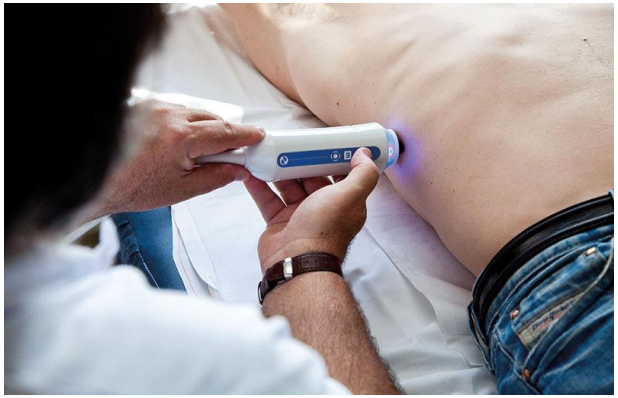


Tsukiyama-Kohara K et. al. Int J Mol Sci. 2017

Fibrosis Staging





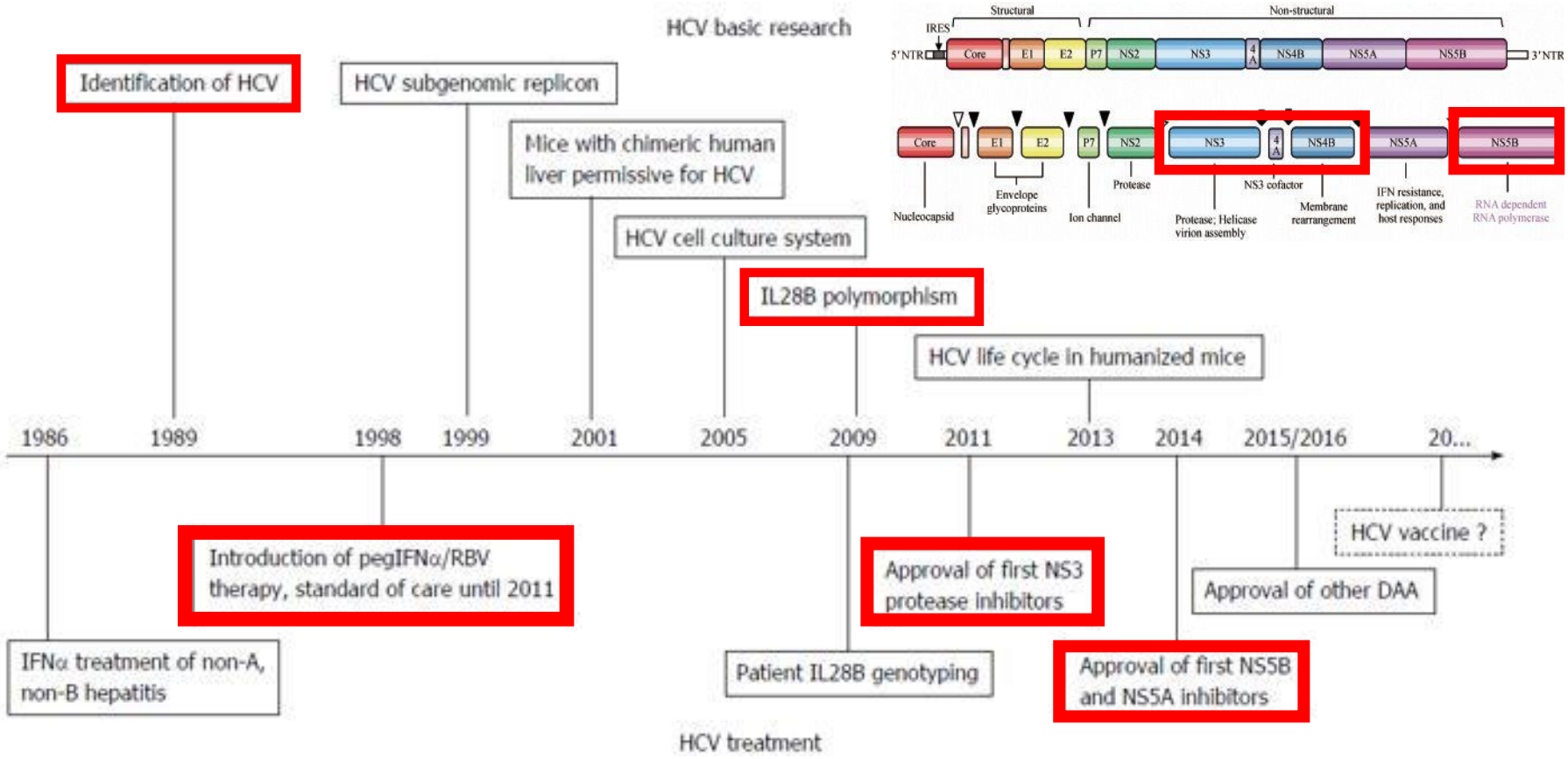


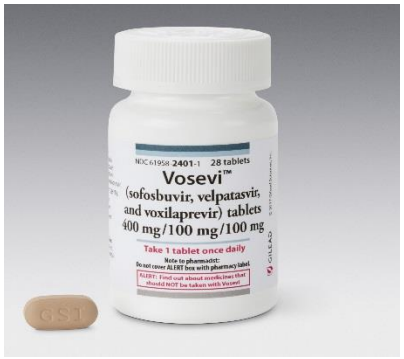
Other Components of the Medical Workup

- Blood work
  - Assess liver function
  - Hemoglobin/hematocrit
  - Hepatitis A and B immunity
  - Fibrosis can be assessed through blood markers

- If advanced fibrosis
  - Ultrasound or liver imaging to screen for liver cancer
  - Upper endoscopy to screen for esophageal varices

Medical Treatment of HCV





https://www.hcvguidelines.org/

Results with Direct Acting Therapy

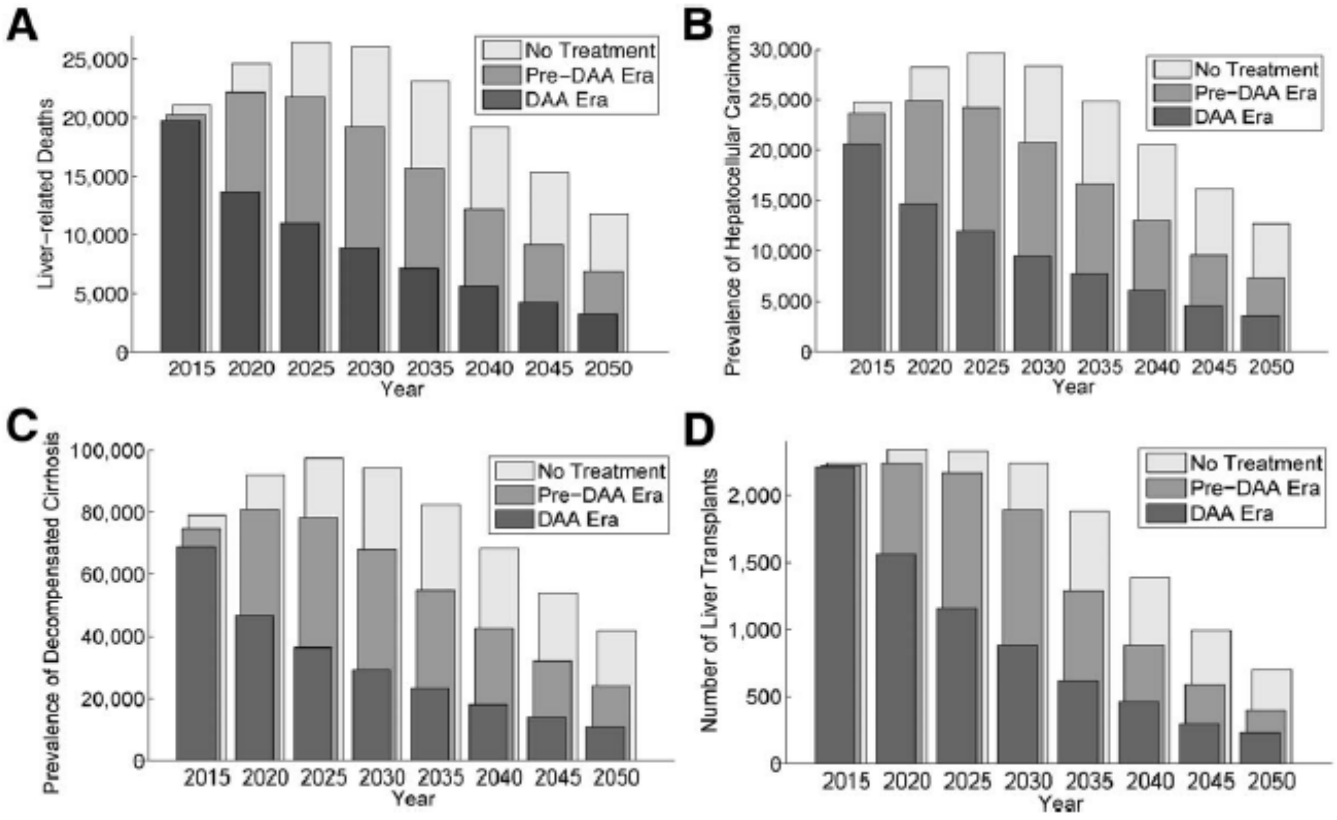
- Single tablet regimens, pan genotypic, often no more than 3 months

- Previous “difficult to treat” populations have options
  - Previous treatment experience
  - Advanced fibrosis and decompensated cirrhosis
  - HIV co-infection
  - End Stage Renal Disease/Dialysis

- Excellent results and tolerability are corroborated by several “real world” registries

Kim JK et, al. Clin Gastroenterol Hepatol. 2018

Are we making a difference?



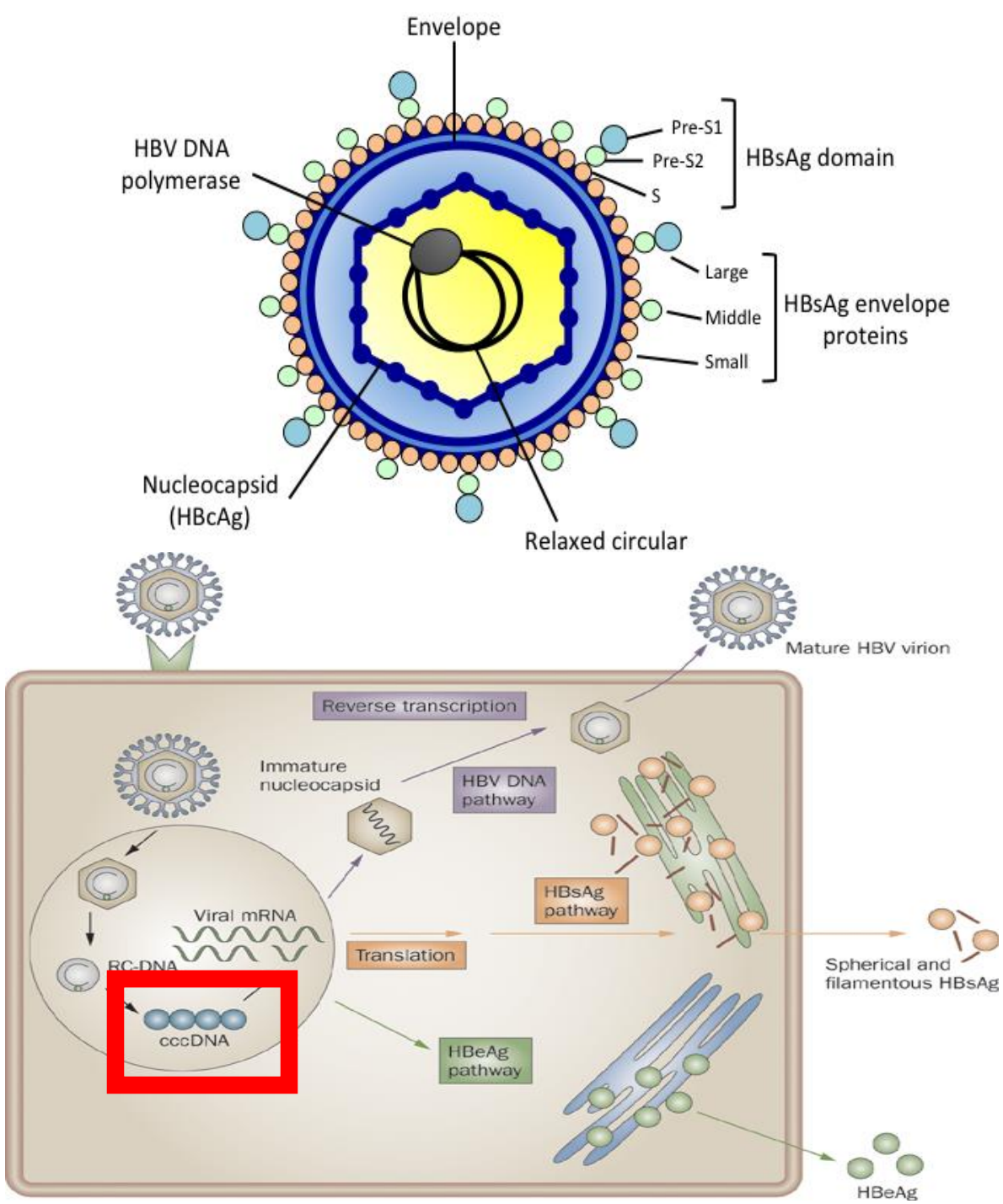
Chhatwal et, al. Hepatology 2016

Hepatitis B

- Most common chronic liver disease worldwide
- ~ 2 billion exposed; >300 million carriers
- Varying prevalence around the world
  - High: China, Southeast Asia, Sub-Saharan Africa
    - Common mode: perinatal/vertical transmission
  - Low: North America and Western Europe
    - Common mode: sexual and IVDU

Hepatitis B

- DNA virus, hepadnavirus family
- Genotypes A-H
- A common cause of *chronic* liver disease however can be "spontaneously cleared" 80-90%
  - Vertical (young): progression to chronicity common
  - Acquired (older): often cleared
- Causes damage…but in the context of a host immune response/inflammation
- Oncogenic virus (regardless of cirrhosis)



Double stranded DNA Virus makes 4 Proteins:

Surface: attachment

Core: inner core included e

Polymerase: replication

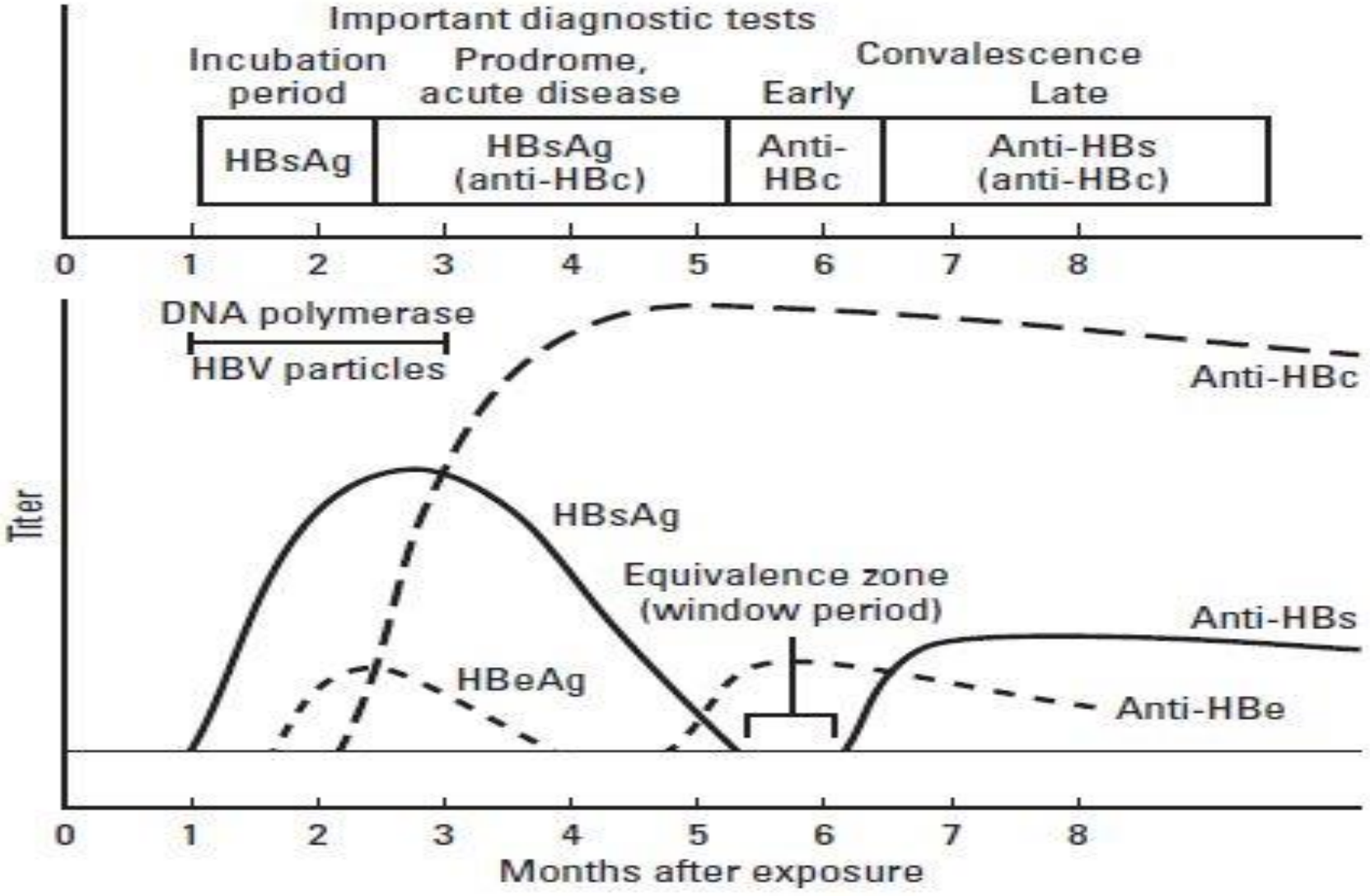
X: causes cancer

cccDNA: protected shell of HBV DNA in the hepatocyte nucleus THAT NEVER GOES AWAY!!!

What we can measure:

Surface Ag and Ab
Core Ab
E Ag and Antibody
HBV DNA

Acute Hepatitis B



“Rules for Acute Hepatitis B”

- Start with surface Antigen: if reactive, assume they have hepatitis B (acute or chronic)
- Detailed history of exposure
- If not reactive….verify with core
  - Core IgM: reactive is acute HBV
  - Core Total (IgG): implies exposure
- eAg expression implies recent acquisition
- Track CMP and PT/INR
- Antiviral therapy is not indicated unless there is liver failure, spontaneous clearance about 80% of the time
- Reassessment in about 6 months in the outpatient setting to check for surface antibody……

Chronic Hepatitis B: The Four Phases

- For those who don't acquire sAb at 6 months or who obtain vertically…progression to chronicity

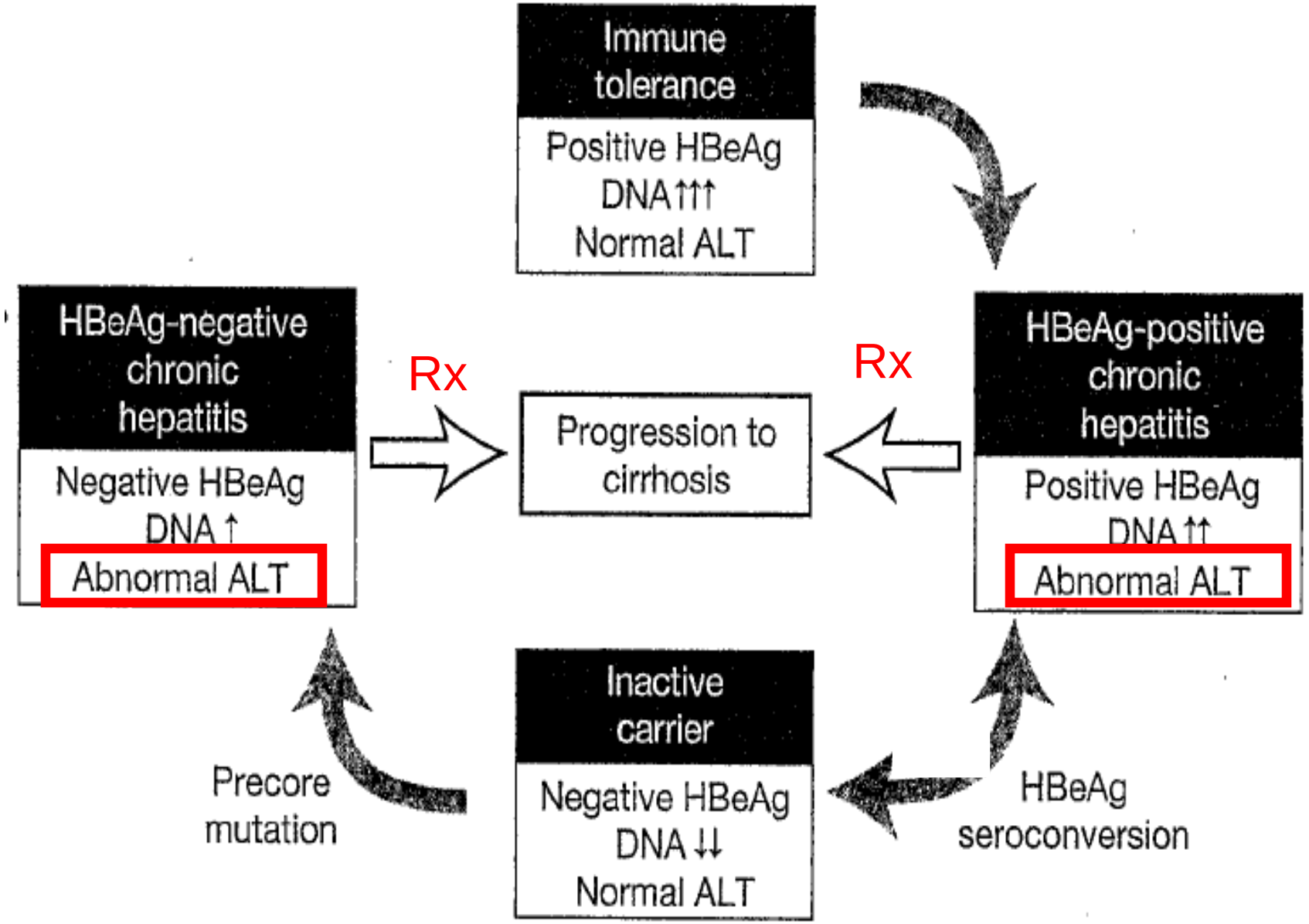
- Phase 1: Immune Tolerant
  - sAg: pos, eAg pos, HBV DNA High, LFTs normal

- Phase 2: "eAg positive" Chronic hepatitis B
  - sAg: pos, eAg pos, HBV DNA wherever, **LFTs abnormal**

- Phase 3: Chronic carrier
  - sAg: pos, eAg negative, eAb pos, HBV DNA Low, LFTs normal

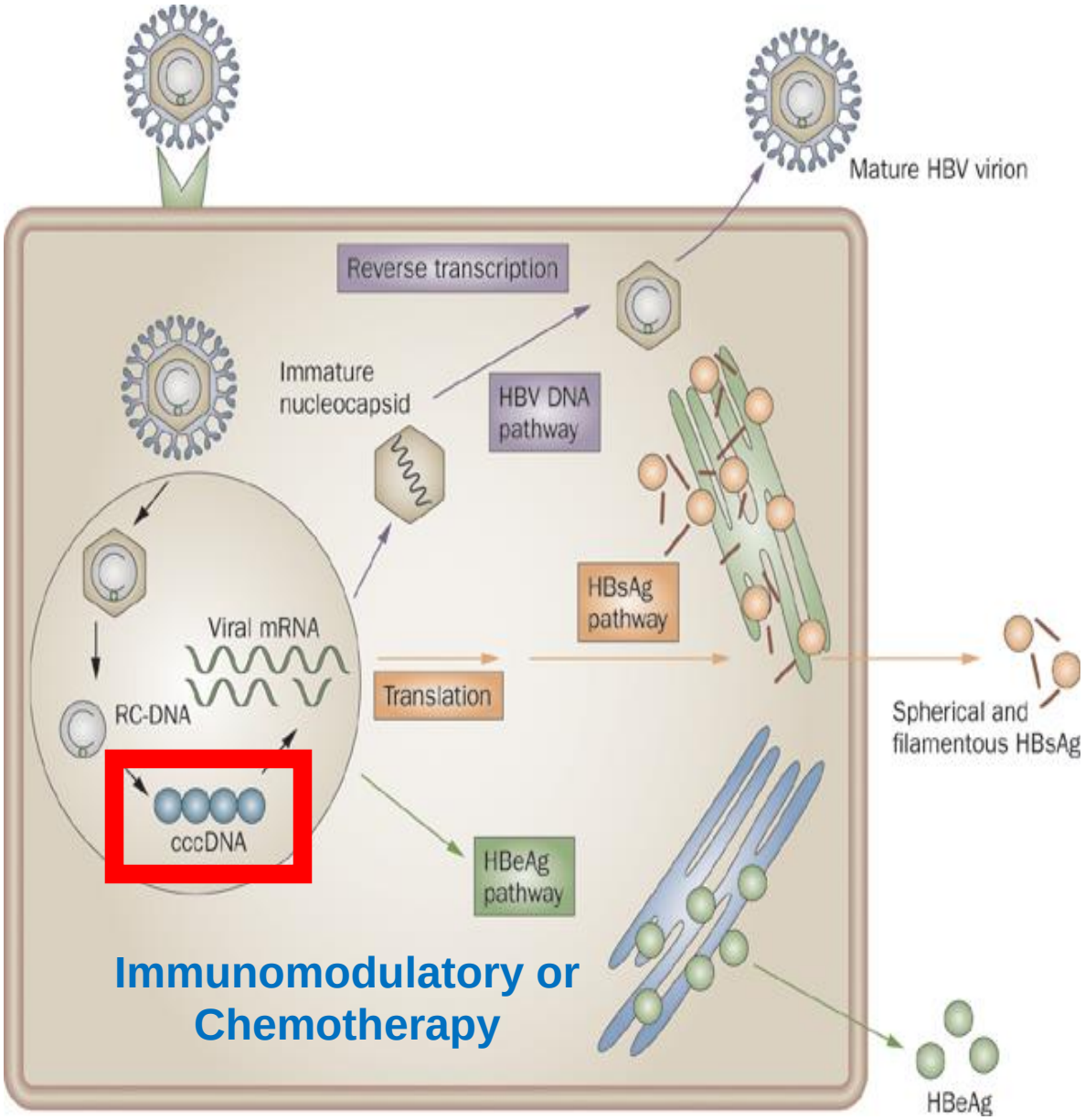
- Phase 4: "eAg negative" Chronic hepatitis B
  - sAg: pos, eAg negative, eAb pos, HBV DNA wherever, **LFTs abnormal**

Chronic Hepatitis B: The Four Phases



Hep B SAg	Anti HBs	IgM Anti-HBc	IgG Anti-HBc	HepB eAg	HepB Anti HBe	ALT	
+	-	+	-	+	-	HIGH	Acute HBV
+	-	-	+	+	-	HIGH	eAg pos CHB
+	-	-	+	-	+	LOW	Chronic Carrier
+	-	-	+	-	+	HIGH	eAg neg CHB
-	+	-	-	-	-	LOW	Immunized
-	+	-	+	-	+	LOW	Exposed

HBV Reactivation



People with "resolved" infection

sAb: NonReactive
cAb: Reactive

sAb: Reactive
cAb: Reactive

Are at risk for reactivation

Prior to starting biologic or chemotherapy: Assess for sAb AND core total antibody

If core total is present….consider antiviral

Hepatitis D Virus

- Hepatitis D virus: defective RNA virus, requires HBV to help with replication
- Can cause pathogenesis in 2 forms
  - Co-infection
  - Superinfection
- Treatment or immunization against HBV should treat/prevent HDV
- Uncontrolled co-infection increases risk for liver failure
- Viruses travel in groups….document HCV and HIV status

Hepatocellular Cancer

- Hepatitis B Virus is a carcinogen
- Risk of hepatocellular cancer increases with
  - Increased duration of infection
  - Higher levels of HBV DNA
- Risk for HCC exists irrespective of cirrhosis
- Guidelines are age based for those from areas of endemicity

Treatment of HBV

- Immunization
  - Series: birth, 2, 6 mos
  - If mother infected: HBIG at birth/immunizations

- Treatment
  - Nucleos(t)ide analogs
    - Tenofovir (Viread) (Vemlidy)
    - Entecavir (Barraclude)