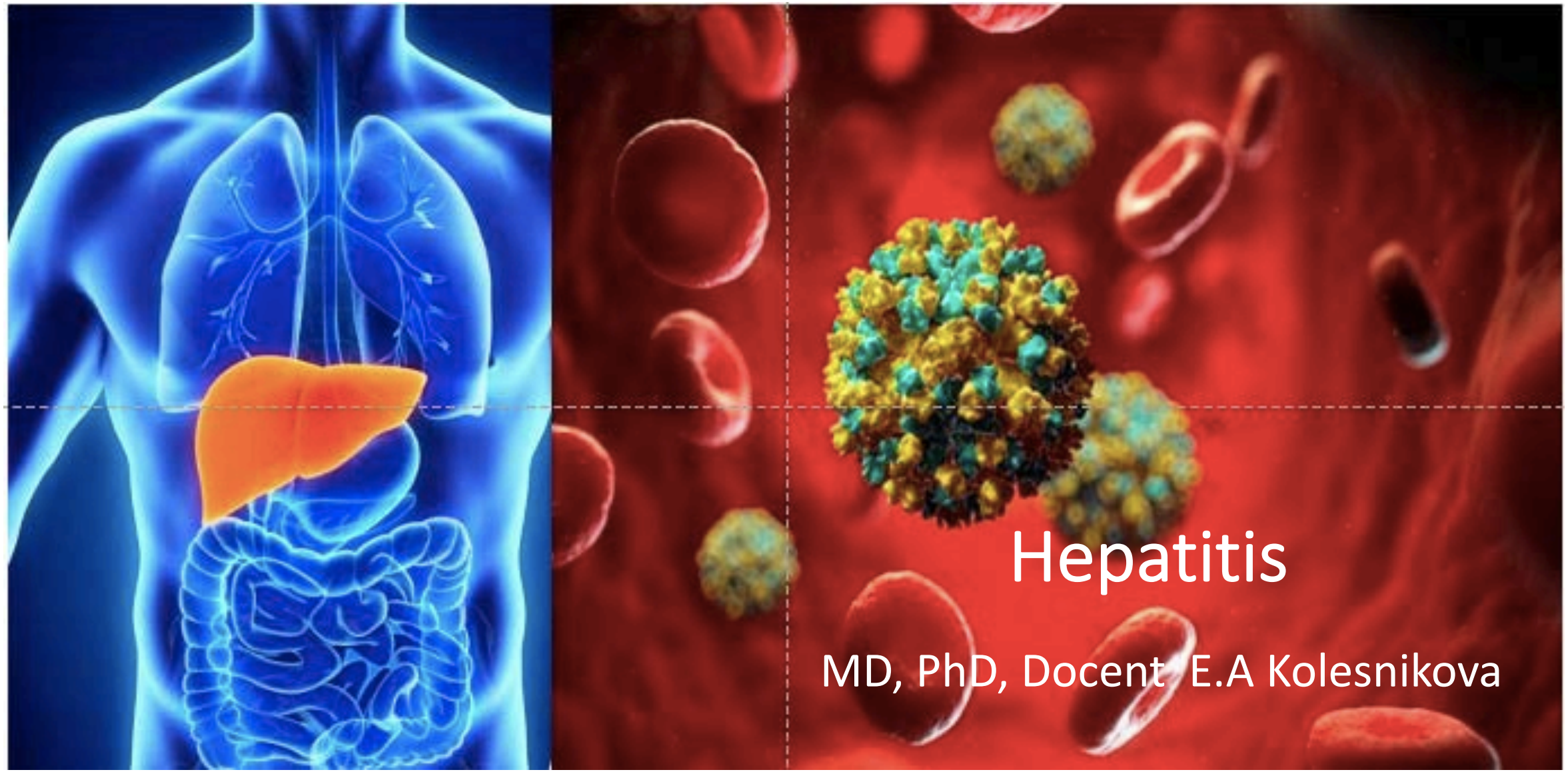


Hepatitis

MD, PhD, Docent E.A Kolesnikova

Classification

Etiology

- Infectious
  - Viral
  - Bacterial (leptospirosis)
  - Parasitic (toxoplasmosis, amebiasis)
- Toxic
  - Alcoholic
  - Drugs induced
  - Chemical

Duration

- Acute
- Chronic
  - more 6 months

Viruses affecting the liver

Major hepatotropic viruses	A, B, C, D, E
Minor hepatotropic viruses	G, transfusion-transmitted virus (TTV)
Systemic viruses capable of causing hepatitis	Herpesviruses (HSV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), varicella virus, adenovirus
Tropical viruses	Yellow fever, dengue, haemorrhagic viruses

Transmission routs

❖ Faeco - Oral

Infected person

Infects food or water

New infected person

❖Parenteral

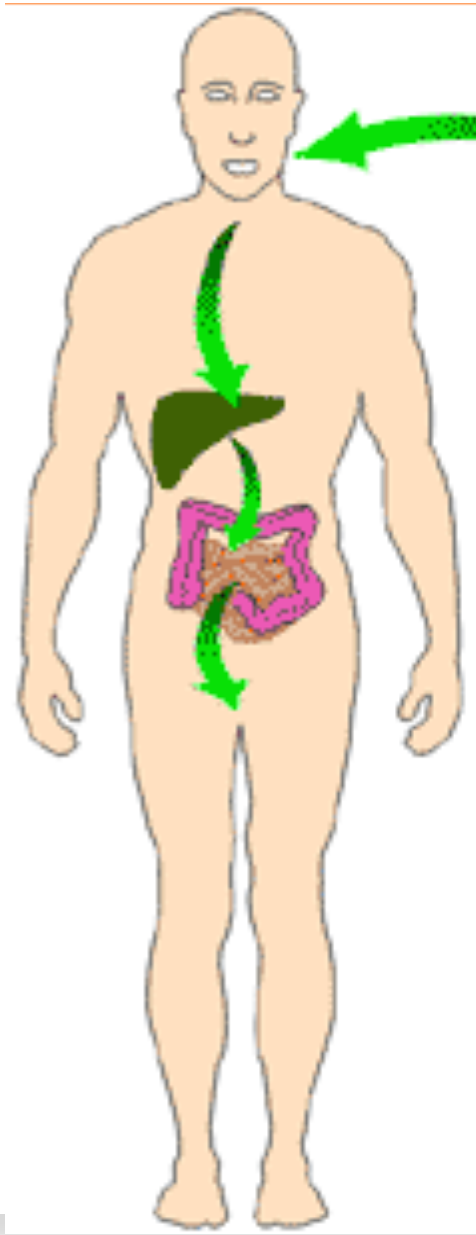
- Blood
  - Sub-cutaneous
  - Intravenous
  - Intramuscular
- Perinatal
- Sexual intercourse

Typical signs

	HAV	HBV	HCV	HDV	HEV
Type	RNA	DNA (p. double strand)	RNA	RNA	RNA
Incubation period	30ds	90 ds	40 ds	Needs HBV	50 ds
Rout	F-O	Parenteral	Parenteral	Parental	F-O
Type of infection	Acute	Acute Chronic	Acute Chronic	Chronic	Acute

Resistance of HBV

- The virus is extremely resistant to various physical and chemical factors: low and high temperatures (including boiling), repeated freezing and thawing, and prolonged exposure to acidic environments.
- In the external environment at room temperature :
  - in blood spots, on a razor blade, or at the end of a needle - **up to several weeks**
- In blood serum:
  - at a temperature of +30°C - **for 6 months,**
  - at a temperature of -20°C for about **15 years**;
  - in dry plasma - **25 years**.
- Inactivated by autoclaving for 30 minutes, dry heat sterilization at 160°C for 60 minutes, warming up at 60°C for 10 hours.



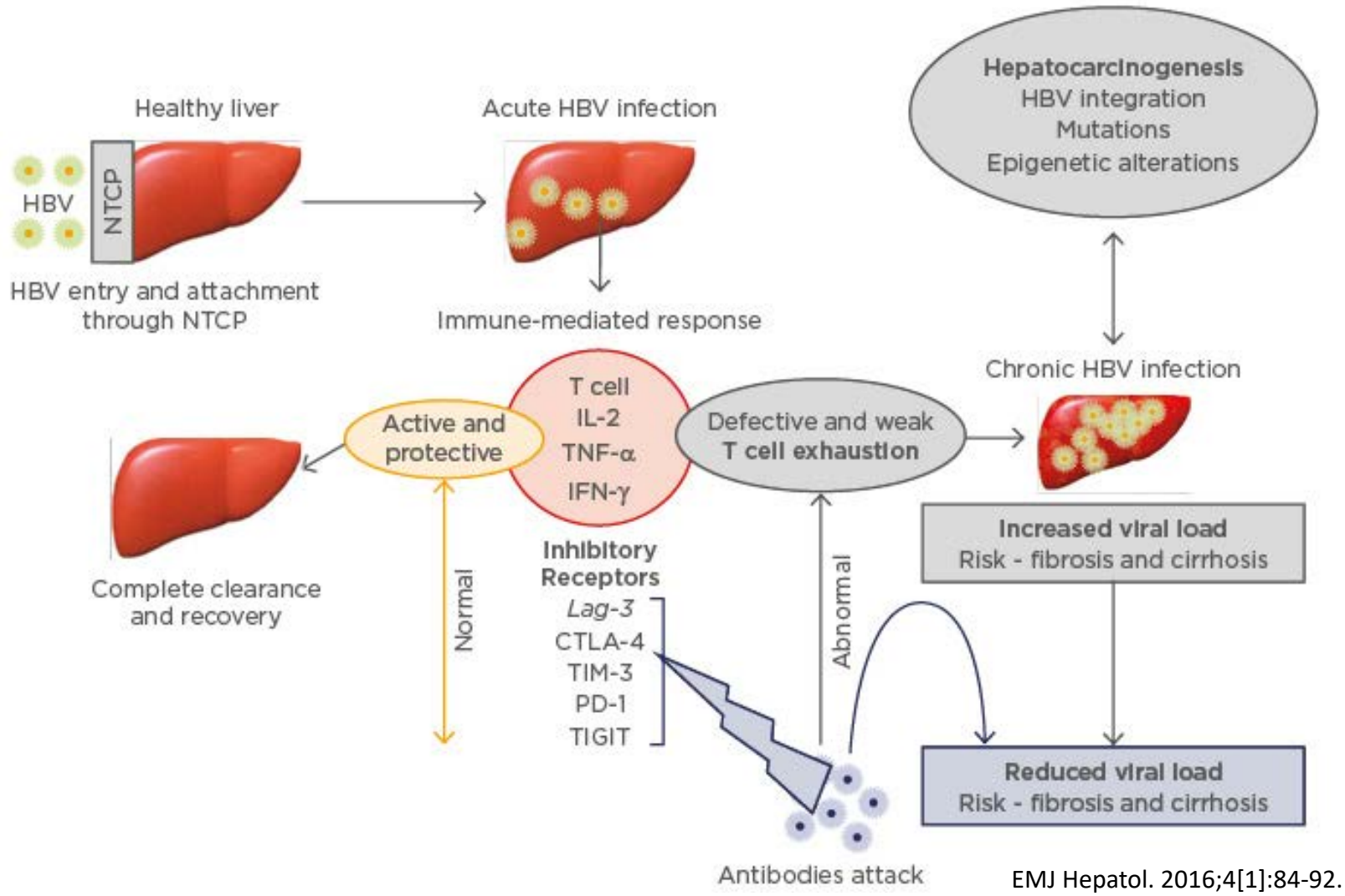
Hepatitis A Pathogenesis

- Ingestion
- Replication in oropharynx/GI tract
- Transported to liver - major site of replication
- Shed in bile, transported to intestines
- Shed in feces
- Brief viremia
- Cellular immune response: clinical disease and control

Incubation Period (15-50 days)

Pathogenesis
HAV/ HEV

Pathogenesis HBV

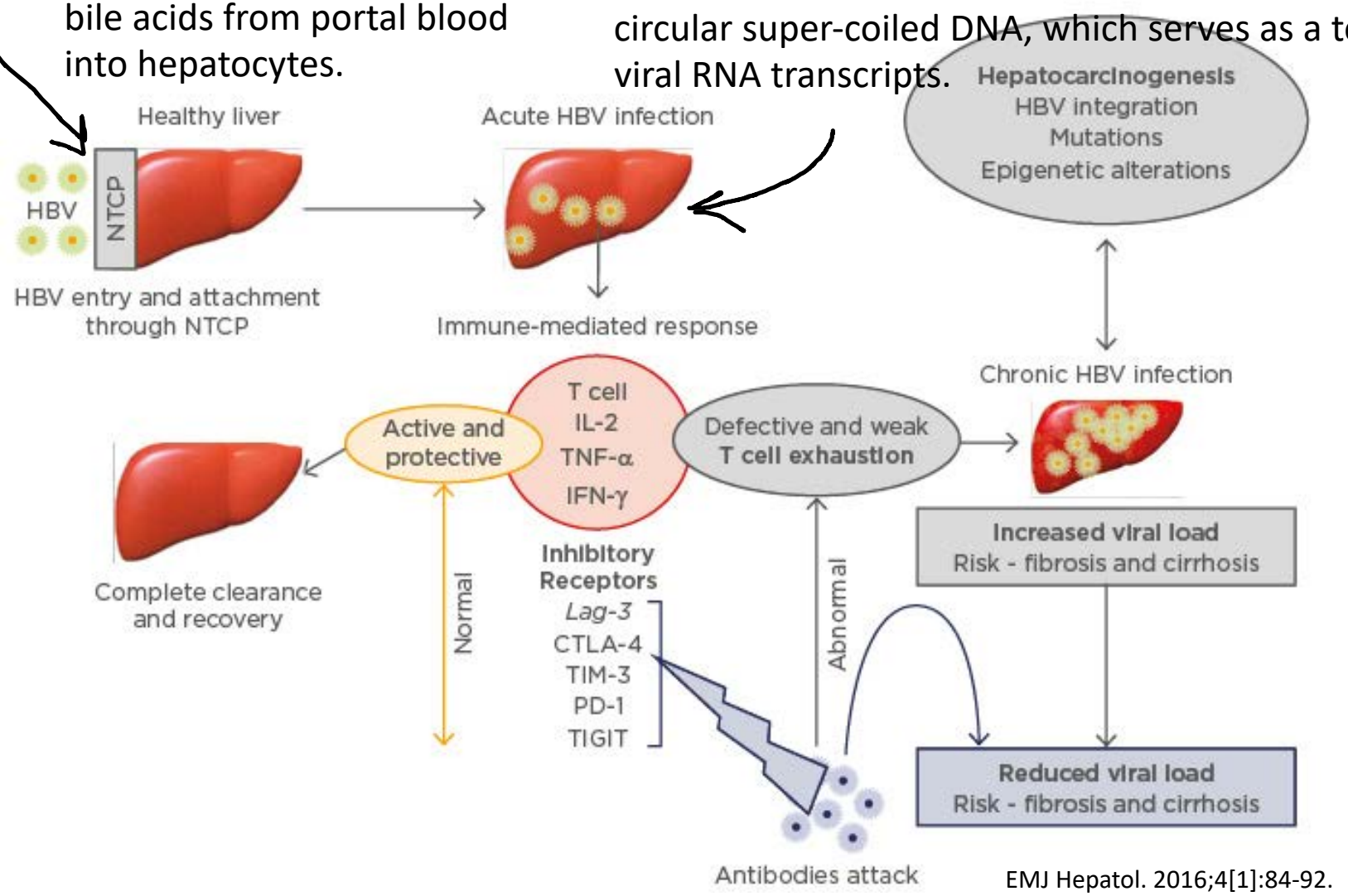


EMJ Hepatol. 2016;4[1]:84-92.

Pathogenesis HBV

NTCP is abundantly expressed in the liver. It is involved in the transportation and clearance of bile acids from portal blood into hepatocytes.

Following entry into the hepatocytes, a HBV nucleocapsid is released into the cytoplasm and transported into the host cell's nucleus to deliver relaxed circular (rc)DNA. In the nucleus, the rcDNA is repaired and converted to covalently closed circular super-coiled DNA, which serves as a template for the transcription of four viral RNA transcripts.



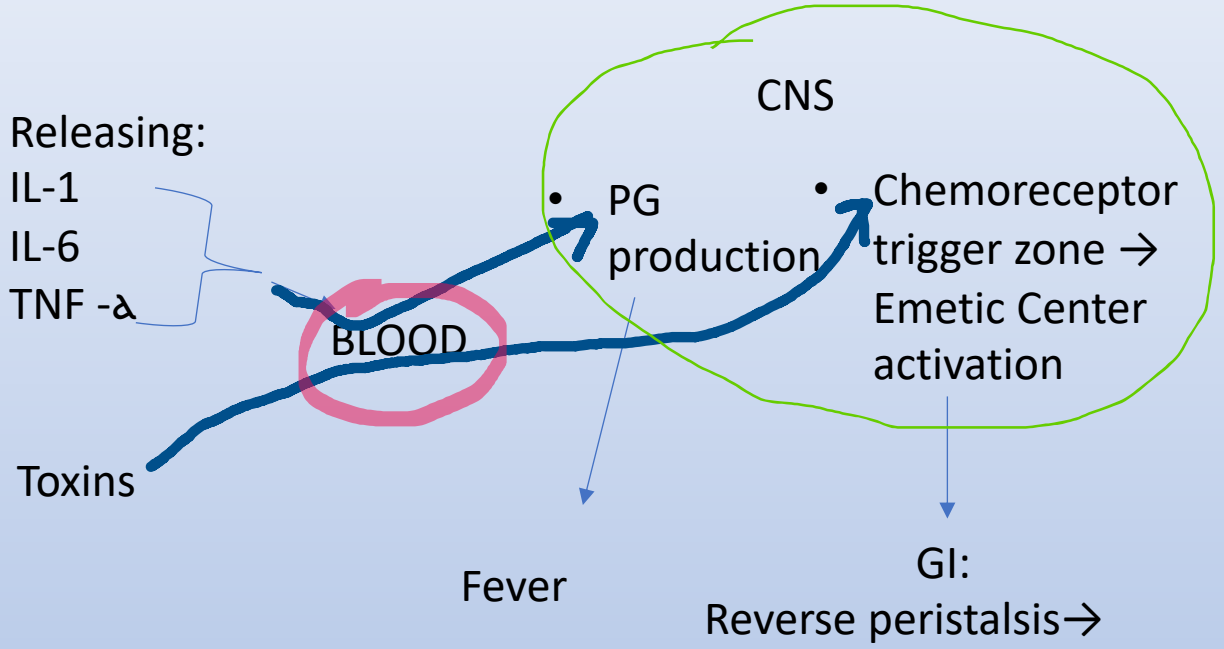
EMJ Hepatol. 2016;4[1]:84-92.

Risk Factors

- Working in the healthcare
- Blood transfusions
- Dialysis
- Living with an infected person
- Travel to countries where infection rate is high
- Tattoo
- Acupuncture
- Manicure
- Dental cure and prosthetic dentistry

Pathogenesis. Clinical signs

- Virus
- Cell
  - Replication
- Lysis of Hepatocytes
- Apoptosis

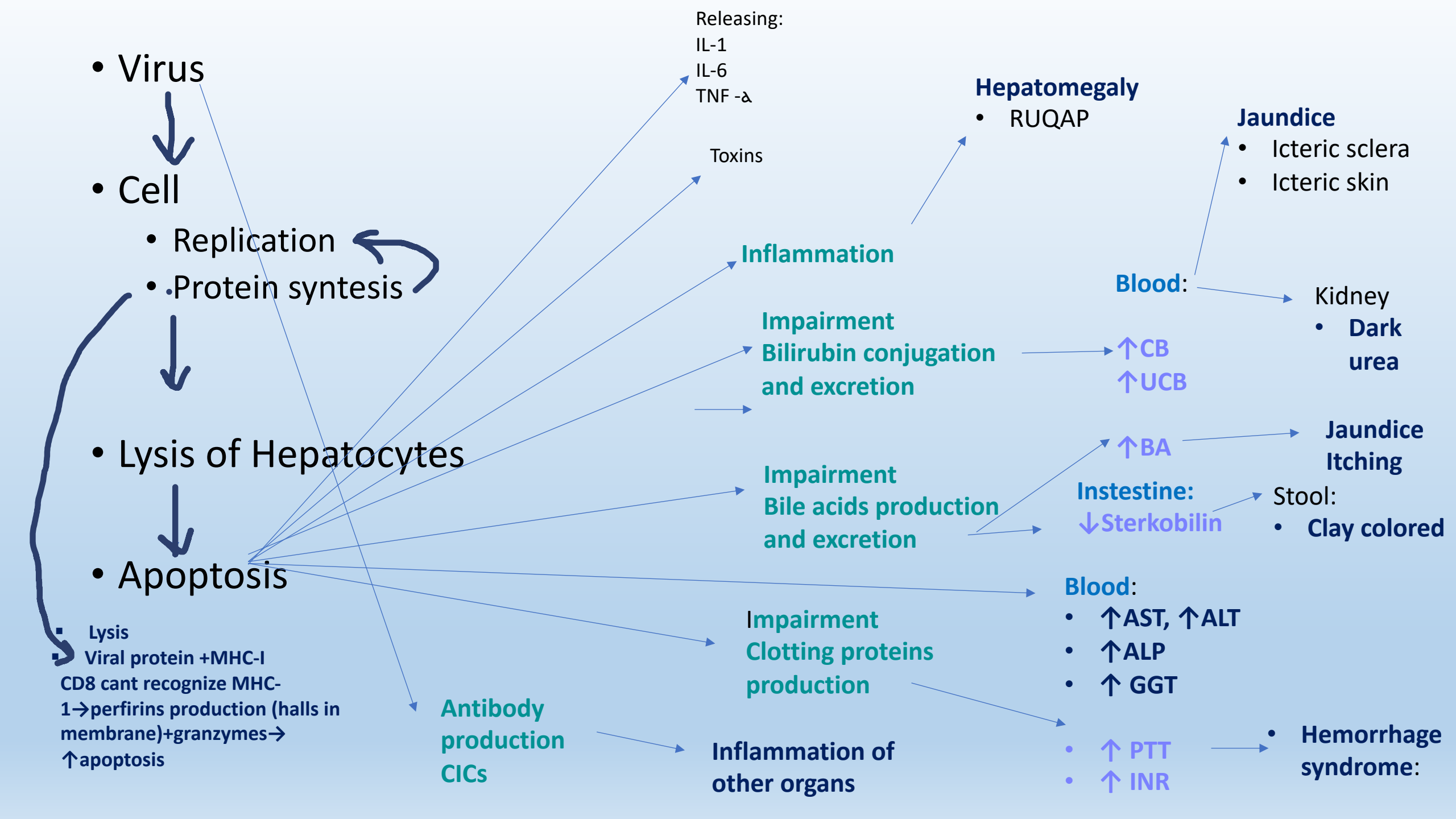


- Nausea, vomiting
- Dehydration
- Diarrhea
- Electrolytes change
- Weight loss

Complains:

➢ Prodromal Phase

- Fever
- Malaise
- Nausea, vomiting
- Dehydration
- Diarrhea
- Electrolytes change
- Weight loss


• Virus
• Cell
• Replication
• Protein syntesis
• Lysis of Hepatocytes
• Apoptosis
Releasing:
IL-1
IL-6
TNF -ə
Toxins
Hepatomegaly
• RUQAP
Jaundice
• Icteric sclera
• Icteric skin
Inflammation
Blood:
Kidney
• Dark urea
Impairment
Bilirubin conjugation and excretion
↑CB
↑UCB
↑BA
Jaundice
Itching
Impairment
Bile acids production and excretion
Instestine:
↓Sterkobilin
Stool:
• Clay colored
Blood:
• ↑AST, ↑ALT
• ↑ALP
• ↑ GGT
Impairment
Clotting proteins production
• ↑ PTT
• ↑ INR
• Hemorrhage syndrome:
Antibody production
CICs
Inflammation of other organs
Lysis
Viral protein +MHC-I
CD8 cant recognize MHC-1→perfirins production (halls in membrane)+granzymes→ ↑apoptosis

Complains:

➢Icteric Phase

- Jaundice
- RUQAP
- Dark urea
- Acholic stool
- Hemorrhage syndrome

Complains. Signs. Diagnostic procedures

➢Icteric Phase

✓Jaundice Syndrome
- Icteric skin and mucosa
- Dark urea
- Acholic stool

✓RUQAP

- Cholestasis syndrome
  - Icteric skin
  - Itching

✓Hemorrhage syndrome

- Inflammation of other organs – Extrahepatic signs
  - Arthritis
  - Vasculitis
  - Myocarditis, pericarditis
  - Glomerulonephritis
  - Hemolytic anemia
  - Neutropenia
  - ↑Lymphocyte
  - Thrombocytopenia

➢Lab Tests

- ↑CB
- ↑ UCB
- ↑ Bile acids
- ↑ ALP
- ↑ GGT
- ↑ ALT
- ↑ AST
- ↑ PTT
- ↑INR
- ↓PLT
- ↓Neut
- ↑Lymph
- ↓RBC

Physical examination. Interview

- Risk factors
- Appetite
- Weight (decrease, increase)
- Urea
- Stool

Physical examination. Observation

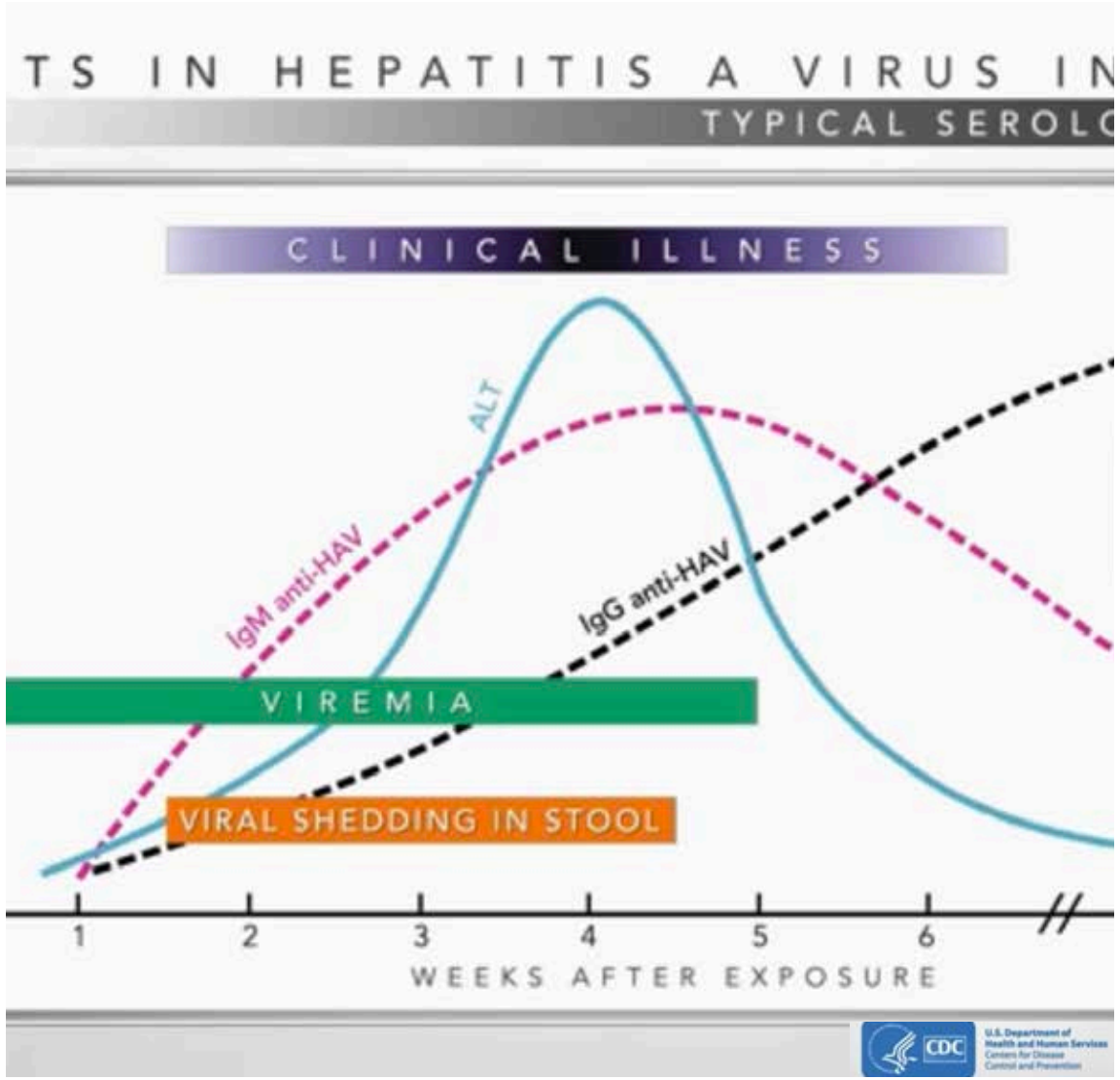
- ✓Mental condition
- ✓Mucosae color, skin color
- ✓Hemorrhage syndrome signs
- ✓Signs of skin scratching
- ✓(Spider navy, palmar erythema, etc)
- ✓(Oedemas)
- ✓(Signs of portal hypertension)

Physical examination. Palpation

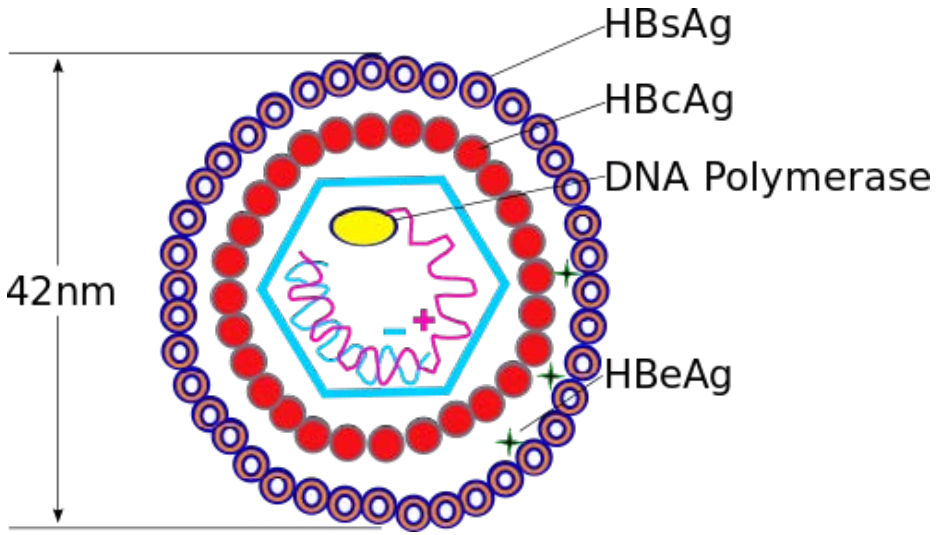
- ✓Tender enlarged liver
- ✓(Oedemas)

HAV

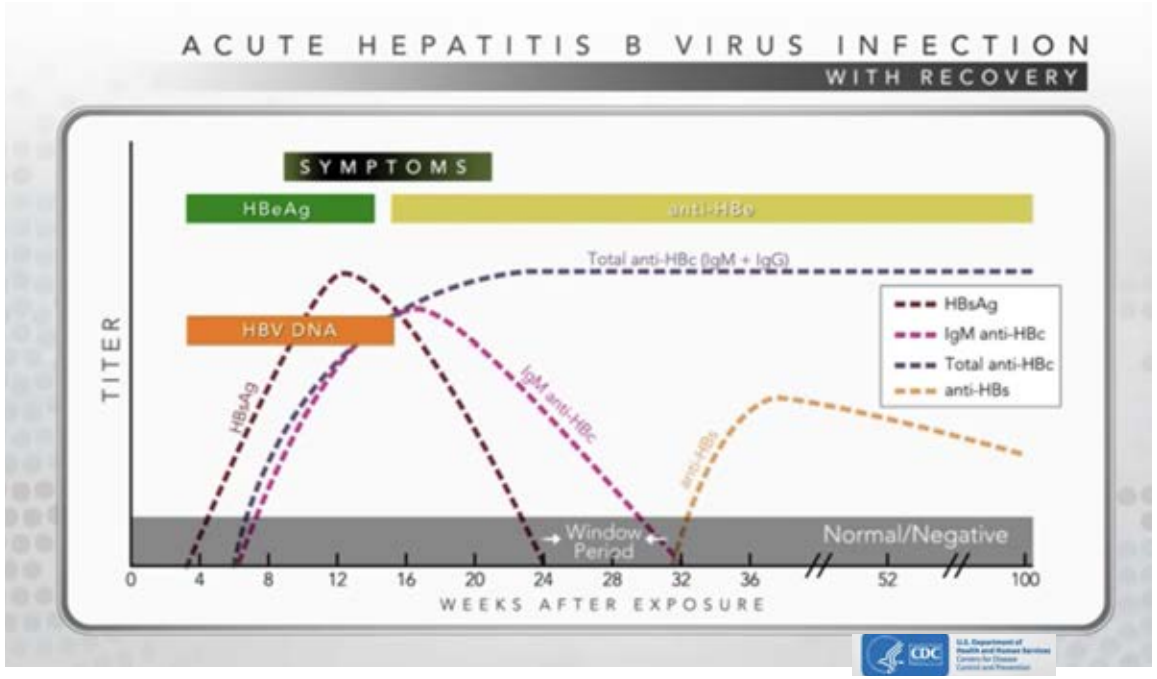
- IgM anti HAV in 1 week after exposure, max in 28 days (4-6 weeks)
- IgG anti HAV in 1 week after exposure
- Virus in stole 1,5- 4, 5 weeks after exposure (jaundice appearance)



HBV

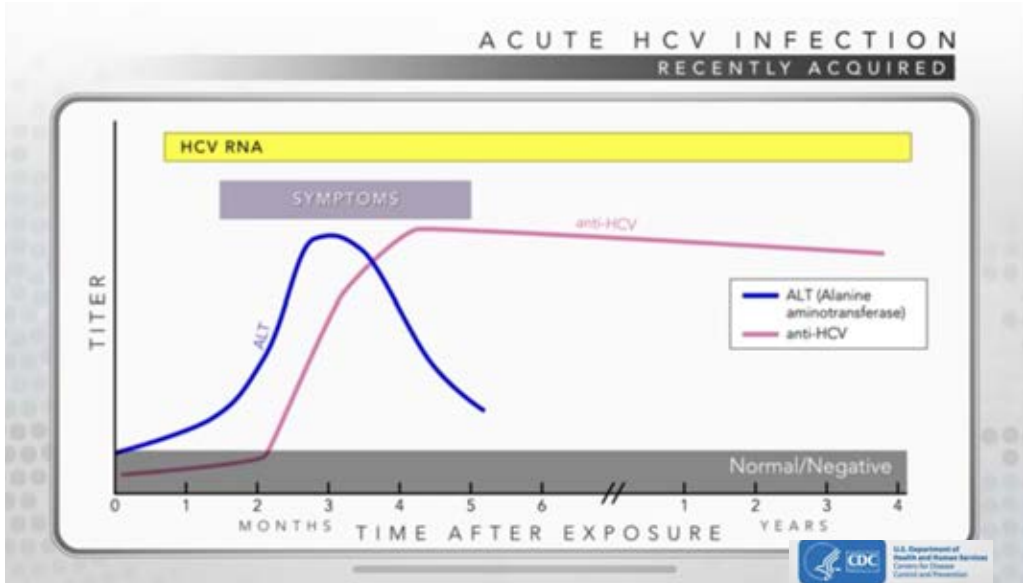


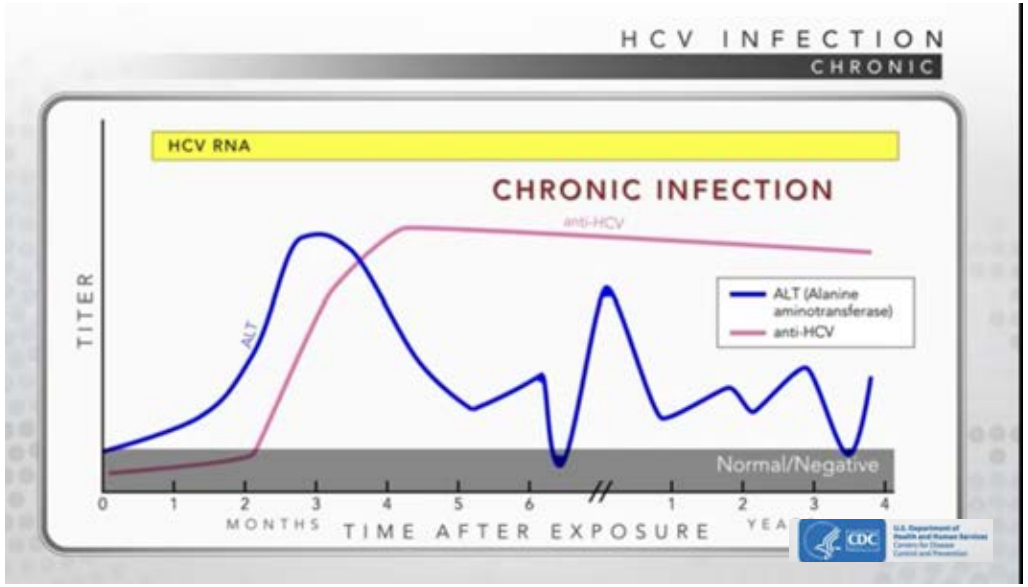
- HBsAG in 2 weeks after exposure
- HBV DNA
- HBeAg – high infectivity
- IgM anti HBc – 6-32 weeks
- Anti- HBs after 32 week or vaccination



HCV

- Anti – HCV in 10-11 weeks after expoluser (80 % increase in 15 weeks)
- HCV RNA (marker of viremia) – startig in 1-2 weeks after exposure
- ALT





Variations on the clinical course of acute hepatitis

- ✓ In anicteric hepatitis jaundice does not occur, and the episode is asymptomatic or dismissed as 'flu-like'. This may in fact be a more frequent pattern than a clinically recognized episode, as evidenced by serological surveys for immunity to hepatitis viruses in populations.
- ✓ In cholestatic hepatitis, jaundice with pruritus, pale stools, and dark urine persists for up to 2 or 3 months before recovery.
- ✓ In relapsing hepatitis there is a transient worsening of jaundice after an initial improvement before recovery eventually occurs.
- ✓ Acute hepatitis is only rarely fatal. If it is, patients usually rapidly develop hepatic encephalopathy, and the timing of onset of this has been used to define subtypes of acute severe hepatitis.
- ✓ In 'fulminant hepatitis' encephalopathy develops within 2 weeks of jaundice.
- ✓ In 'subfulminant hepatitis' encephalopathy develops later.

Hepatitis A virus (HAV)

- faecal-oral transmission; incubation 2-6 weeks; acute self-limited hepatitis; no specific treatment.
- Transmission generally follows the ingestion of food or water contaminated with faeces from an HAV-infected individual.
- Viral shedding in the faeces ceases at approximately the onset of clinical symptoms
- Clinically the disease is often anicteric or mild, particularly in young children.
- About 10% of patients have a relapse before recovery. The mortality rate is low, about 0.3%.
- Deaths occur predominantly in older people, among whom mortality rates may exceed 2%, and pre-existing chronic viral hepatitis B or C may predispose to a fatal outcome.

Hepatitis B virus (HBV)

- parenteral transmission

Horizontal transmission routes include blood transfusion and blood products, the use of contaminated needles medically or by drug addicts, exposure in dialysis units, tattooing, and sexual contact

- incubation 4-24 weeks;
- may present with acute hepatitis,
- with prodrome sometimes including prominent arthritis, fever, and urticarial rash,
- anicteric attacks are common;
- most (>90%) patients clear HBV after acute infection,
- but failure to clear HBsAg (hepatitis B surface antigen) within 6 months defines 'chronic carriage', which is associated with a spectrum of histological damage and clinical manifestations ranging from being clinically silent to producing cirrhosis and hepatocellular cancer.

Hepatitis C virus (HCV)

- parenteral transmission; I
- ncubation 2 to 26 weeks;
- acute episode most often subclinical;
- 70% of patients fail to clear the virus and become chronic carriers,
- often leads to cirrhosis after 15 to 25 years and then predisposes to hepatocellular cancer;

Hepatitis D virus (HDV)

- an RNA virus 'parasitic' on HBV,
- dual infection produces more severe liver disease;
- treatment is as for hepatitis B.

Hepatitis E virus (HEV)—

- faecal-oral transmission;
- incubation about 6 weeks;
- high risk of fulminant hepatitis if acquired during mid-trimester pregnancy;
- no specific treatment.