

Paediatric hepatitis

Vibeke Brix Christensen

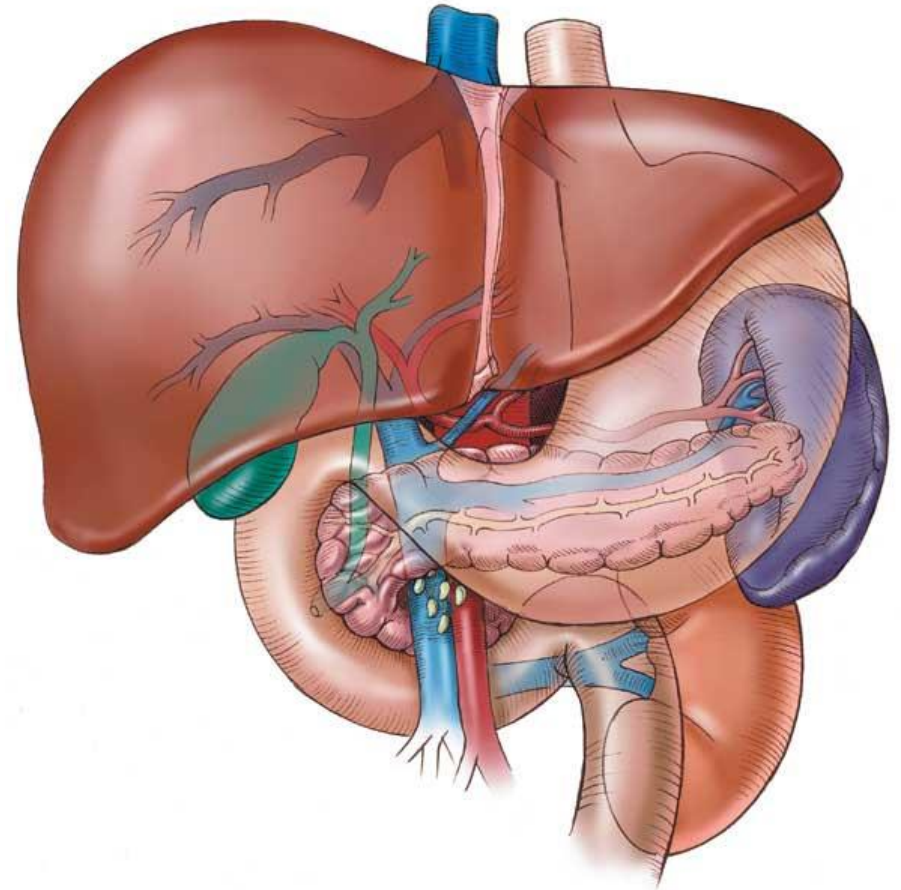
MD, PhD, DMSc

Paediatric hepatologist

Rigshospitalet,

Denmark

vibeke.brix.christensen@regionh.dk



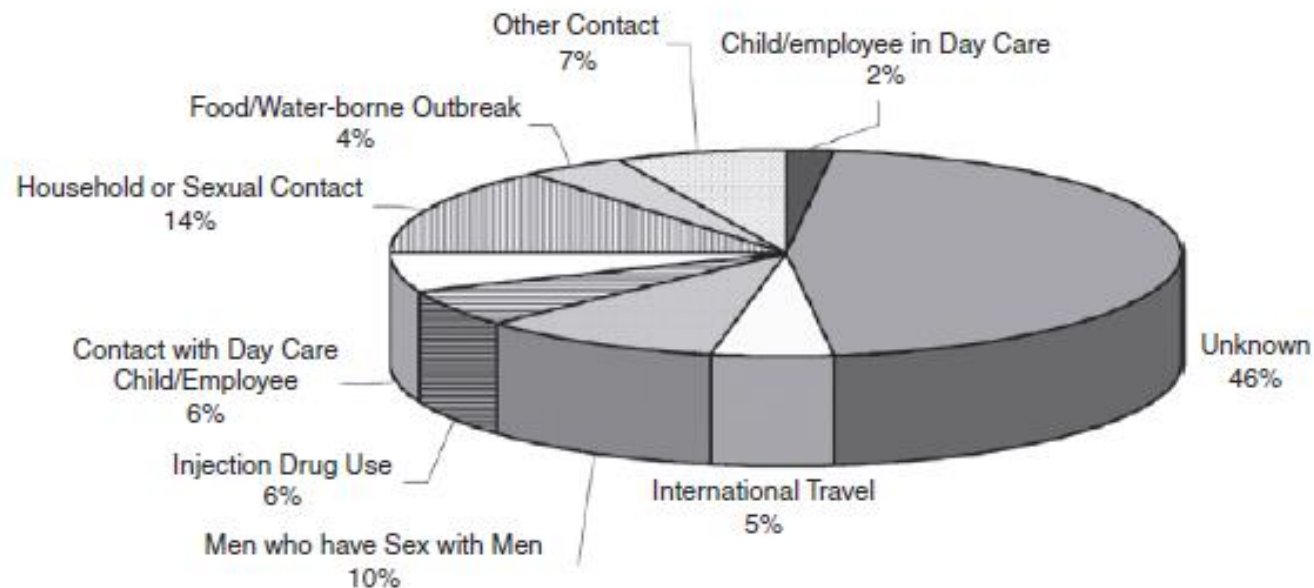
What is Hepatitis ?

- Hepatitis is a viral infection that causes inflammation of the liver
- 5 main types of viral hepatitis: A, B, C, D, E
 - Hepatitis A and E are typically caused by ingestion of contaminated food or water
 - Hepatitis B, C and D are typically caused by contact with contaminated blood or body fluids
- Type B and C lead to chronic disease in hundreds of millions of people and, together, are the most common cause of liver cirrhosis and cancer
- About 1 million people die each year from causes related to viral hepatitis

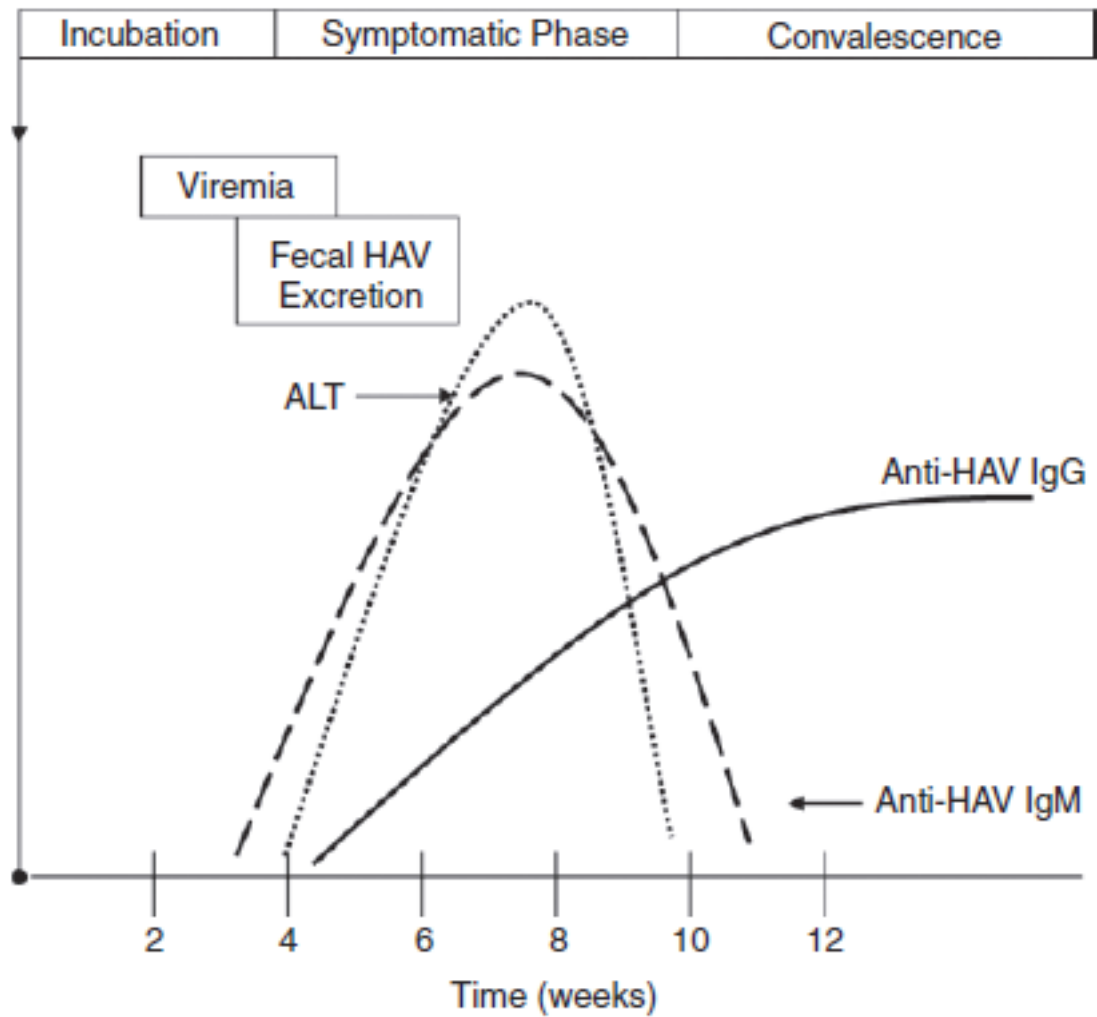
Source: www.who.org

Hepatitis A

- Mild, self-limiting disease
- > 5 Y: fever, nausea, icterus, abdominal pain, diarrhea, dark urine



Hep A



Prevention

Vaccinate!

Viral hepatitis

- HBV epidemiology

- 400 million people infected worldwide
- Most prevalent
 - Asia
 - Africa
 - Southern Europe
 - Latin America



HBsAg rate 2-20%

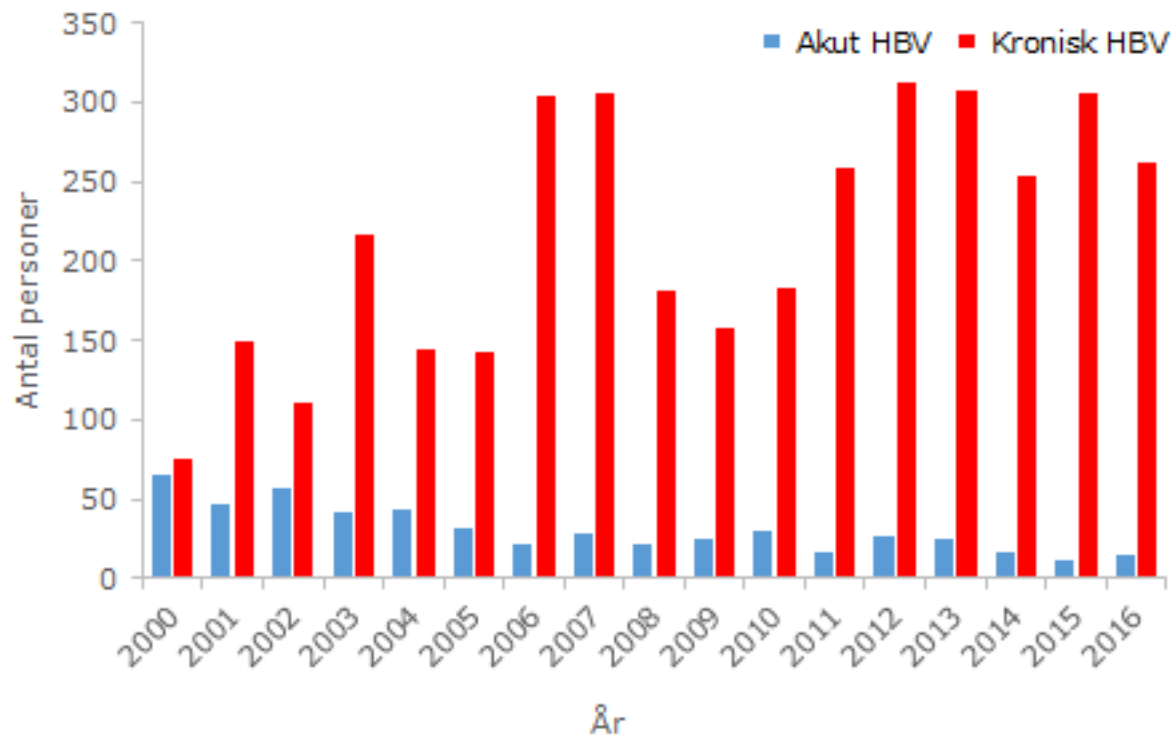
Hep B

- Asymptomatic acute HBV infection
- In the prodromal phase: nausea, vomit, anorexia og subfebrilia
- Incubation period of 1-6 month. Then icterus and ALAT increase
- Symptoms like hep A, but worse. Skin and joint manifestations
- Acute liver failure at 0,1 til 0,5 % of patients.
- Mortality less than 0,5 %.

- 8 genotypes (A- H)

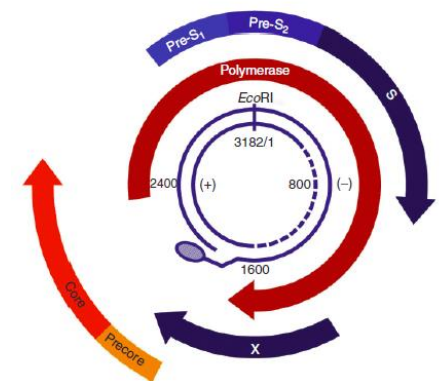
Hep B in Denmark

Figur 2. Antal anmeldte tilfælde af akut og kronisk hepatitis B, 2000-2016

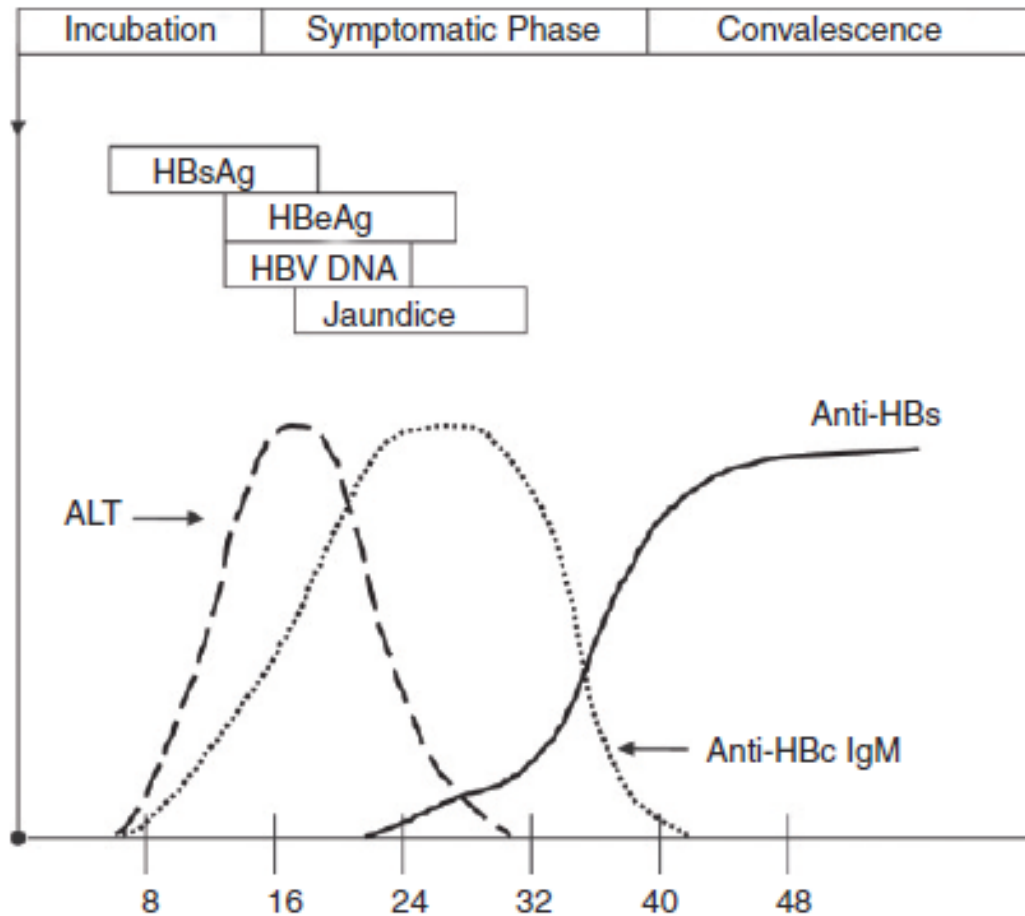


Monitoring HBV

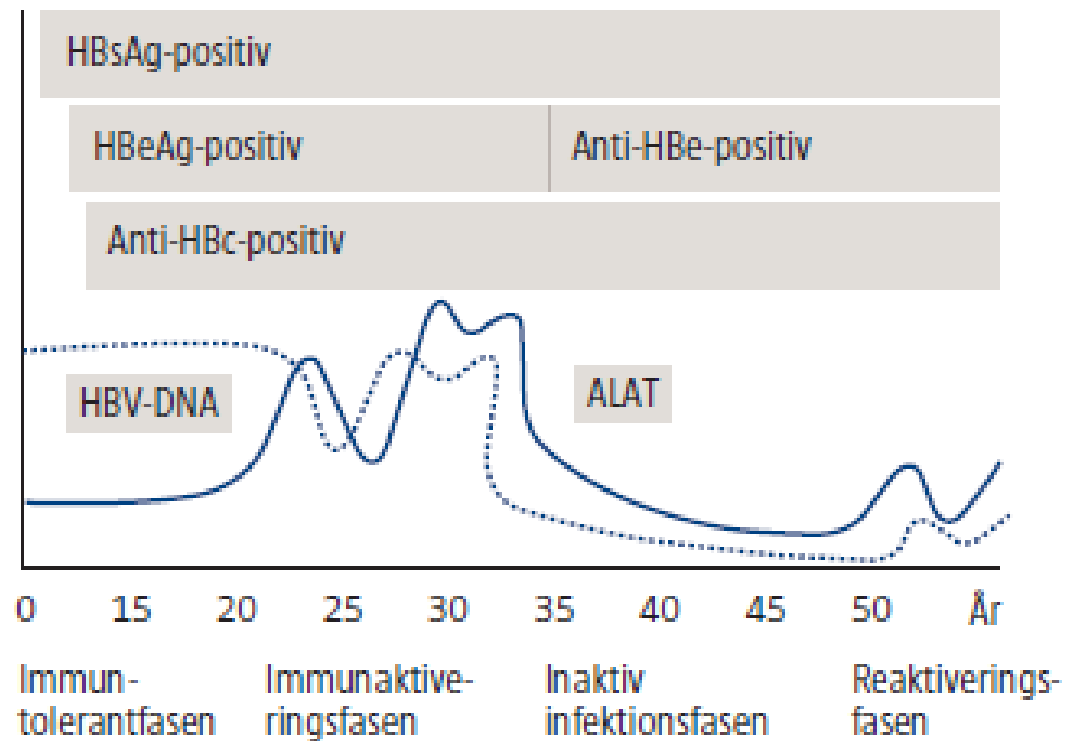
- **HBV DNA:** copies of viral genome (copies vs units)
- **HBsAg:** surface Ag (presence of virus)
- **HBeAg:** actively replicating virus
- **Anti-HBe Ab:**
 - ->first step in controlling viral replication
- **Anti HBs Ab:** immunity
- **Anti HBc Ab IgM:** recent HBV infection
- **Anti HBc Ab IgG:** old HBV infection



Acute HBV infection



Chronic HBV infection



Hep B

Natural history and assessment of patients with chronic HBV infection

HBV markers

HBsAg
HBeAg/anti-HBe
HBV DNA

Liver disease

Biochemical parameters: ALT
Fibrosis markers: non-invasive markers of fibrosis (elastography or biomarkers) or liver biopsy in selected cases

Chronic Hep B.

New categories

	HBeAg positive		HBeAg negative	
	Chronic infection	Chronic hepatitis	Chronic infection	Chronic hepatitis
HBsAg	High	High/intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10 ⁷ IU/ml	10 ⁴ -10 ⁷ IU/ml	<2,000 IU/ml**	>2,000 IU/ml
ALT	Normal	Elevated	Normal	Elevated*
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis

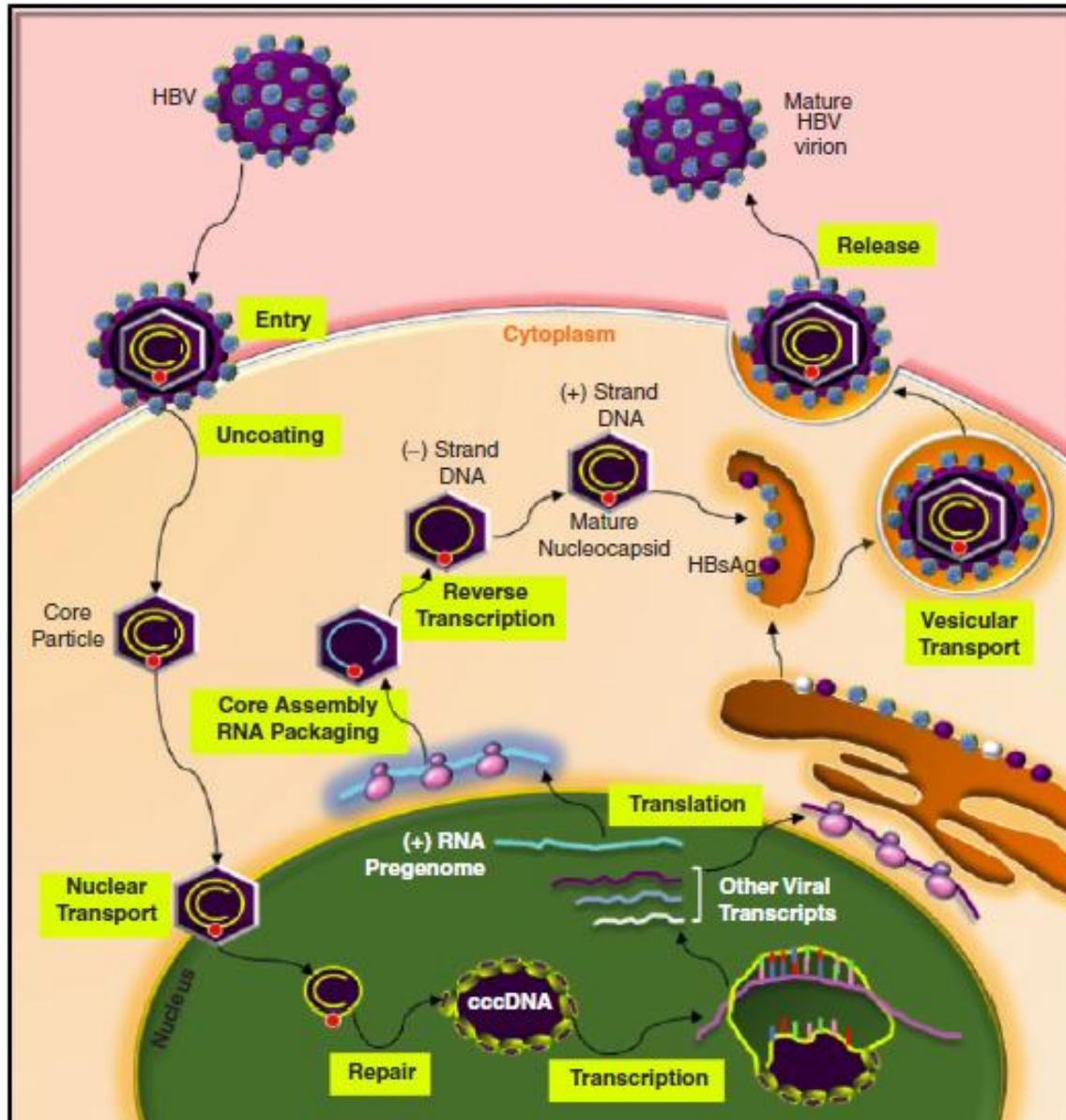
Fig. 1. Natural history and assessment of patients with chronic HBV infection based upon HBV and liver disease markers. *Persistently or intermittently. **HBV DNA levels can be between 2,000 and 20,000 IU/ml in some patients without signs of chronic hepatitis.



A



B



Concentration of Hep B virus

High

Moderate

Low

blood

vaginal secretion

urine

wound secretion

semen

feces

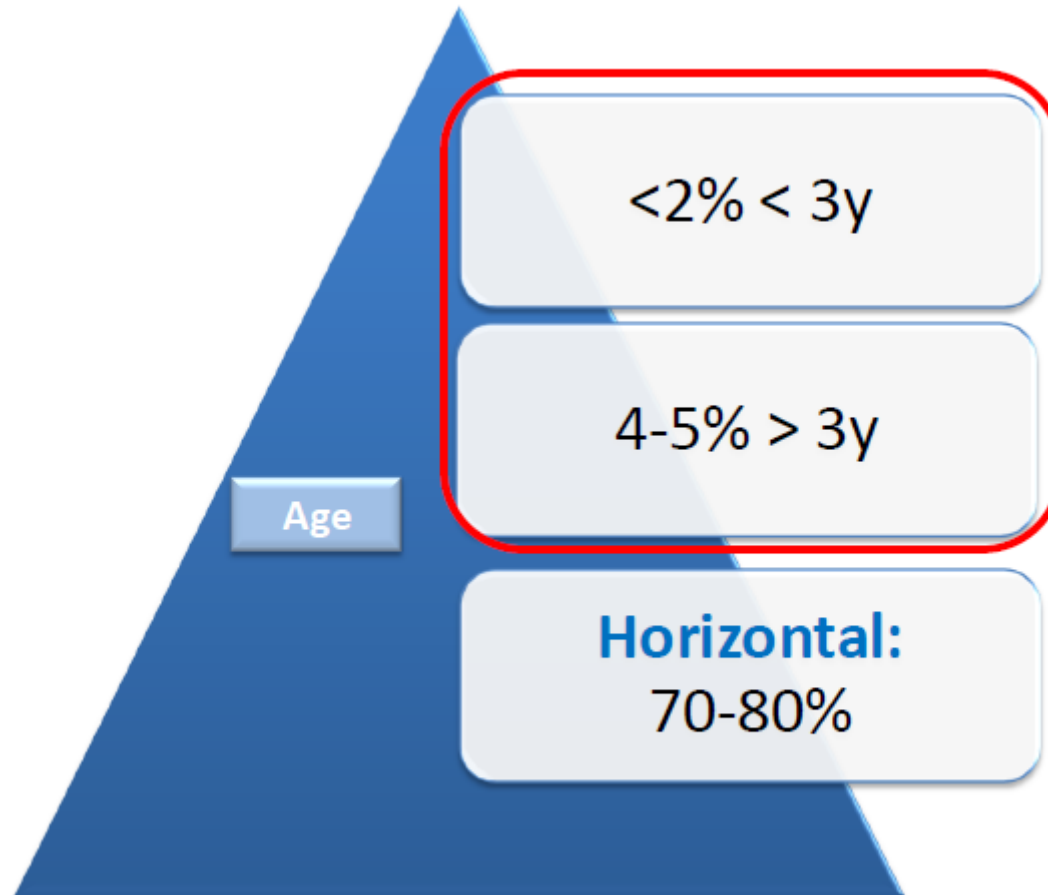
saliva

sweat

tears

breast milk

Spontaneous seroconversion



Treat who?

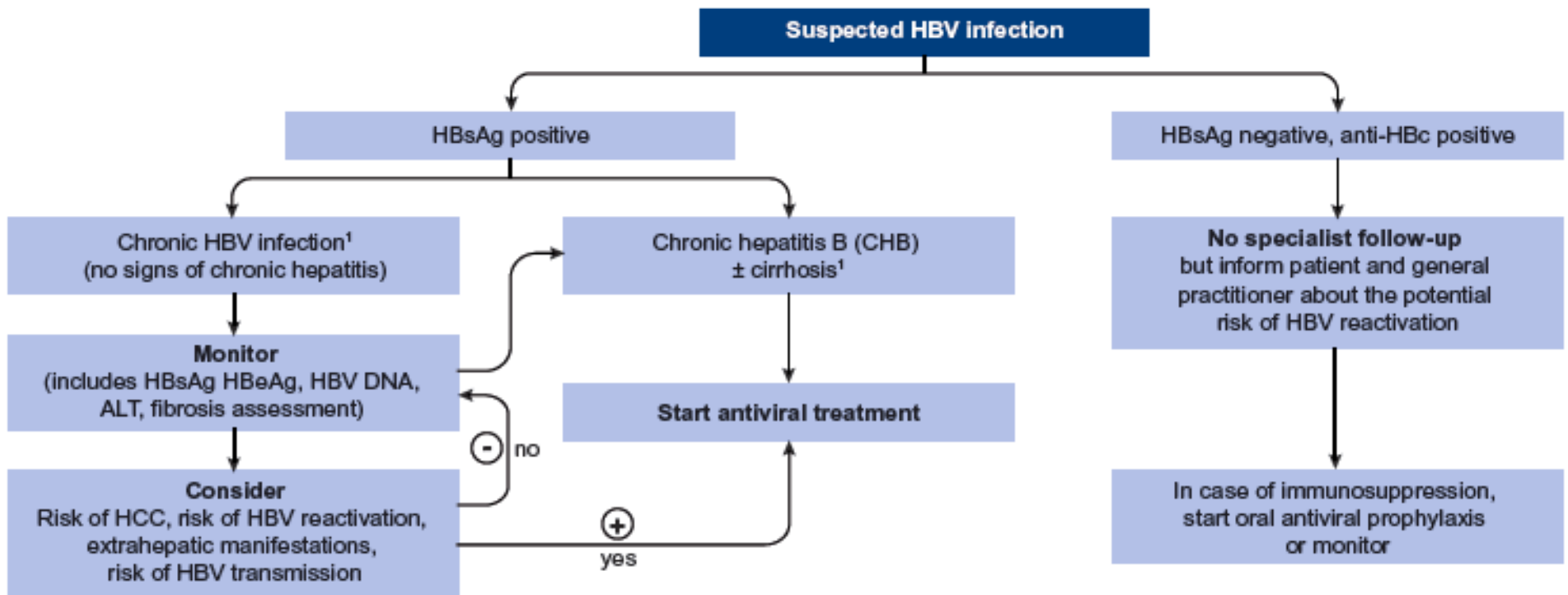
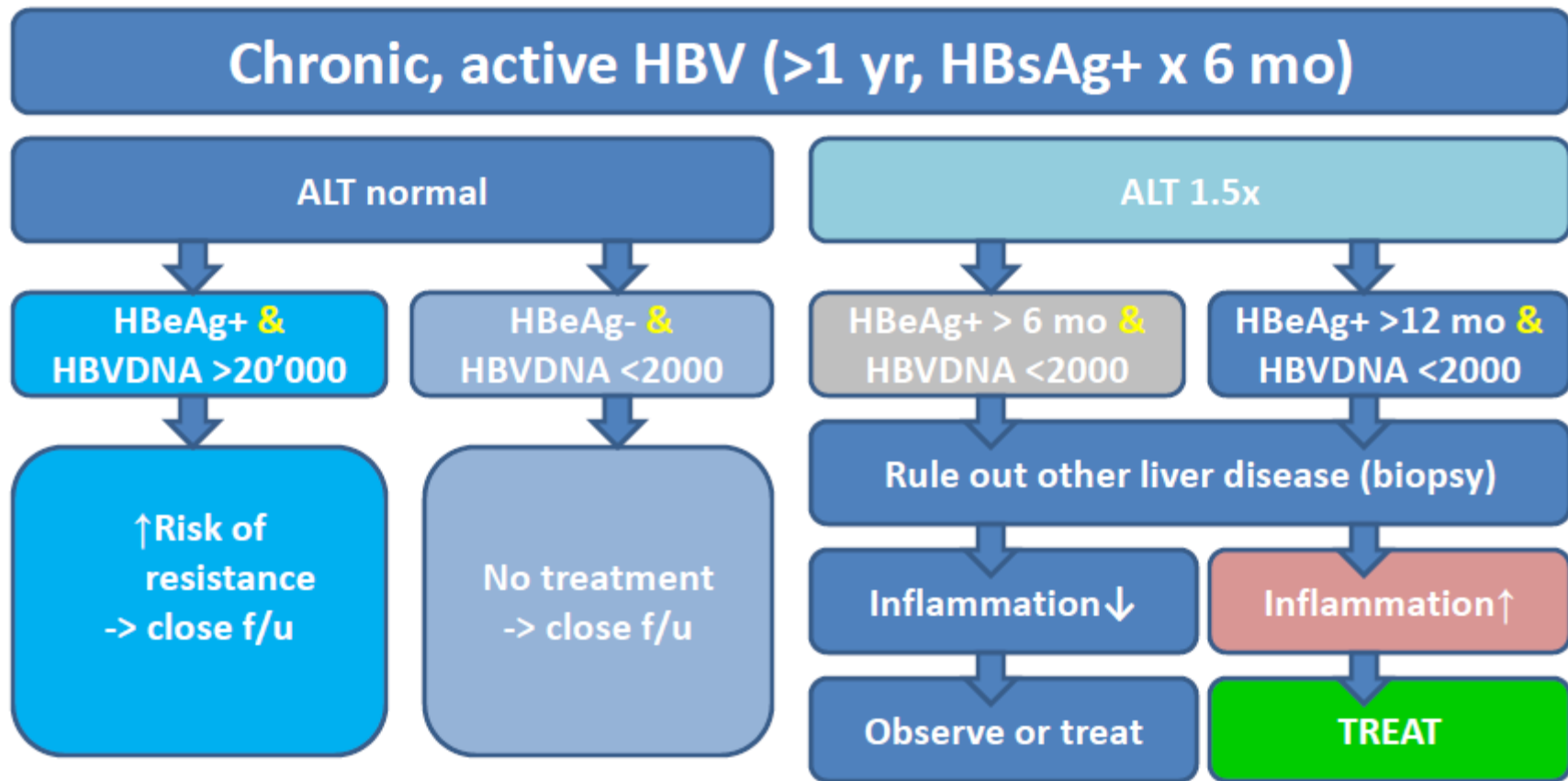
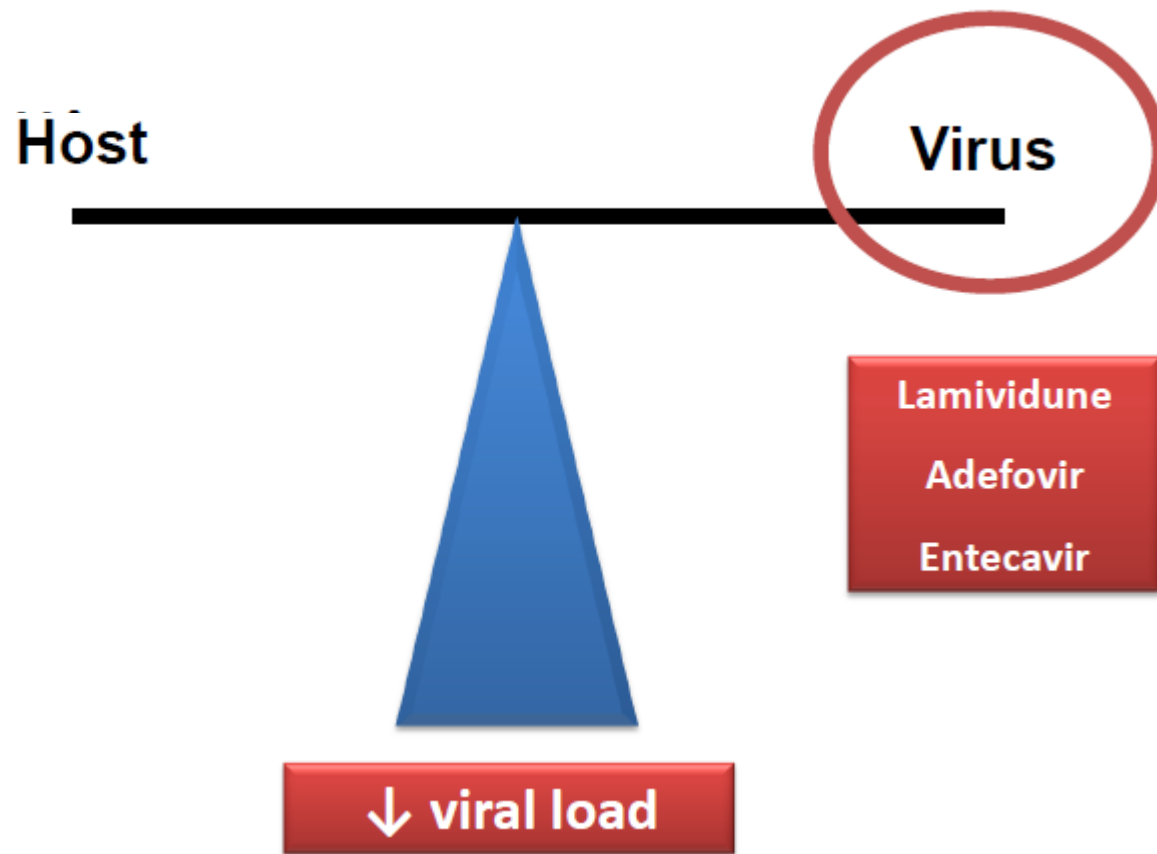


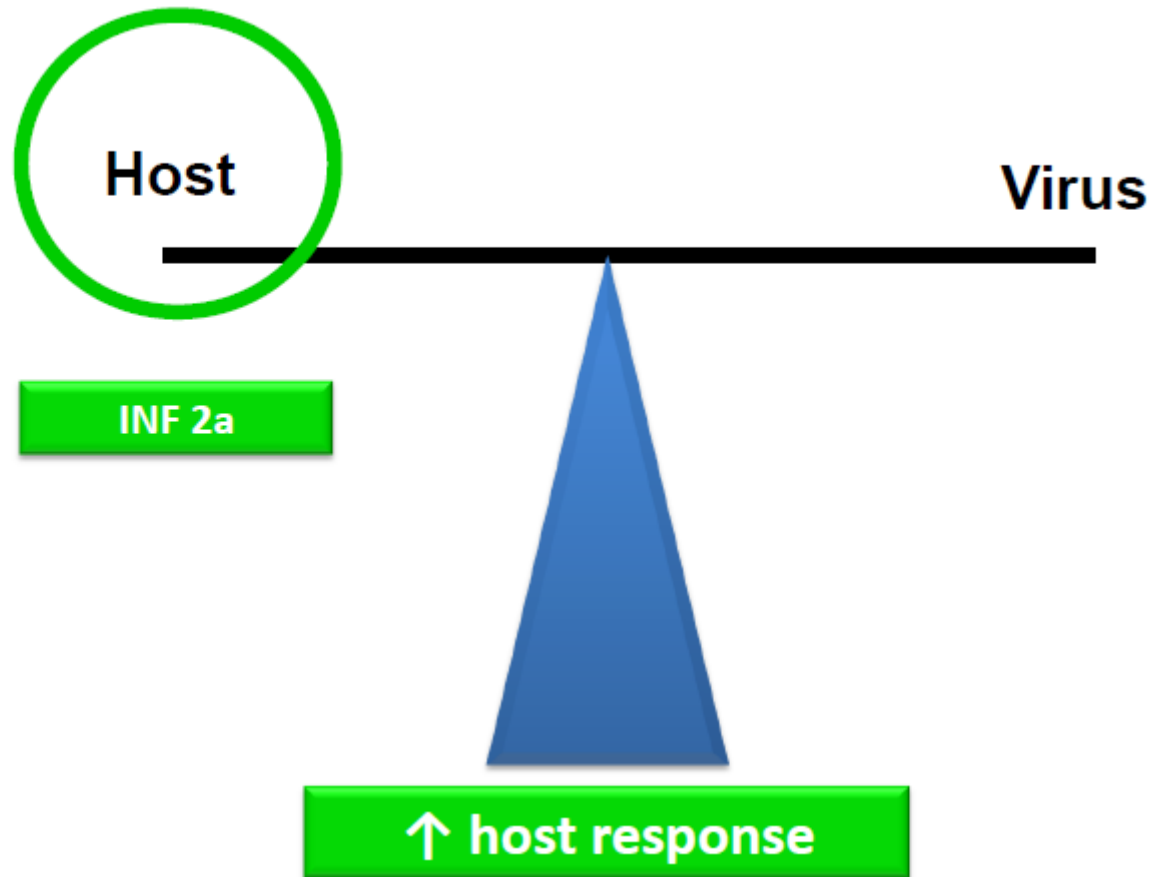
Fig. 2. Algorithm for the management of HBV infection. ¹see definitions in text and Fig. 1.



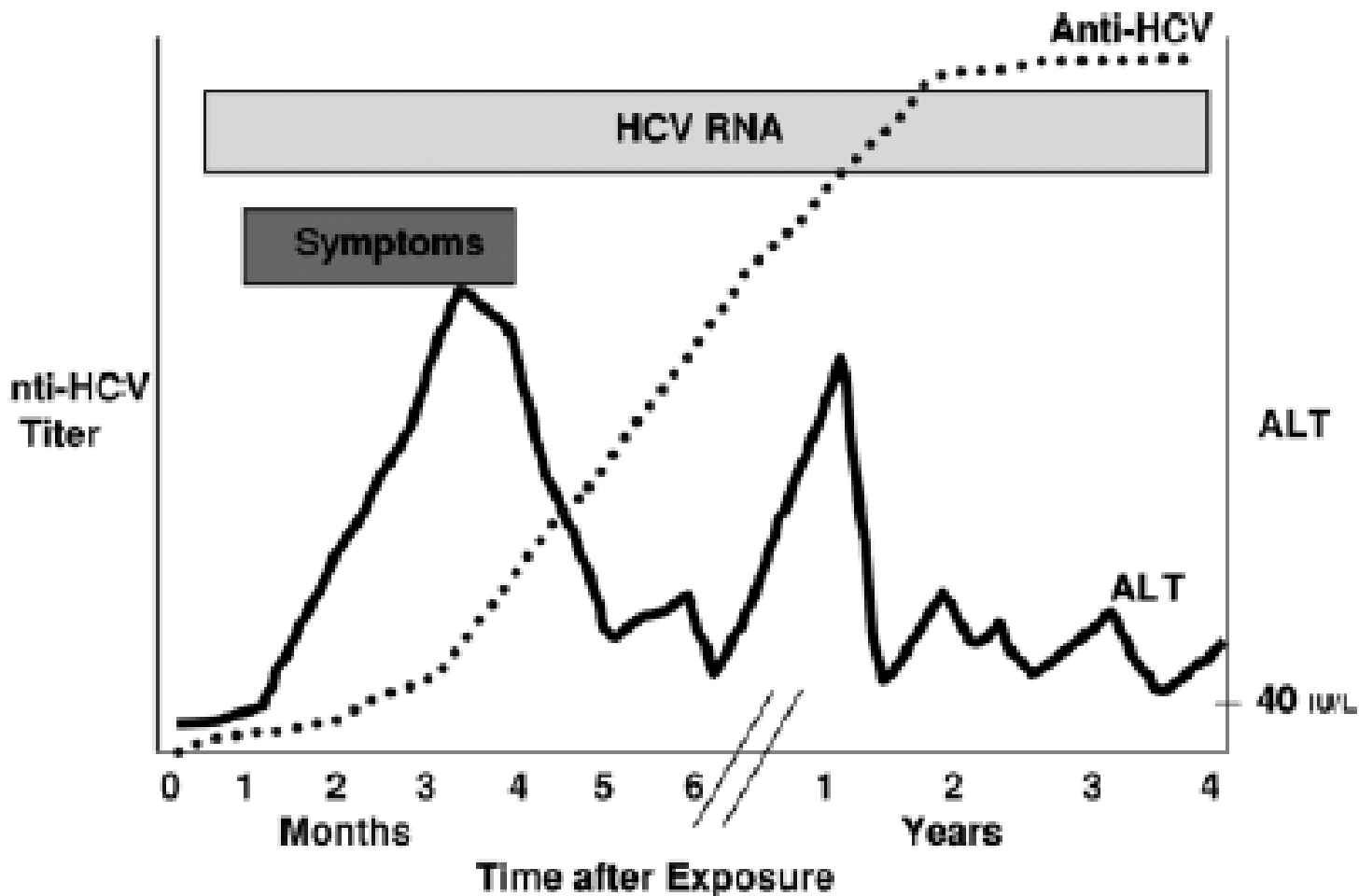
Which treatment?



Which treatment?



HCV infection



HCV infection

- Anti HCV does not discriminate between acute, chronic or post-infection
- Progressive development with cirrhosis and liverfailure over 20 to 40 years
- Exstrahepatic manifestations is seen
- Nye effektive behandlinger eradikerer virus hos 90 %

The new treatment ?

- Direct Acting Agents (DAA)
- Phase 2, multicenter, open-label study of 100 patients 12-17 Y with Ledipasvir + sofosbuvir daily for 12 W

» Balistreri et al. Hepatology. Dec 2016

Global burden hep B and hep C

- The global burden of disease due to acute hepatitis B and C, and cancer and cirrhosis of the liver, accounts for about 2.7% of all deaths.
- An estimated 57% of liver cirrhosis and 78% of primary liver cancer are due to HBV or HCV infection
- In total, about 2 billion people have been infected with HBV; about 600 000 people die each year due to the consequences of hepatitis B
- About 150 million people are chronically infected with HCV (about 10 times higher than HIV estimates); >350 000 people die each year from hepatitis C-related liver diseases

Transmission mode hep B and hep C

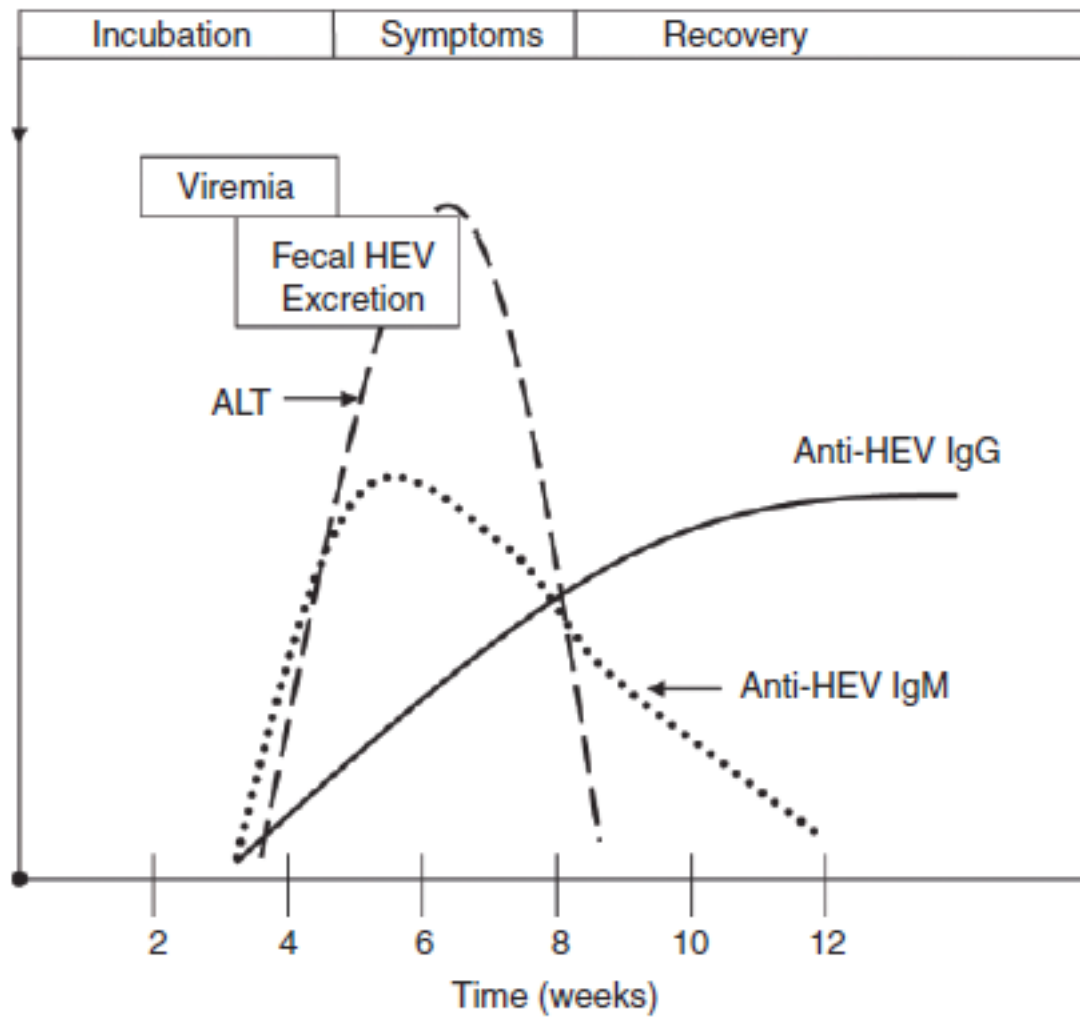
HBV:

- Sexual contact
- Mother-to-child transmission
- Blood-to-blood contact by unsafe injecting practices, blood transfusion, unsterile medical equipment

HCV:

- Blood-to-blood contact by unsafe injecting practices (main transmission mode in the WHO European Region), blood transfusion, unsterile medical equipment
- Sexual contact (less common)
- HBV and HCV are many more times infective than HIV

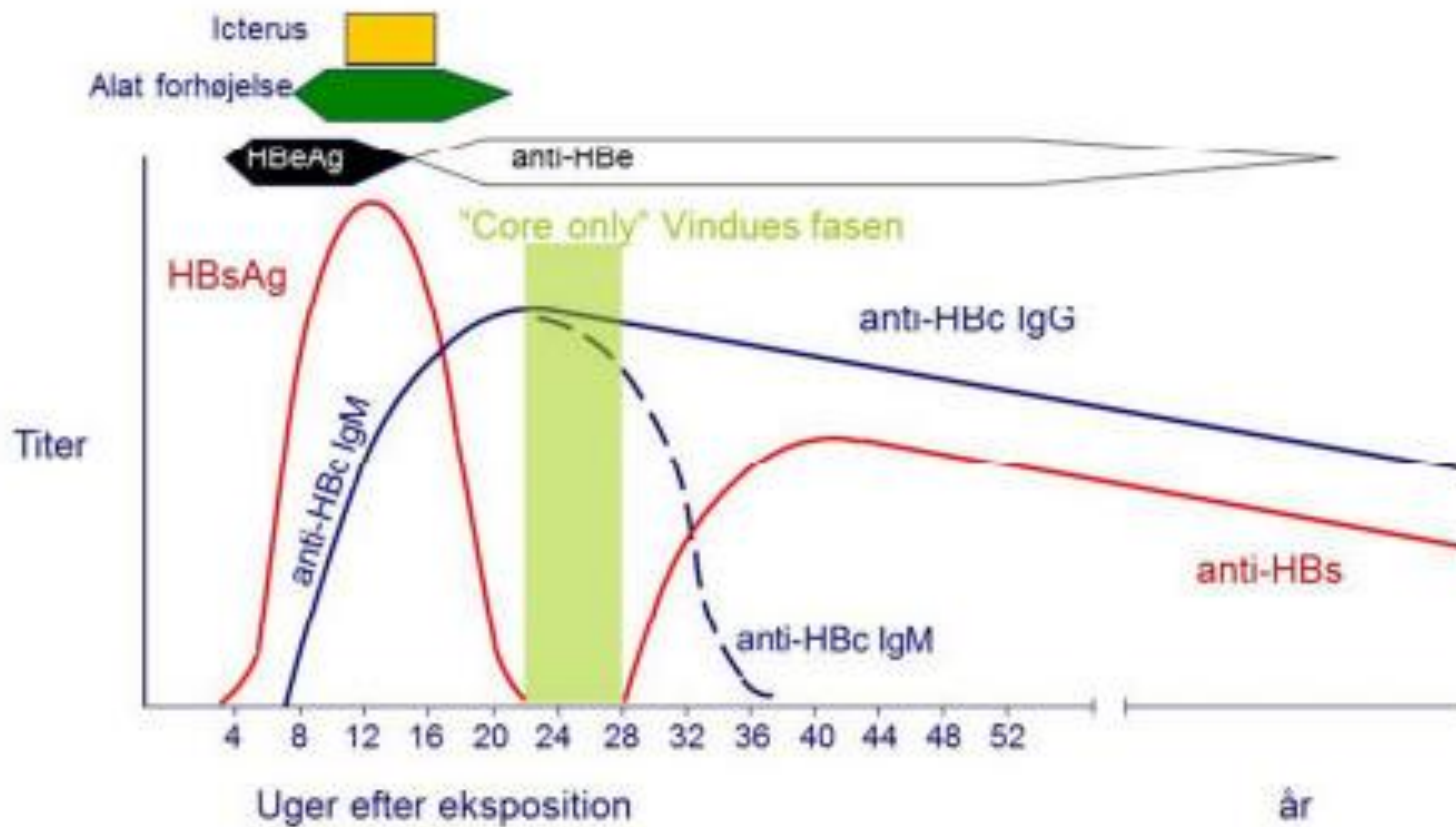
Hep E



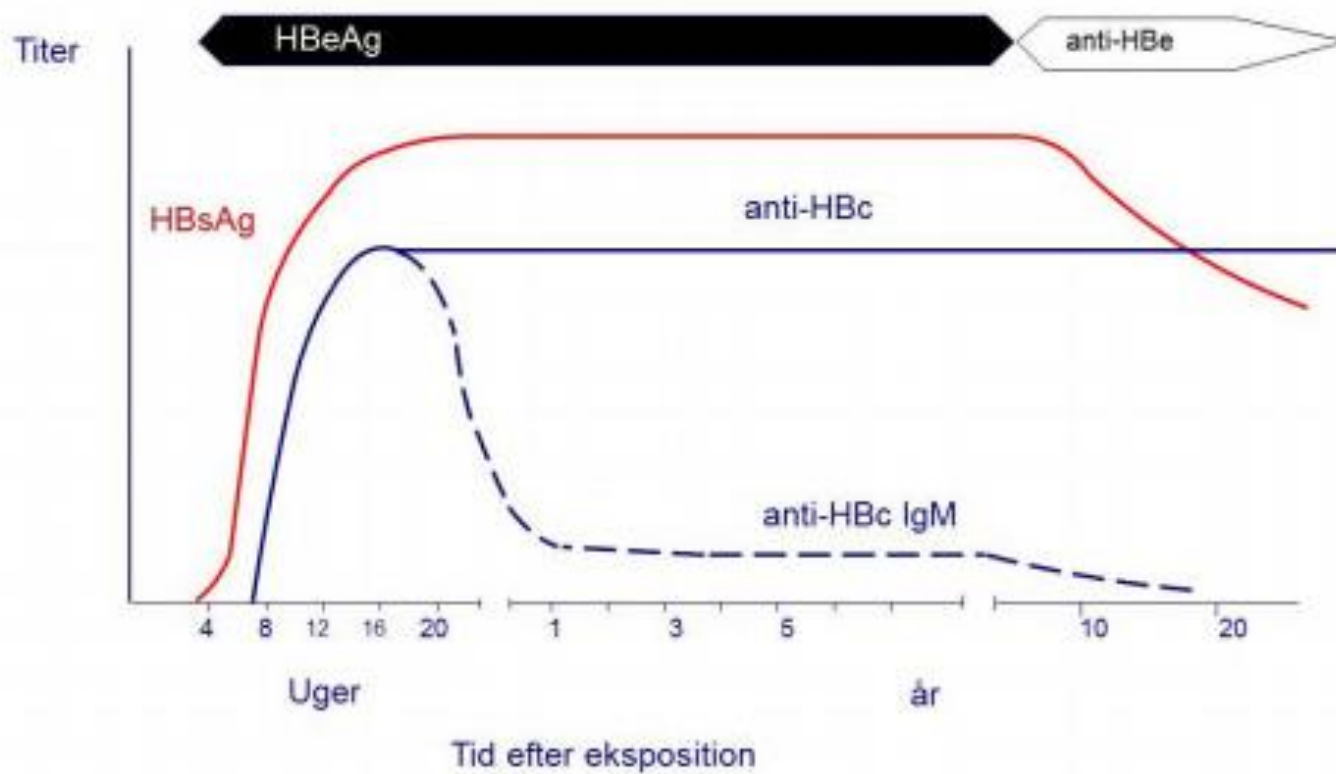
Questions ?



AKUT HBV INFEKTION



KRONISK HBV-INFEKTION



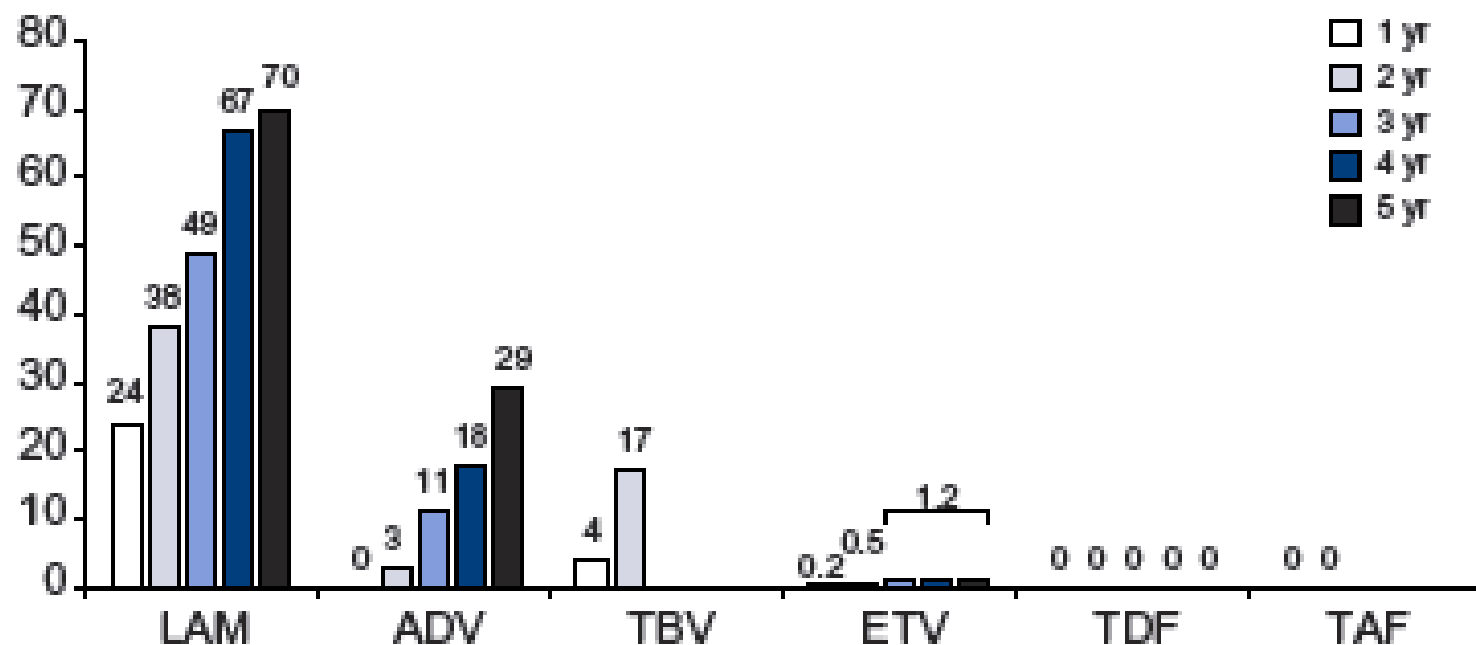


Fig. 3. Cumulative incidence of HBV resistance for lamivudine (LAM), adefovir (ADV), entecavir (ETV), telbivudine (TBV), tenofovir (TDF) and tenofovir alafenamide (TAF) in pivotal trials in nucleos(t)ide-naïve patients with chronic hepatitis B. (Collation of currently available data – not from head-to-head studies). No evidence of resistance has been shown after 8 years of TDF treatment.⁶⁹