

HEPATITIS VIRUS AKUT

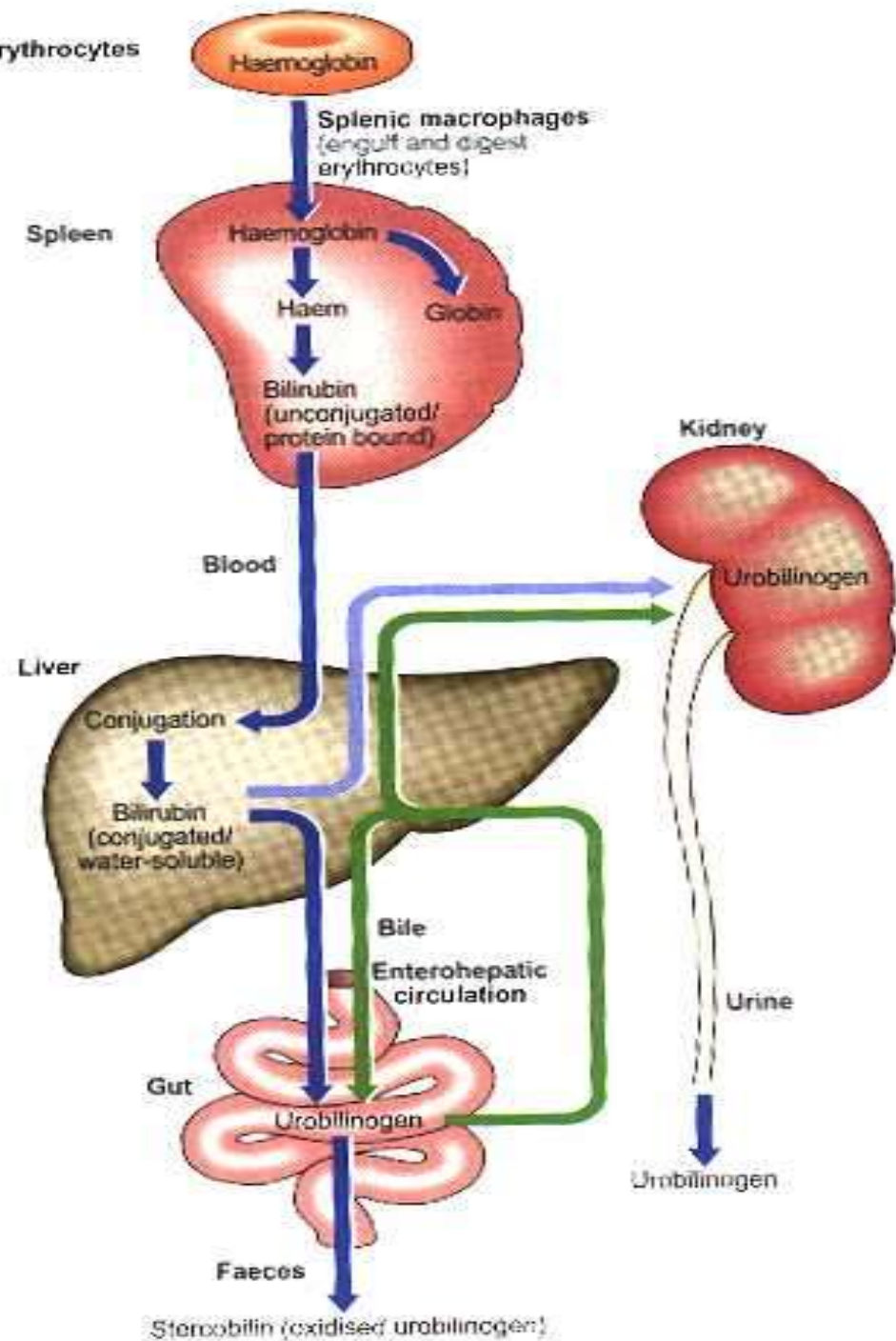
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ANATOMI

- ▶ Berat normal 1400 – 1600 gram (2,5%)
- ▶ Tdd 4 lobus :
 - Kanan → anterior & posterior
 - Kiri → lateral & medial
- ▶ Dipasok 2 pembuluh darah:
 - Vena porta 60 – 70 %
 - Arteria hepatica 30 – 40 %



METABOLISME...

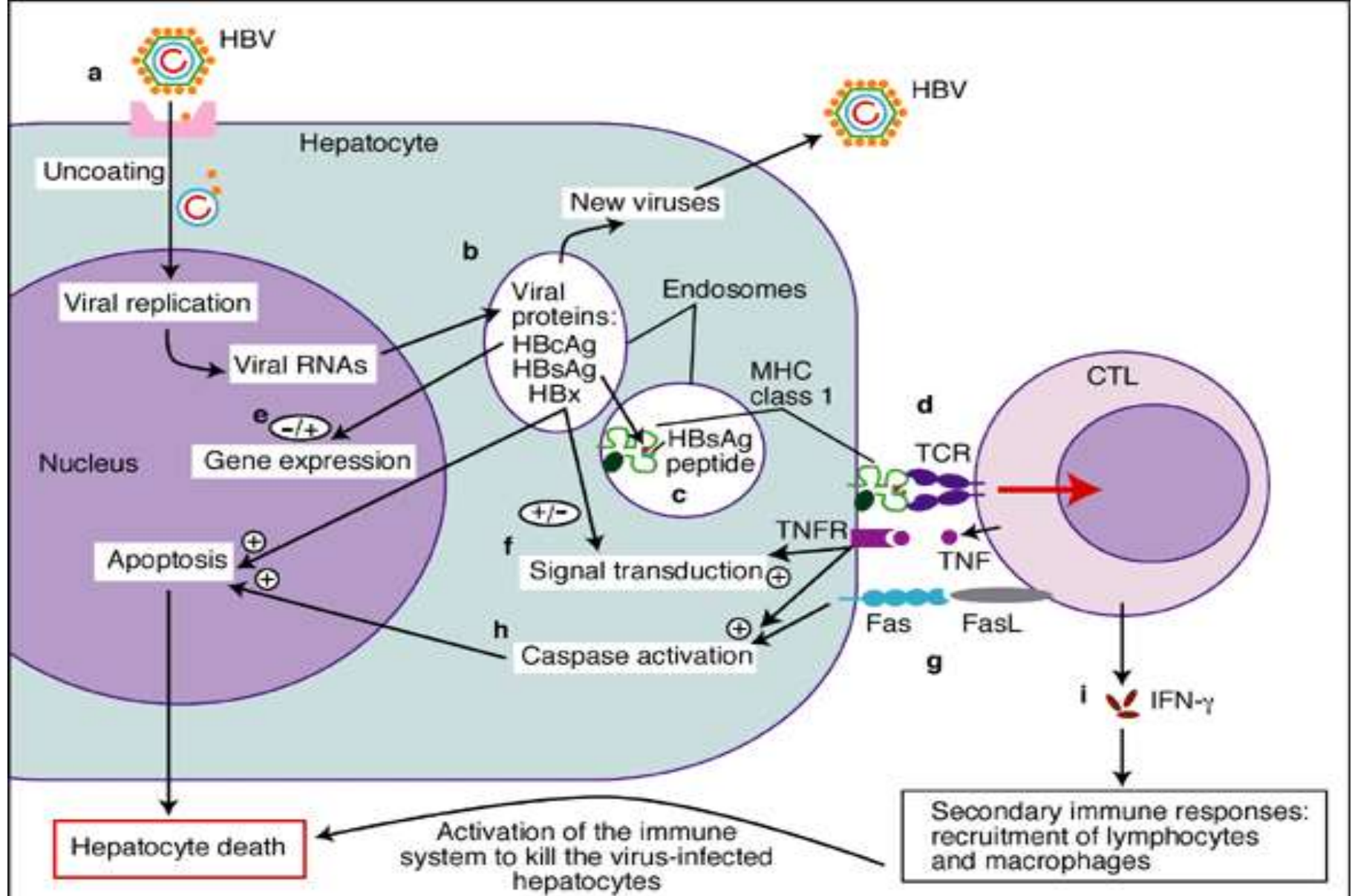


PENDAHULUAN

- ▶ Ada 5 jenis virus yaitu A,B,C,D, dan E
- ▶ Semua jenis hepatitis virus yang menyerang manusia merupakan virus RNA kecuali HBV.
- ▶ Hepatitis dibagi menjadi 4 tahap:
 - Fase inkubasi
 - Fase prodormal
 - Fase ikterus
 - Fase konvalesen

PATOFISIOLOGI

- ▶ Sistem imun yang bertanggung jawab untuk terjadinya kerusakan sel hati:
 - Melibatkan respon CD8 dan CD4 sel T
 - Produksi sitokin di hati dan sistemik
- ▶ Efek sitopatik langsung dari virus.
- ▶ Agen penyebab hepatitis virus diklasifikasikan berdasarkan transmisinya:
 - Transmisi secara enterik (HVA & HVB)
 - Transmisi melalui darah (HVB, HVD & HVC)



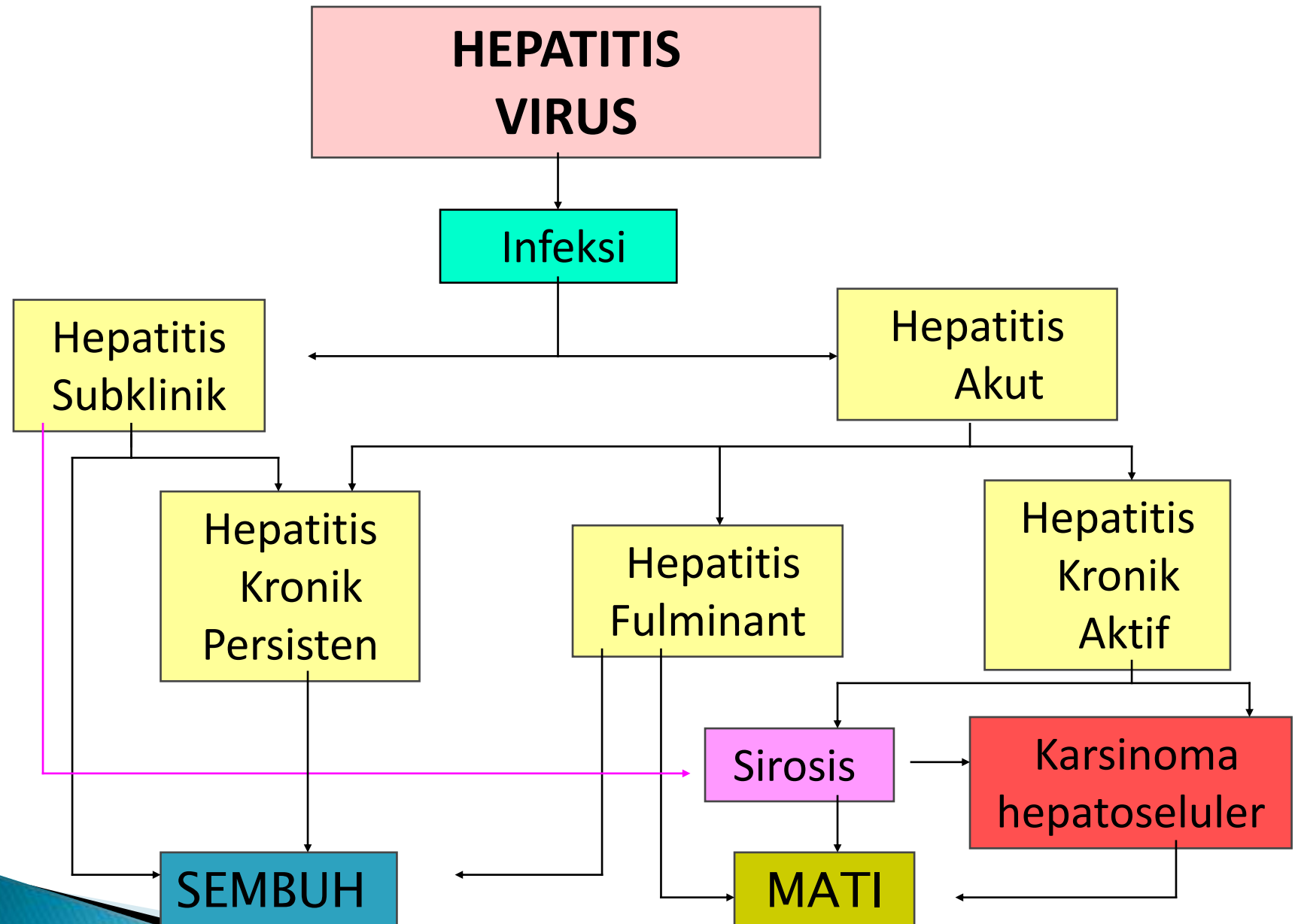
Virus-specific cytotoxic T lymphocyte (CTL) responses, and roles of proteins of hepatitis B virus

Figure 1. Virus-specific cytotoxic T lymphocyte (CTL) responses, and roles of proteins of hepatitis B virus.

- ▶ ***(a)*** After hepatitis B virus (HBV) enters a hepatocyte through an unknown virus receptor,
- ▶ ***(b)*** a number of viral proteins are synthesised, including HBc antigen (HBcAg), HBsAg and HBx protein. At the same time, the virus undergoes self-replication.
- ▶ ***(c)*** HBsAg peptide is presented at the hepatocyte cell surface by the major histocompatibility complex (MHC) and

- ▶ *(d) induces an antigen-specific CTL response through the T-cell receptor (TCR).*
- ▶ *(e) Core protein (HBcAg) can move into the nucleus of the cell and modulate expression of host genes.*
- ▶ *(f) HBx protein can interfere with signal transduction and promote the apoptosis pathway.*

- ▶ *(h) Subsequently, the caspase pathway is activated, which leads to hepatocyte apoptosis.*
- ▶ *(i) In addition, HBsAg-specific CTLs secrete interferon γ (IFN- γ) and activate secondary immunoresponses, which lead to recruitment of lymphocytes and macrophages and activation of the immune system to kill the virus-infected cell.*
- ▶ *(g) Surface antigen (HBsAg)-specific CTLs send a death signal to hepatocytes through Fas-Fas ligand (FasL) interaction and the binding of tumour necrosis factor (TNF) to its receptor (TNFR).*



Hepatitis Viruses



Virus Family	Hepatitis A Picornavirus	Hepatitis E Calicivirus	Hepatitis B Hepadnavirus	Hepatitis C Flavivirus	Delta virus Satellite virus (only in combination with HBV)
Commonality	All generate conditions of illness in the liver				
Symptoms (acute)	All the same – malaise, dark urine, anorexia, nausea, vomiting, jaundice				
Transmission	Enteric (food and water)		Sex, blood and close contact		
Chronic condition	No	No	Yes	Yes	Yes
Virus genome	+ss RNA	+ss RNA	DNA with reverse transcriptase activity	+ss RNA	-ss RNA
Virus antigens	HA Ag	HEV ORF2 proteins	HBsAg HBcAg HBeAg	Many – core E1 E2 NS3	Delta antigen
Incubation	1 month (15 – 50 d)		4 months (45 – 160 d)	2 months (15 – 150 d)	1 – 2 months
Current therapeutics	No specific treatment	No specific treatment	Interferon alpha, Lamivudine, Adefovir, Etecovir	Interferon alpha + ribavirin, Pegylated Interferon	Follow HBV therapy
Vaccines available?	Yes Havrix (GSK) Vacta (Merck)	No	Yes Engerix-B (rHBsAg) GSK Recombivax B (Merck)	No	Can be prevented by vaccination against HBV

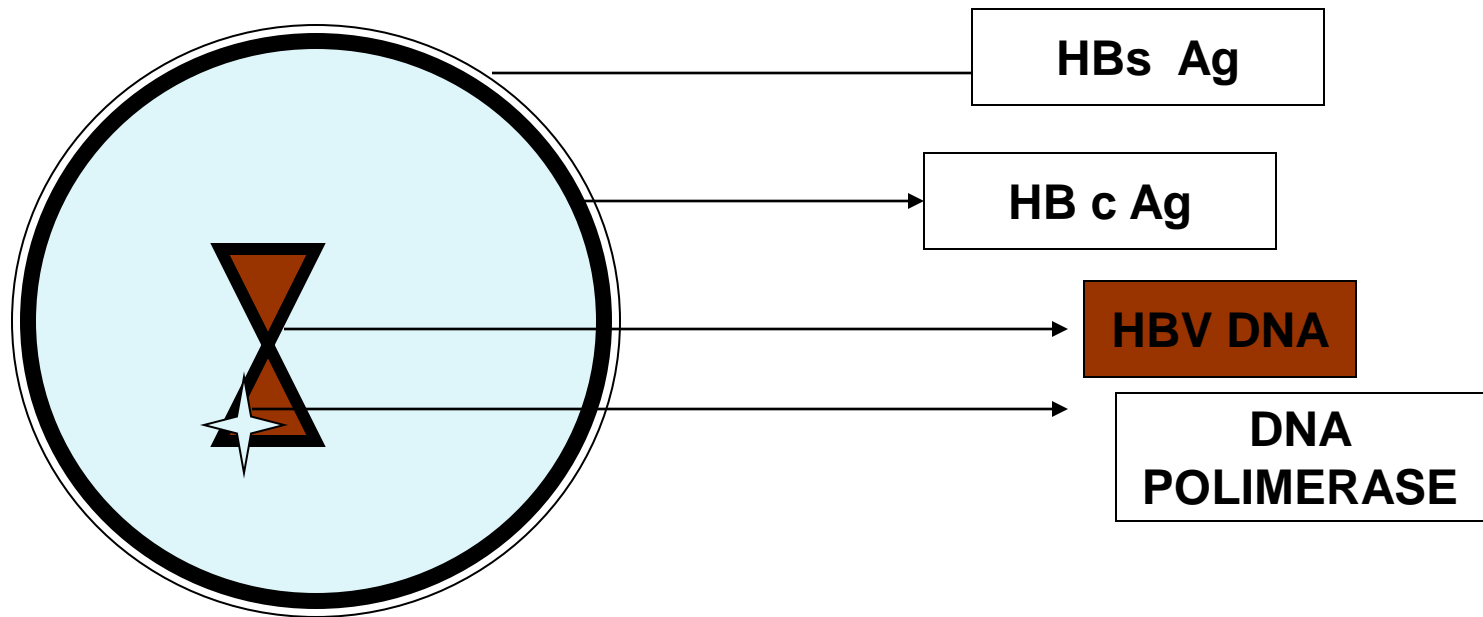
Gejala Klinis

- ▶ **Fase inkubasi** → wkt antara msknya virus dan timbulnya gejala atau ikterus
 - tergantung dosis inokulum yang ditularkan dan jalur penularan, mkn besar dosis inokulum, mkn pendek fase inkubasi.
- ▶ **Fase prodromal (praikterik)** → 1 - 2 minggu
 - fase tjd keluhan utama
 - malaise, mialgia, mudah lelah, gejala sal nafas atas dan anoreksia, diare, konstipasi
 - nyeri abdomen ringan dan menetap si kuadran kanan atas (epigastrium)

- ▶ **Fase ikterus** → 4 – 6 minggu
 - pada fase ini jrg tjd perburukan gejala klinis malah tjd perbaikan gejala klinis yang nyata, ikterus didahului dgn urin gelap, pruritus (ringan dan sementara)
- ▶ **Fase konvalesen (perbaikan)** → dimulai 1 –2 minggu setelah ikterus dan berlangsung 2 – 6 minggu
 - tdk ada ikterus dan keluhan lain
 - (+) hepatomegali dan abnormal fgs hati (+)
 - lbh sehat, nafsu makan kembali
 - akut membaik 2 – 3 minggu
 - perbaikan Hep.A lengkap = 9 minggu, Hep.B = 16 minggu

VIRUS HEPATITIS B

(VIRUS DNA –sepasang rantai mol DNA)



HBe Ag?

Non struktural (soluble)

Dibentuk dlm proses replikasi virus

Dibentuk dlm sel hati, disekresikan kedlm darah

Pemeriksaan penunjang

1. AST(SGOT) = *aspartate aminotransferase* (N = 5-40 units/l)
2. ALT(SGPT) = *alanine aminotransferase* (N = 5-40 units/ l)
 - pada hepatitis > 1000 u/l
 - sensitif , tapi tidak spesifik utk kerusakan hati
 - ALT > AST → viral hepatitis
3. Bilirubin (total = 0,3-1 mg/dl, direk = 0,1-0,3 mg/dl, indirek = 0,2 - 0,7 mg/dl)
 - ▶ normalnya bilirubin tidak terdapat di urin.
 - ▶ pada hepatitis, bilirubin **meningkat**
4. Leukopenia dan nertopenia transien yang akan diikuti dengan relatif limfositosis
5. USG abdomen
6. Serologi

Serologi Hepatitis

TABLE 285-4 Simplified Diagnostic Approach in Patients Presenting with Acute Hepatitis

Serologic Tests of Patient's Serum

<i>HBsAg</i>	<i>IgM Anti-HAV</i>	<i>IgM Anti-HBc</i>	<i>Anti-HCV</i>	<i>Diagnostic Interpretation</i>
+	—	+	—	Acute hepatitis B
+	—	—	—	Chronic hepatitis B
+	+	—	—	Acute hepatitis A superimposed on chronic hepatitis B
+	+	+	—	Acute hepatitis A and B
—	+	—	—	Acute hepatitis A
—	+	+	—	Acute hepatitis A and B (HBsAg below detection threshold)
—	—	+	—	Acute hepatitis B (HBsAg below detection threshold)
—	—	—	+	Acute hepatitis C

Hepatitis A

- ▶ IgM anti HAV = infeksi akut, konvalesen
- ▶ IgG = infeksi lama, imun thp HAV
- ▶ HAV- RNA = mendeteksi infektivitas

Hepatitis B

- ▶ HbsAg = pada awitan dan infeksi akut ; karier HBV
- ▶ HbeAg = berhubungan dengan daya infeksi yang tinggi
- ▶ HbcAg = dalam hepatosit, tdk mudah dideteksi dalam serum
- ▶ Anti - HBs memberikan imunitas thp HBV
- ▶ IgM anti- HBc timbul pada infeksi baru terjadi hingga 6 bulan
- ▶ Anti HBe timbul segera setelah resolusi infeksi akut
- ▶ DNA HBV = mendeteksi infektivitas

TABLE 285-3 Commonly Encountered Serologic Patterns of Hepatitis B Infection

HBsAg	Anti-HBs	Anti-HBc	HBeAg	Anti-HBe	Interpretation
+	-	IgM	+	-	Acute hepatitis B, high infectivity
+	-	IgG	+	-	Chronic hepatitis B, high infectivity
+	-	IgG	-	+	1. Late acute or chronic hepatitis B, low infectivity 2. HBeAg-negative ("precore-mutant") hepatitis B (chronic or, rarely, acute)
+	+	+	+/-	+/-	1. HBsAg of one subtype and heterotypic anti-HBs (common) 2. Process of seroconversion from HBsAg to anti-HBs (rare)
-	-	IgM	+/-	+/-	1. Acute hepatitis B 2. Anti-HBc "window"
-	-	IgG	-	+/-	1. Low-level hepatitis B carrier 2. Hepatitis B in remote past
-	+	IgG	-	+/-	Recovery from hepatitis B
-	+	-	-	-	1. Immunization with HBsAg (after vaccination) 2. Hepatitis B in the remote past (?) 3. False-positive

Hepatitis C

- ▶ AST dan ALT berfluktuasi tidak seperti pada hepatitis A, B
- ▶ RNA HCV = terdeteksi dalam serum dari 1 – 3 minggu peningkatan transaminase
- ▶ Anti – HCV dan RNA HCV = mendeteksi infektivitas
- ▶ EIA dan RIBA mendeteksi anti HCV yang positif
- ▶ Skrining donor darah, organ, atau jaringan penting dilakukan

TERAPI

- ▶ Kalori dan cairan yang adekuat
- ▶ Istirahat
- ▶ Tidak ada pengobatan spesifik untuk hepatitis A, E, D.
- ▶ IFN α pd hepatitis C akut \rightarrow menurunkan resiko infeksi kronik.
- ▶ Lamivudin & adefovir pada hepatitis B akut
- ▶ Kortkosteroid \rightarrow tidak bermanfaat.

KOMPLIKASI (SERING)

- ▶ Relaps hepatitis
- ▶ Hepatitis fulminan
- ▶ Edema otak
- ▶ Kompresi batang otak
- ▶ Kolaps kardiovaskuler

TERIMA KASIH.....

