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PATOFISIOLOGI PENYAKIT TIDAK MENULAR GANGGUAN HATI DAN KANDUNG EMPEDU

MERTIEN SA'PANG
ILMU GIZI / FAKULTAS ILMU KESEHATAN

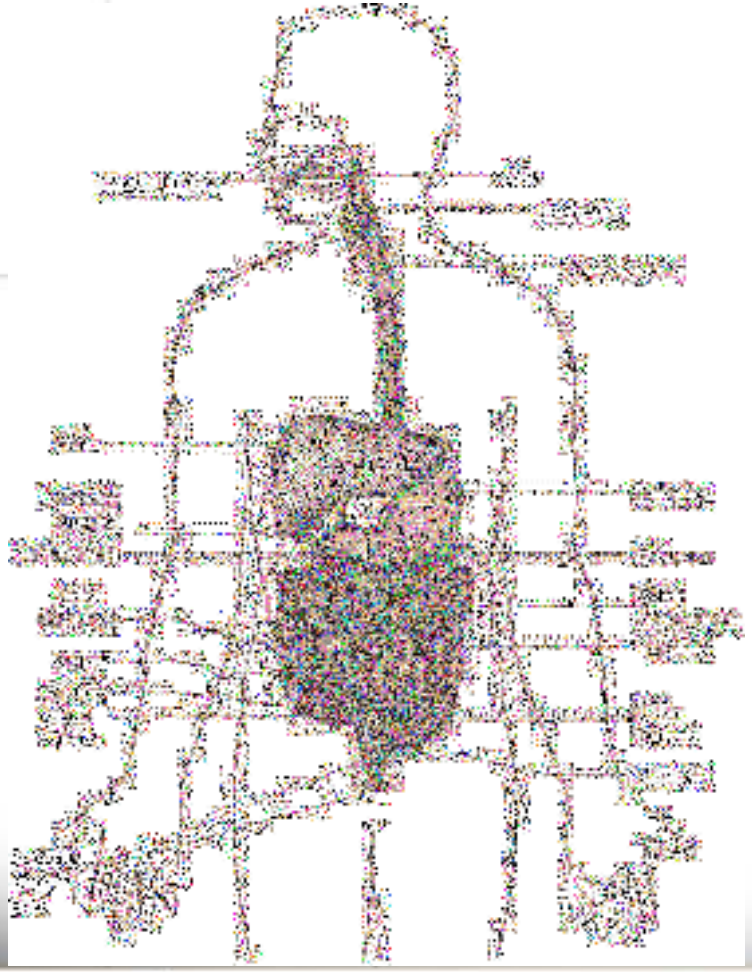
KEMAMPUAN AKHIR YANG DIHARAPKAN

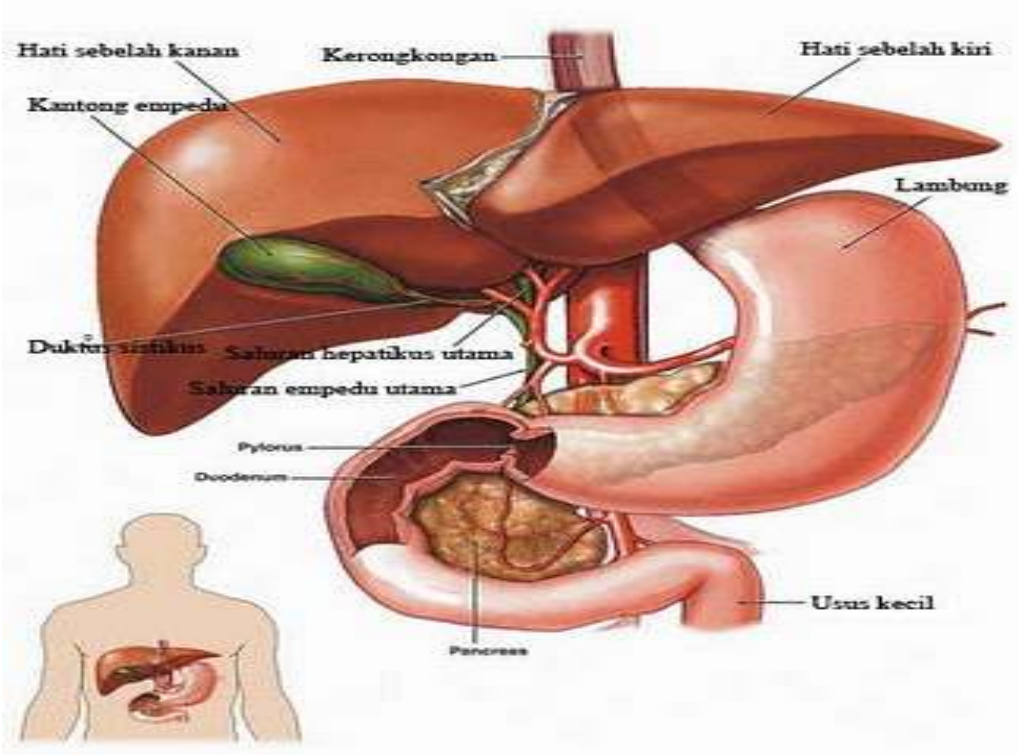
- Mampu menjelaskan fisiologi hati
- Mampu menjelaskan patofisiologi gangg. Hati dan pankreas

Sumber:

- Krause's,Kathleen Mahan, Sylvia Escoot Stump. Food, Nutrition, & Diet Therapy. edisi ke 14, Saunders, 2017
- Guyton & Hall, 1997, Buku ajar Fisiologi Kedoteran, EGC
- Price & Wilson, 2005, Patofisiologi Konsep Klinis Proses-proses penakit, EGC

Anatomi Hati, Kandung Empedu dan Pankreas

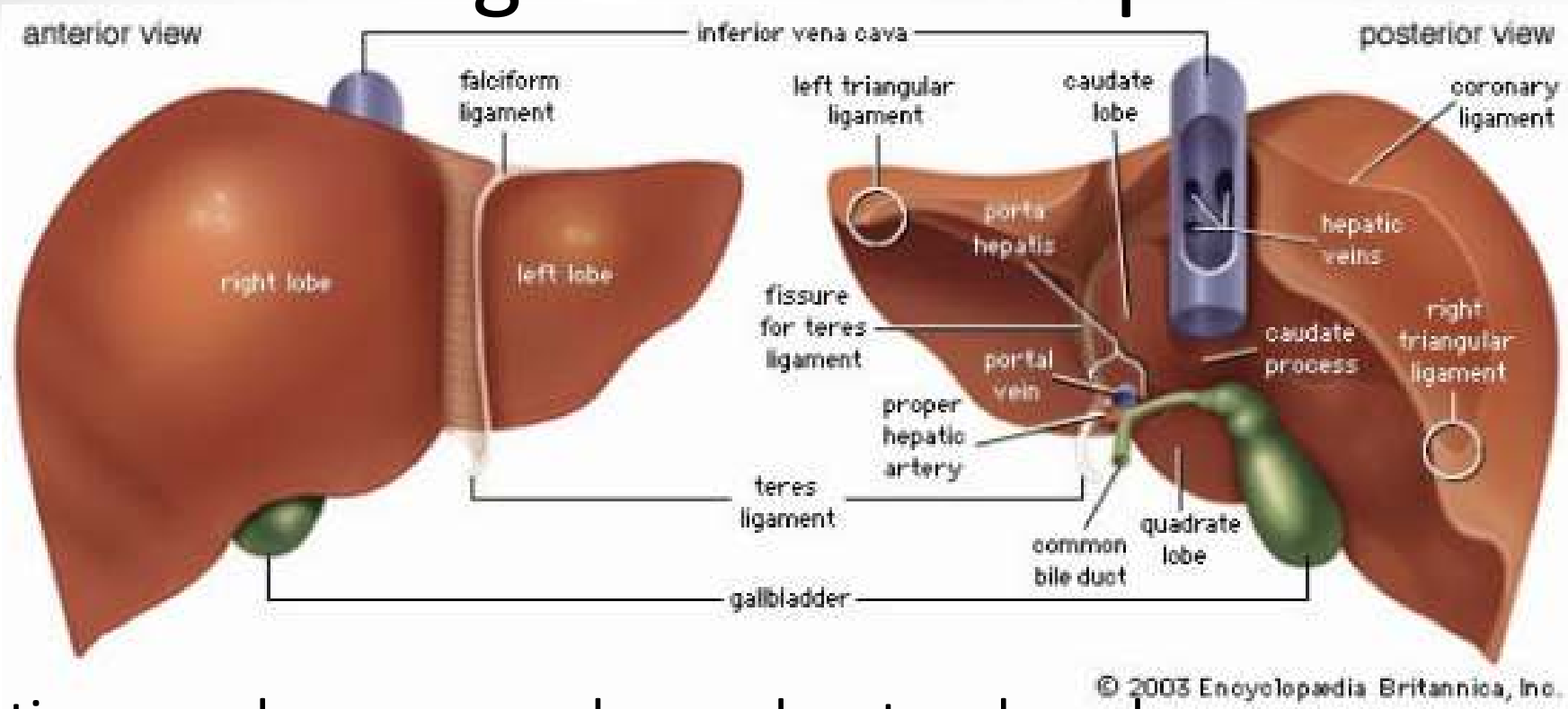




Hati

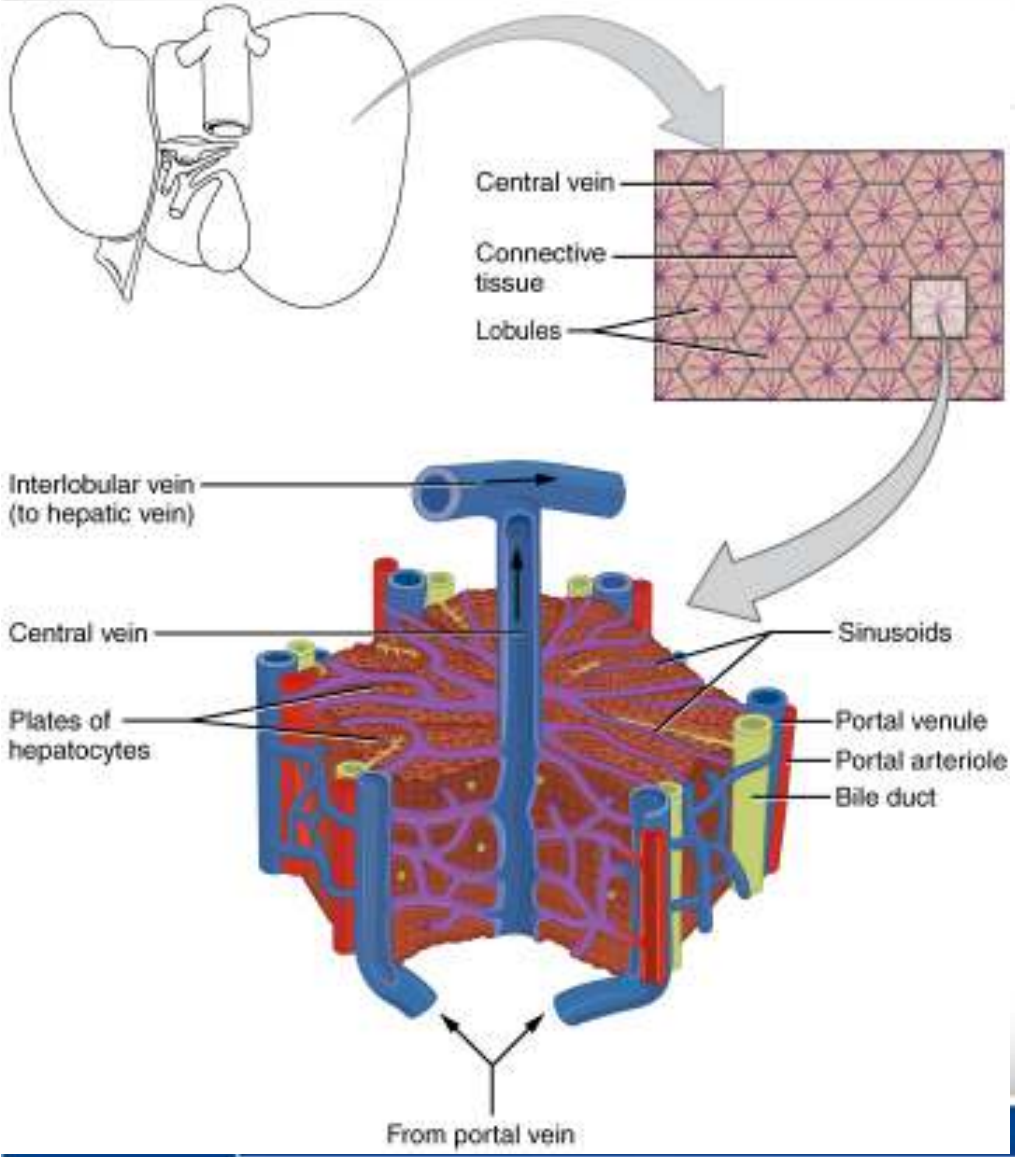
- Hati adalah kelejer terbesar dlm tubuh, berat rata2 1500 gram/ 2% BB org dewasa
- Fungsi dasar hati:
  - Fungsi vaskular untuk menyimpan dan menyaring darah
  - Fungsi Metabolisme yg berhub dgn sebag besar metabolisme tubuh
  - Fungsi sekresi dan eksresi yg berperan membentuk cairan empedu yg mengalir ke saluran pencernaan

Fungsi Vaskular Hepar



Hati merupakan organ yg besar, dapat meluas dan organ venosa yg mampu bekerja sebagai tempat penampungan darah disaat vol darah berlebihan dan mampu mensuplai darah ekstra saat kekurangan vol darah

Lanjutan....



- Hati manusia memiliki max 100.000 lobulus
- Diantara lempengan sel hati terdapat sinusoid yg merupakan cab. Vena porta arteria hepatika
- Tidak seperti kapiler lain, sinusoid dibatasi oleh sel fagositik dan sel Kupffer

Sel *Kupffer*

- Sel *Kupffer* merupakan sistem monosit-makrofag yg memiliki fungsi utama menelan bakteri dan nbenda asik lain dlm darah
- 50% makrofag dlm hati adalah sel *Kupffer,* sehingga hati merupakan salah satu organ peting dlm pertahanan melawan invasi bakteri dan agen toksik.

Fungsi Metabolik Hati

- Metabolisme KH
  - Menyimpan glikogen
  - Mengubah galaktosa dan fruktosa menjadi glukosa
  - Glukoneogenesis
  - Membentuk banyak senawa kimia penting hasil perantara metabolisme KH

Lanjutan....

- Metabolisme Lemak
  - Hidrolisis trigliserida, kolesterol, fosfolipid, dan lipoprotein (diabsorpsi dari usus) menjadi asam lemak dan gliserol
  - Sintesis kolesterol, sebagian besar diubah mjdi garam empedu dan diseksresi ke dlm empedu sisana diangkut o/ lipoprotein utk diangkut ke semua jaringan tubuh
  - Penimbunan Lemak, pengubahan sejumlah KH dan protein menjadi lemak

Lanjutan....

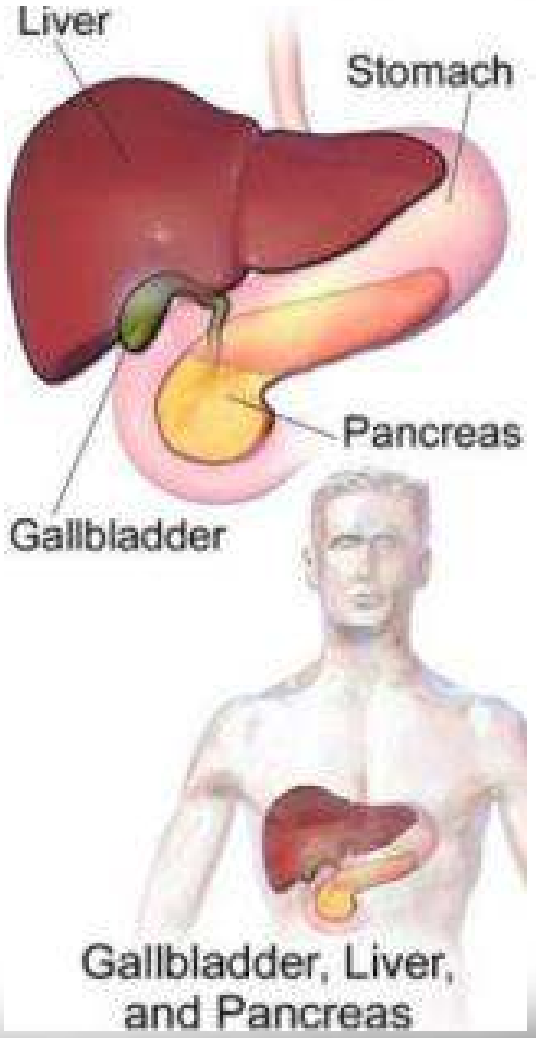
- Metabolisme Protein
  - Deaminasi asam amin
  - Pembentukan ureum utk mengeluarkan amonia dari cairan tubuh melalui urine dan feses
  - Sintesis protein plasma
- Metabolisme lainnya
  - Penyimpanan vitamin dan mineral ; Vitamin larut Lemak (Vit. A,D, E, K), vitamin B12, zat besi
  - Eksresi obat-obatan, hormon, dan zat lain

Fungsi Sekresi dan Eksresi

- Pembentukan dan eksresi empedu
  - Metabolisme garam empedu: Garam empedu berfungsi utk pencernaan dan absorpsi lemak serta vit larut lemak di dlm usus
  - Metabolisme pigmen empedu: Bilirubin (pigmen empedu utama) mrpkn hasil akhir metabolisme pemecahan eritrosit yg sudah tua, proses konjugasi berlangsung dlm hati dan dieksresi ke dlm empedu
- Detoksifikasi : Hati bertanggung-jawab atas biotransformasi zat-zat berbahaya mjdi tdk berbahaya g kemudian dieksresi o/ ginjal

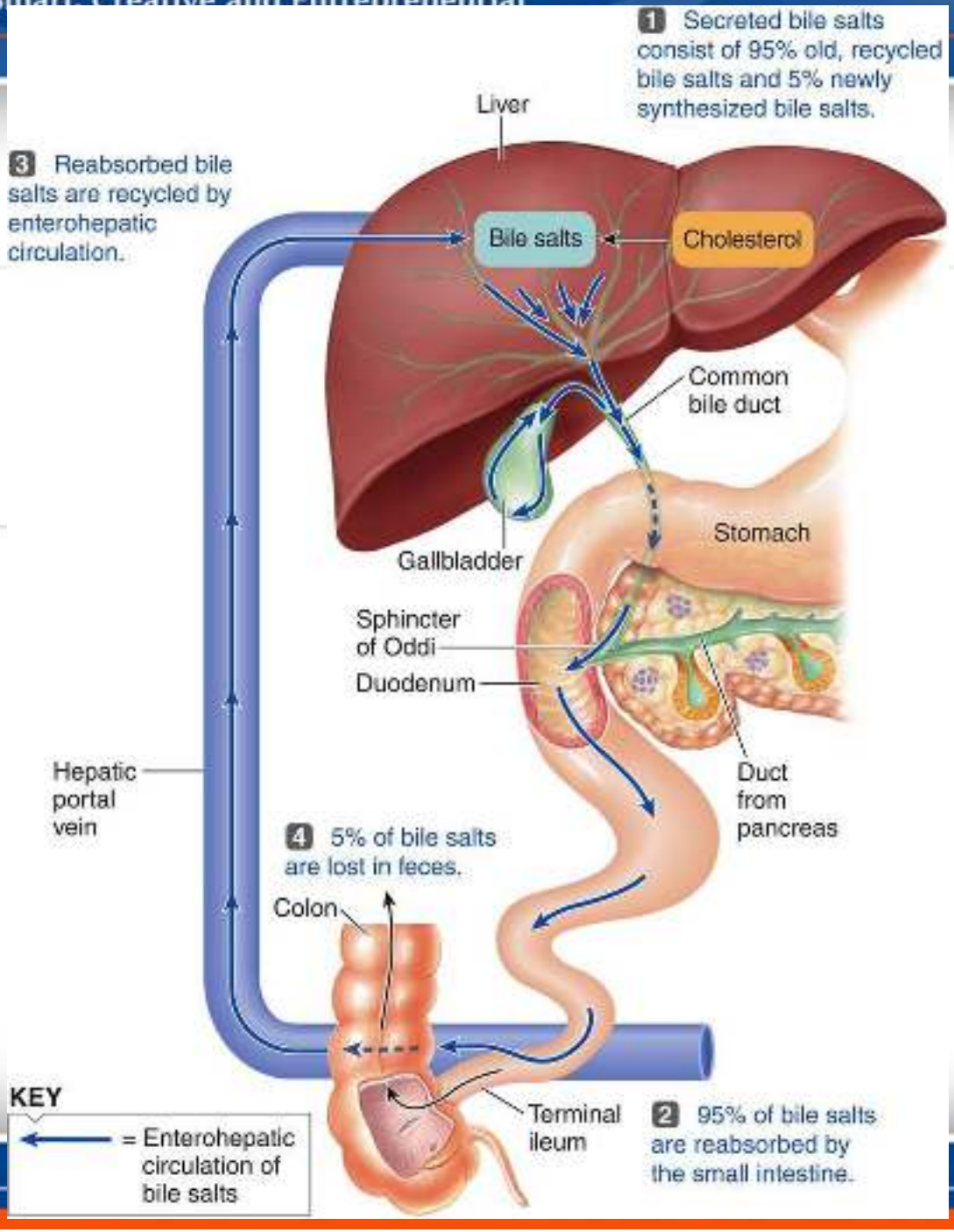
Kandung Empedu

- Fungsi utama: menyimpan dan memekatkan cairan empedu
- Sec. Berkala kandung empedu mengosongkan isinya ke dalam duodenum melalui konstraksi simultan lapisan ototnya (dirangsang o/ hormon kolesistokinin (CCK)) dan relaksasi sfingter oddi



Pankreas

- Pankreas dibentuk dari 2 sel dasar:
  - Sel-sel eksokrin: menghasilkan unsur getah pankreas (Tripsin, Kimotripsin, karbosipeptidae, nuklease, lipase pankreas, dan amilase pankreas)
  - Sel-sel endokrin/pula langerhans: menghasilkan sekret endokrin yaitu insulin dan glukagon
- Sekresi getah pankreas dirangsang oleh *pankreozimin* (diduga merupakan satu hormon dengan kolesistokin dgn efek yg berbeda)


1 Secreted bile salts consist of 95% old, recycled bile salts and 5% newly synthesized bile salts.
Liver
3 Reabsorbed bile salts are recycled by enterohepatic circulation.
Bile salts
Cholesterol
Common bile duct
Stomach
Gallbladder
Sphincter of Oddi
Duodenum
Hepatic portal vein
Duct from pancreas
4 5% of bile salts are lost in feces.
Colon
Terminal ileum
2 95% of bile salts are reabsorbed by the small intestine.
KEY
= Enterohepatic circulation of bile salts

Pemeriksaan Fungsi Hati

TABLE 29-1 Common Laboratory Tests Used to Test Liver Function

Laboratory Test	Comment
Hepatic Excretion	
Total serum bilirubin	When increased, may indicate bilirubin overproduction or impaired hepatic uptake, conjugation, or excretion
Indirect serum bilirubin	Unconjugated bilirubin; increased with excessive bilirubin production (hemolysis), immaturity of enzyme systems, inherited defects, drug effects
Direct serum bilirubin	Conjugated bilirubin; increased with depressed bilirubin excretion, hepatobiliary disease, intrahepatic or benign postoperative jaundice and sepsis, and congenital conjugated hyperbilirubinemia
Cholestasis	
Serum alkaline phosphatase	Enzyme widely distributed in liver, bone, placenta, intestine, kidney, leukocytes; mainly bound to canalicular membranes in liver; increased levels suggest cholestasis but can be increased with bone disorders, pregnancy, normal growth, and some malignancies
γ-Glutamyl transpeptidase (GGT)	Enzyme found in high concentrations in epithelial cells lining bile ductules in the liver; also present in kidney, pancreas, heart, brain; increased with liver disease, but also after myocardial infarction, in neuromuscular disease, pancreatic disease, pulmonary disease, diabetes mellitus, and during alcohol ingestion
Hepatic Serum Enzymes	
Alanine aminotransferase (ALT, formerly SGPT, serum glutamic pyruvic transaminase)	Located in cytosol of hepatocyte; found in several other body tissues but highest in liver; increased with liver cell damage
Aspartate aminotransferase (AST, formerly SGOT, serum glutamic oxaloacetic transaminase)	Located in cytosol and mitochondria of hepatocyte; also in cardiac and skeletal muscle, heart, brain, pancreas, kidney; increased with liver cell damage
Serum lactic dehydrogenase	Located in liver, red blood cells, cardiac muscle, kidney; increased with liver disease but lacks sensitivity and specificity because it is found in most other body tissues
Serum Proteins	
Prothrombin time (PT)	Most blood coagulation factors are synthesized in the liver; vitamin K deficiency and decreased synthesis of clotting factors increase prothrombin time and risk of bleeding.
International Normalized Ratio (INR)	A standardized way to report PT levels so that levels from different laboratories can be compared

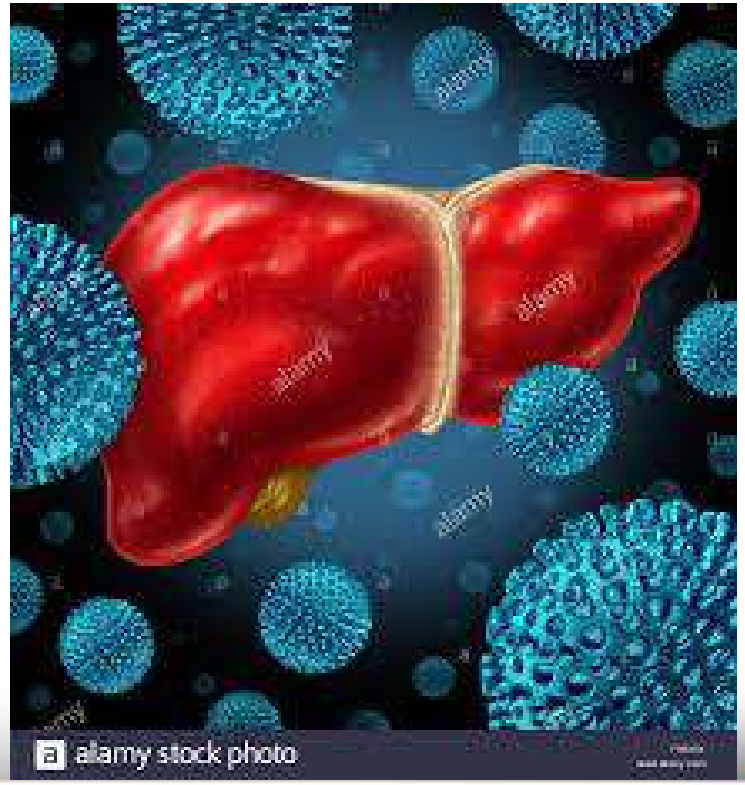
Lanjutan....

TABLE 29-1 Common Laboratory Tests Used to Test Liver Function—cont'd

Laboratory Test	Comment
Serum albumin	Main export protein synthesized in the liver and most important factor in maintaining plasma oncotic pressure; hypoalbuminemia can result from expanded plasma volume or reduced synthesis as well as increased losses as occurs with protein-losing enteropathy, nephrotic syndrome, burns, gastrointestinal bleeding, exfoliative dermatitis.
Serum globulin	Alpha$_1$ and alpha$_2$-globulins are synthesized in the liver; levels increase with chronic liver disease; limited diagnostic use in hepatobiliary disease although the pattern may suggest underlying cause of liver disease (e.g., elevated immunoglobulin [Ig]G suggests autoimmune hepatitis, elevated IgM suggests primary biliary cirrhosis, elevated IgA suggests alcoholic liver disease)
Markers of Specific Liver Diseases	
Serum ferritin	Major iron storage protein; increased level sensitive indicator of genetic hemochromatosis
Ceruloplasmin	Major copper-binding protein synthesized by liver; decreased in Wilson's disease
Alpha-fetoprotein	Major circulating plasma protein; increased with hepatocellular carcinoma
Alpha$_1$-antitrypsin	Main function is to inhibit serum trypsin activity; decreased levels indicate alpha$_1$-antitrypsin deficiency, which can cause liver and lung damage.
Markers for Viral Hepatitis	
Anti-HAV IgM (antibody to hepatitis A virus)	Marker for hepatitis A; indicates current or recent infection or convalescence
HBsAg (hepatitis B surface antigen)	Marker for hepatitis B; positive in most cases of acute or chronic infection
Anti-HBc (antibody to hepatitis B core antigen)	Antibody to hepatitis B core antigen; marker for hepatitis B; Recent or past hepatitis infection
Anti-HBs (antibody to hepatitis B surface antigen)	Antibody to HBsAg; marker for hepatitis B; denotes prior hepatitis B infection or hepatitis B vaccine; protective
HBeAg (hepatitis Be antigen)	Marker for hepatitis B; transiently positive during active virus replication; reflects concentration and infectivity of virus
Anti-HBe (antibody to hepatitis Be antigen)	Marker for hepatitis B; positive in all acute and chronic cases; positive in carriers; not protective
HBV-DNA (hepatitis B deoxyribonucleic acid)	Measures hepatitis B viral load
Anti-HCV (antibody to hepatitis C virus)	Marker for hepatitis C; positive 5-6 weeks after onset of hepatitis C virus; not protective; reflects infectious state and is detectable during and after treatment
HCV-RNA (hepatitis C virus ribonucleic acid)	Measures hepatitis C viral load
Anti-HDV	Marker for hepatitis D; indicates infection; not protective
Miscellaneous	
Ammonia	Liver converts ammonia to urea; may increase with hepatic failure and portal-systemic shunts

Viral Hepatitis

- Merupakan inflamasi hati yang disebabkan oleh berbagai jenis virus hepatitis spti Hepatitis A, B, C, D dan E



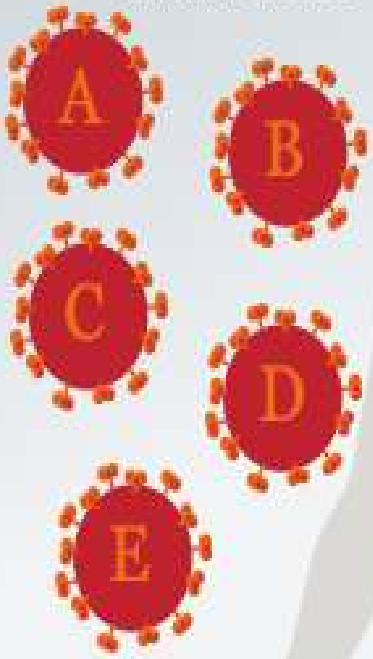
Hepatitis

- Hepatitis dpt bersifat akut atau kronis
- Hepatitis: peradangan hati yang disebabkan o/ keracunan toksik tertentu atau krn infeksi virus
- Penyakit ini disertai anoreksia, demam, rasa mual dan muntah, serta *jaundice* (kuning)

What is hepatitis?

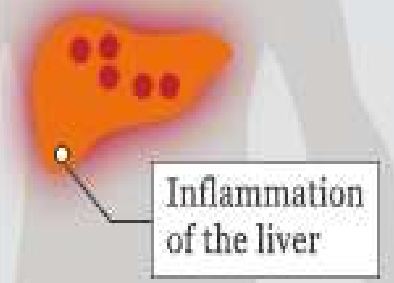
The A, B, C, D and E of hepatitis

There are five main hepatitis viruses



What vaccines are available for which types of hepatitis?

- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis D
- Hepatitis E



Estimated cases world-wide (per year)

Hepatitis B and C:
400 million cases

Gradual death:
1.4 million people die worldwide from hepatitis every year
An estimated

Treatment:
90% of hepatitis C patients can be healed within three to six months

How does the virus spread?

Hepatitis A and E:
Lack of food hygiene, contaminated water and sub-standard sanitary facilities

Hepatitis B, C and D:
Blood, sperm and other bodily fluids

Source: WHO

TABLE 29-2 Types of Viral Hepatitis

Virus	Transmission	Comments
Hepatitis A	Fecal-oral route; is contracted through contaminated drinking water, food, and sewage	Anorexia is the most frequent symptom, and it can be severe. Other common symptoms include nausea, vomiting, right upper quadrant abdominal pain, dark urine, and jaundice (icterus). Recovery is usually complete, and long-term consequences are rare. Serious complications may occur in high-risk patients; subsequently, great attention must be given to adequate nutritional intake.
Hepatitis B and C	HBV and HCV are transmitted via blood, blood products, semen, and saliva. For example, they can be spread from contaminated needles, blood transfusions, open cuts or wounds, splashes of blood into the mouth or eyes, or sexual contact.	HBV and HCV can lead to chronic and carrier states. Chronic active hepatitis also can develop, leading to cirrhosis and liver failure.
Hepatitis D	HDV is rare in the United States and depends on the HBV for survival and propagation in humans.	HDV may be a coinfection (occurring at the same time as HBV) or a superinfection (superimposing itself on the HBV carrier state). This form of hepatitis usually becomes chronic.
Hepatitis E	HEV is transmitted via the oral-fecal route.	HEV is rare in the United States (typically only occurs when imported), but it is reported more frequently in many countries of southern, eastern, and central Asia; northern, eastern, and western Africa; and Mexico. Contaminated water appears to be the source of infection, which usually afflicts people living in crowded and unsanitary conditions. HEV is generally acute rather than chronic.
Hepatitis G/GB	HGV and a virus labeled GBV-C appear to be variants of the same virus.	Although HGV infection is present in a significant proportion of blood donors and is transmitted through blood transfusions, it does not appear to cause liver disease.

Manifestasi Klinis

Manifestasi klinis Hepatitis Akut terbagi kedalam 4 fase:

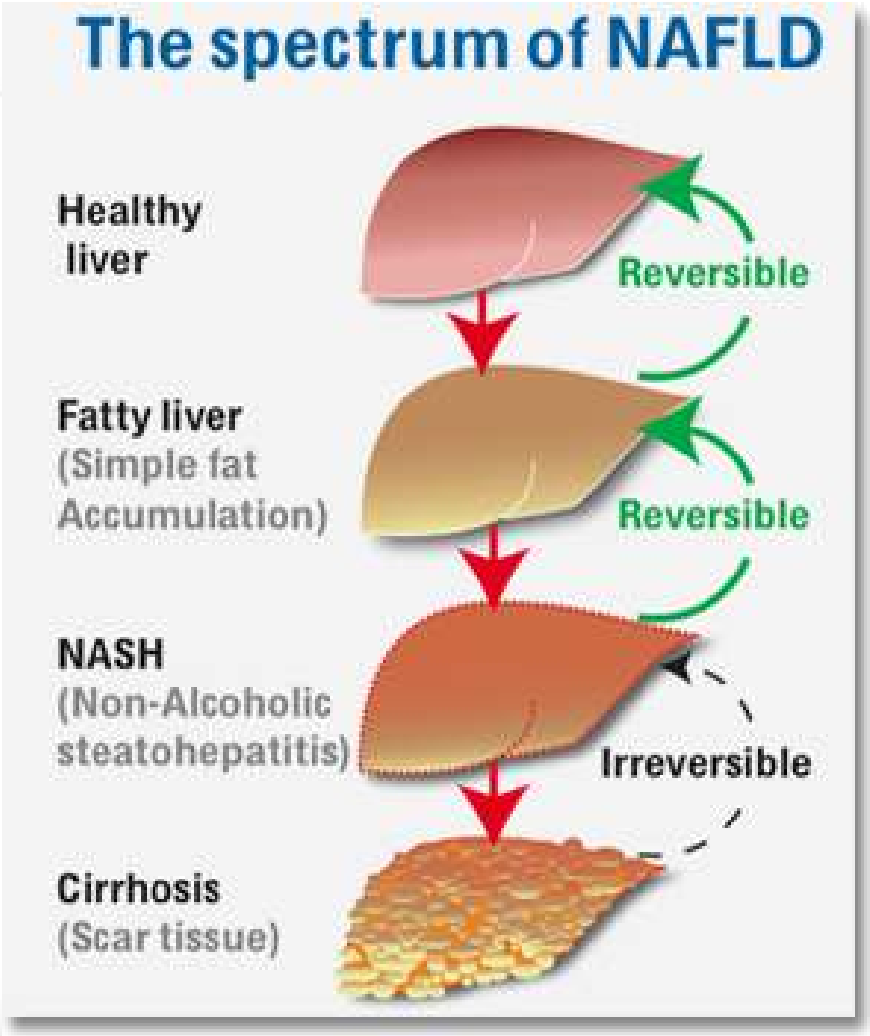
1. Fase inkubasi
   - Gejala tidak spesifik spti: malaise, kehilangan nafsu makan, mual, dan nyeri pada abdomen kuadran kanan atas.
2. Fase Preikterik (Prodromal)
   - Masih menunjukkan gejala tdk spesifik disertai anoreksia dan demam

Lanjutan....

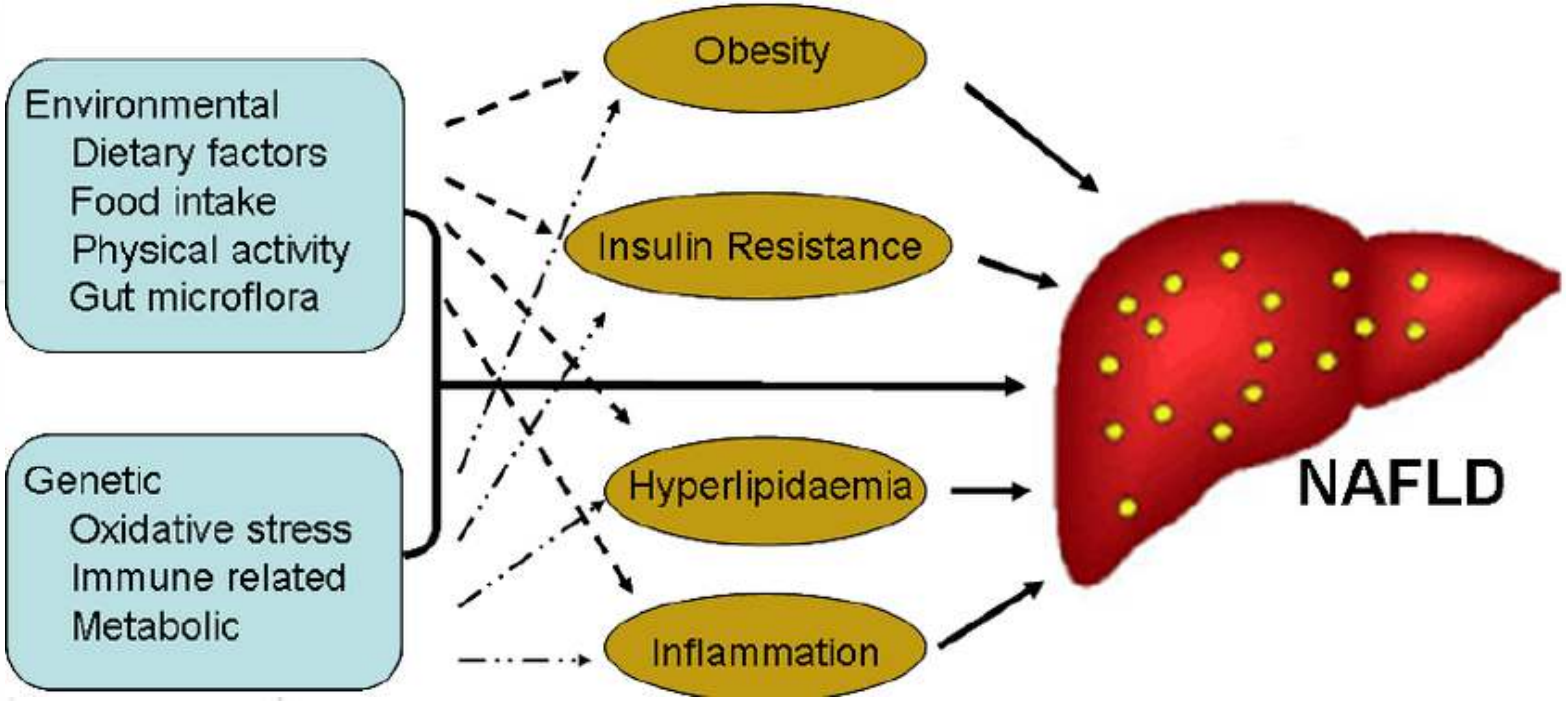
3. Fase Ikterik
   - Gejala non-spesifik bertambah parah disertai hiperbilirubinemia, peningkatan kadar ALT &AST, hati membesar sedang dan terasa nyeri, limpa teraba membesar, jaundice, urne lebih gelap, feses memucat.
   - Biasanya terjadi 4-6 minggu
4. Fase penyembuhan
   - Jaundice dan gejala lain mulai mereda
   - Pd kasus tdk komplikasi fase ini dimulai 1-2 minggu setelah awitan fase ikterik dan berlangsung selama 2-6 minggu

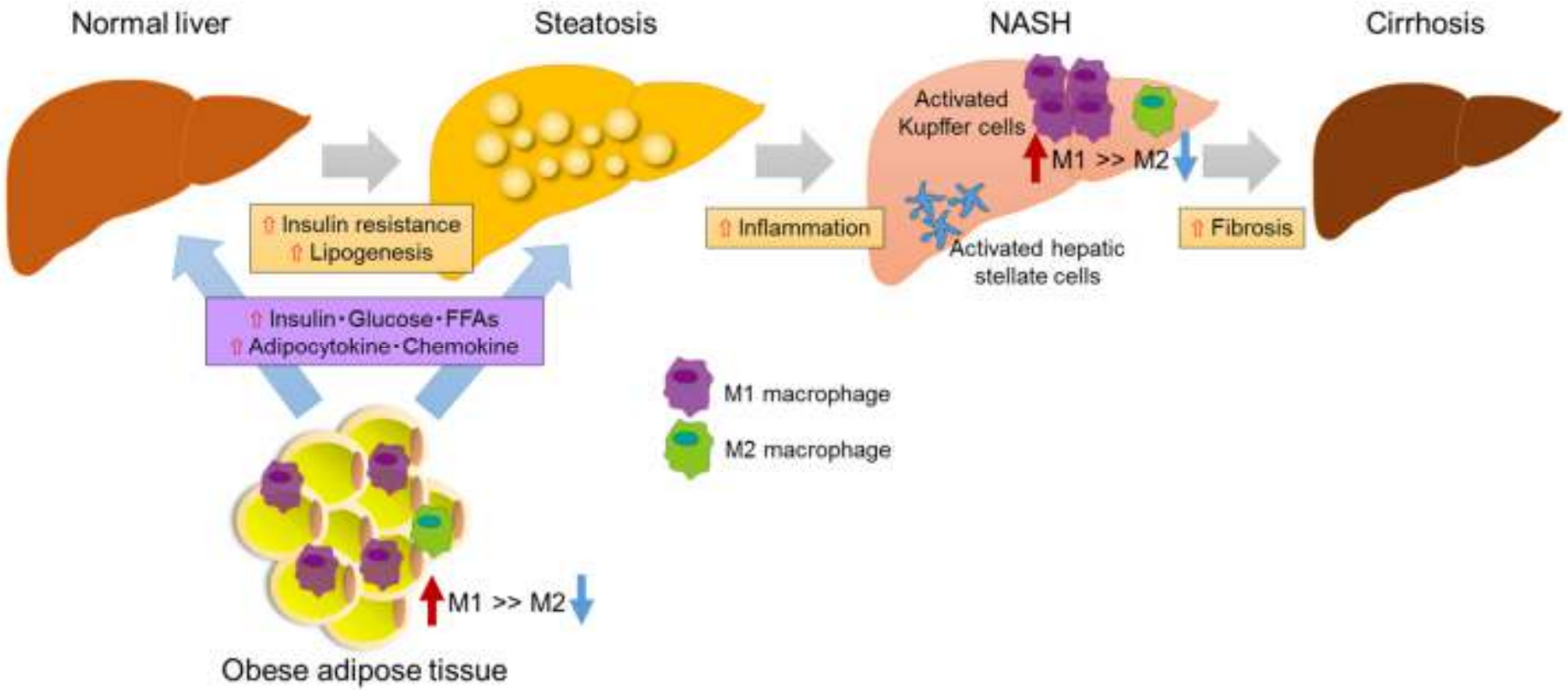
Non-Alcoholic Fatty Liver Disease

- NAFLD: a spectrum of liver disease ranging from steatosis to steatohepatitis and cirrhosis.



NAFLD develops from simple steatosis to steatohepatitis (NASH), and then cirrhosis. Cirrhosis is no more reversible.


Environmental
Dietary factors
Food intake
Physical activity
Gut microflora
Genetic
Oxidative stress
Immune related
Metabolic
Obesity
Insulin Resistance
Hyperlipidaemia
Inflammation
NAFLD


Normal liver
Steatosis
NASH
Cirrhosis
⇧ Insulin resistance
⇧ Lipogenesis
⇧ Insulin・Glucose・FFAs
⇧ Adipocytokine・Chemokine
⇧ Inflammation
Activated Kupffer cells
M1 >> M2
Activated hepatic stellate cells
⇧ Fibrosis
M1 macrophage
M2 macrophage
M1 >> M2
Obese adipose tissue

Alcoholic Liver Disease

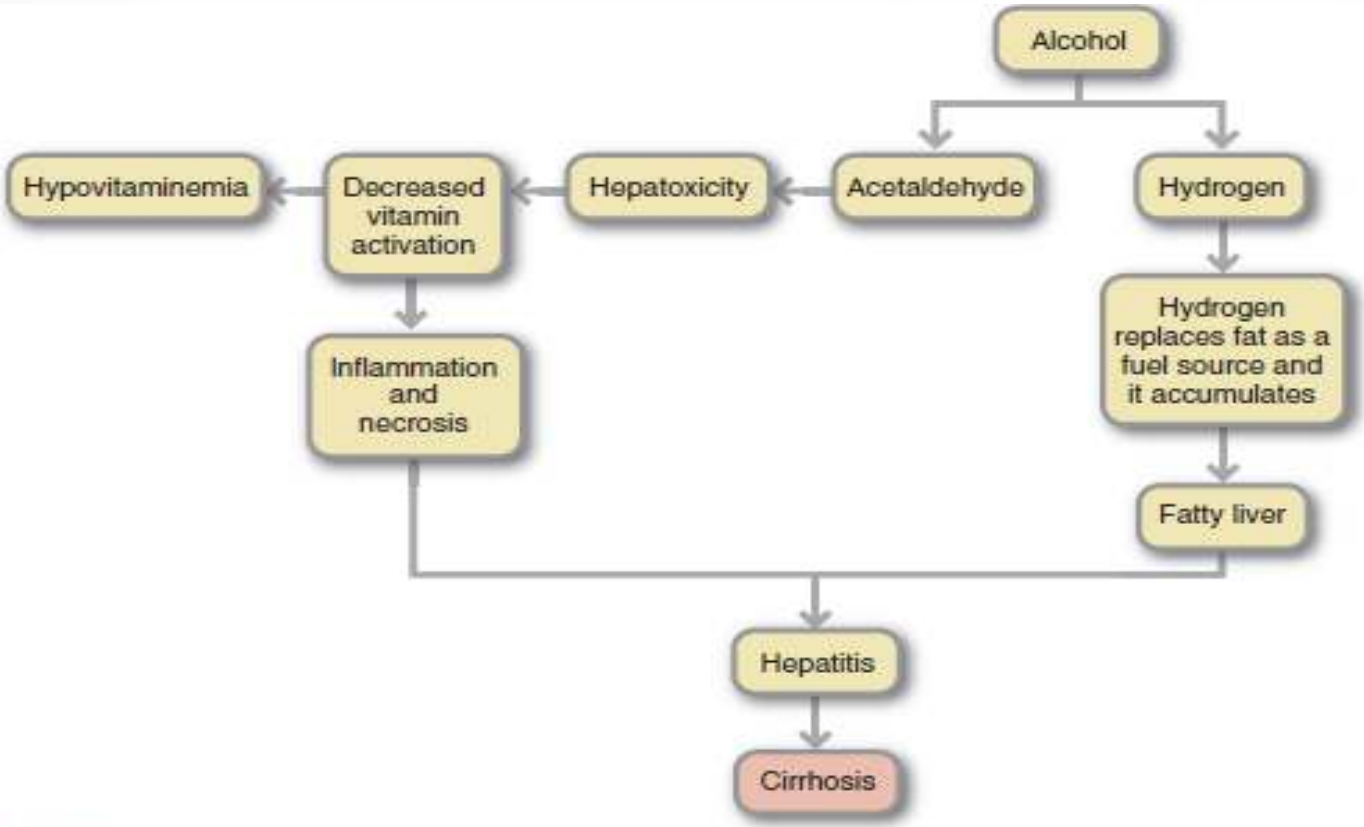
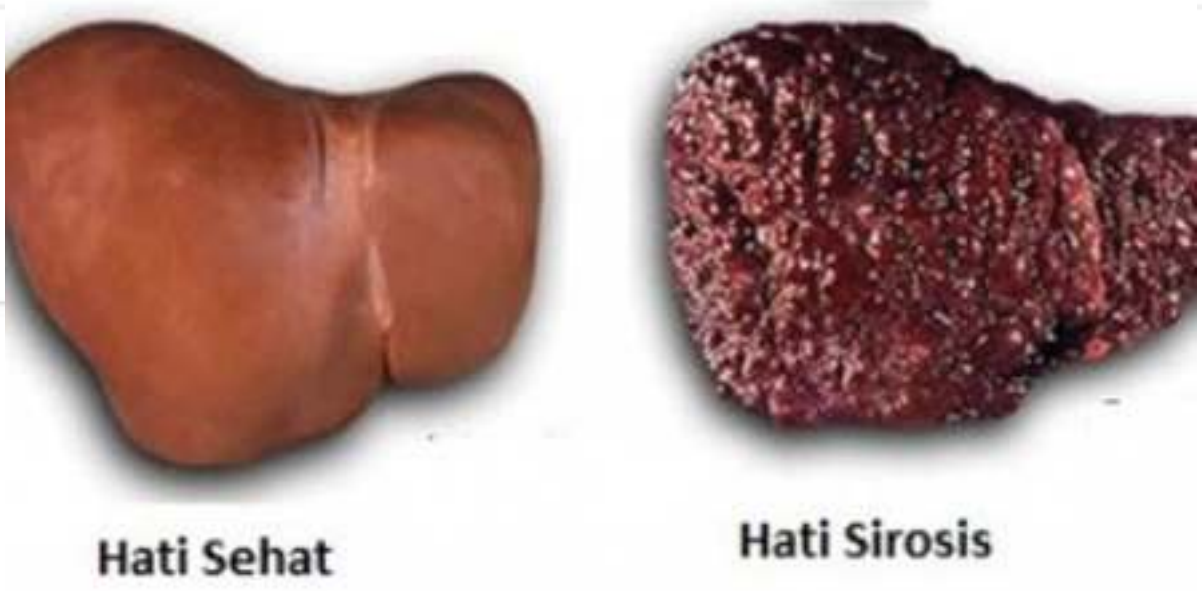


FIGURE 29-2 Complications of excessive alcohol consumption stem largely from excess hydrogen and from acetaldehyde. Hydrogen produces fatty liver and hyperlipemia, high blood lactic acid, and low blood sugar. The accumulation of fat, the effect of acetaldehyde on liver cells, and other factors as yet unknown lead to alcoholic hepatitis. The next step is cirrhosis. The consequent impairment of liver function disturbs blood chemistry, notably causing a high ammonia level that can lead to coma and death. Cirrhosis also distorts liver structure, inhibiting blood flow. High pressure in vessels supplying the liver may cause ruptured varices and accumulation of fluid in the abdominal cavity. Response to alcohol differs among individuals; in particular, not all heavy drinkers develop hepatitis and cirrhosis.

Sirosis Hati



Sirosis hati: kerusakan hati yg menetap, disebabkan o/ hepatitis kronis, alkohol, penyumbatan saluran empedu, dan berbagai kelainan metabolisme

Sirosis

- Jaringan hati sec merata rusak akibat pengerutan dan pengerasan (fibrotik) sehingga fungsi terganggu.
- Gejalanya: kelelahan, kehilangan BB, penurunan daya tahan tubuh, gangg pencernaan, dan *jaundice*
- Dlm keadaan berat disertai asites, hipertensi portal dan hematemesis (muntah darah)-melena (feses berwarna hitam) yang dpt berakhir dgn koma hepatik.

Clinical Manifestations of Cirrhosis

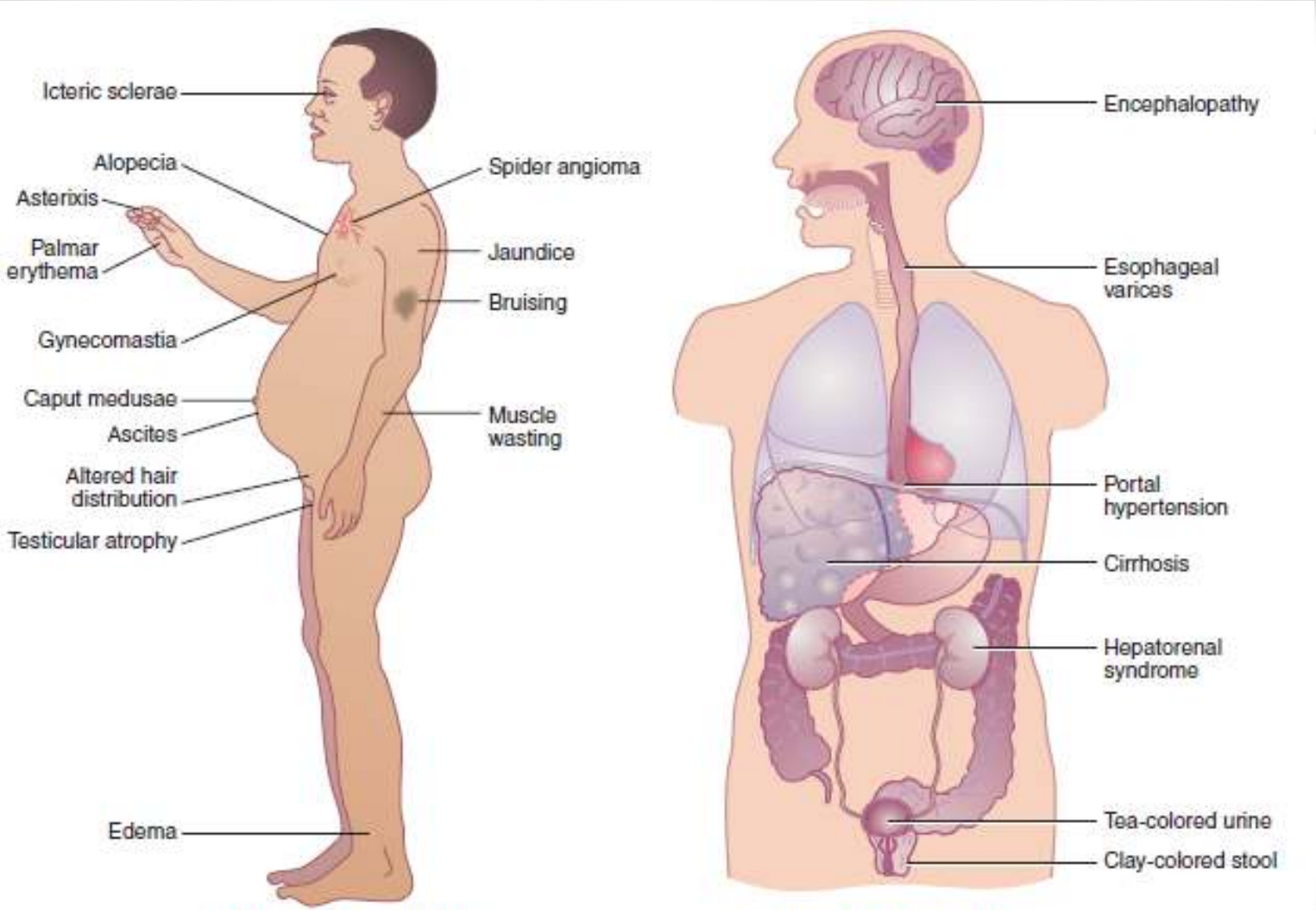
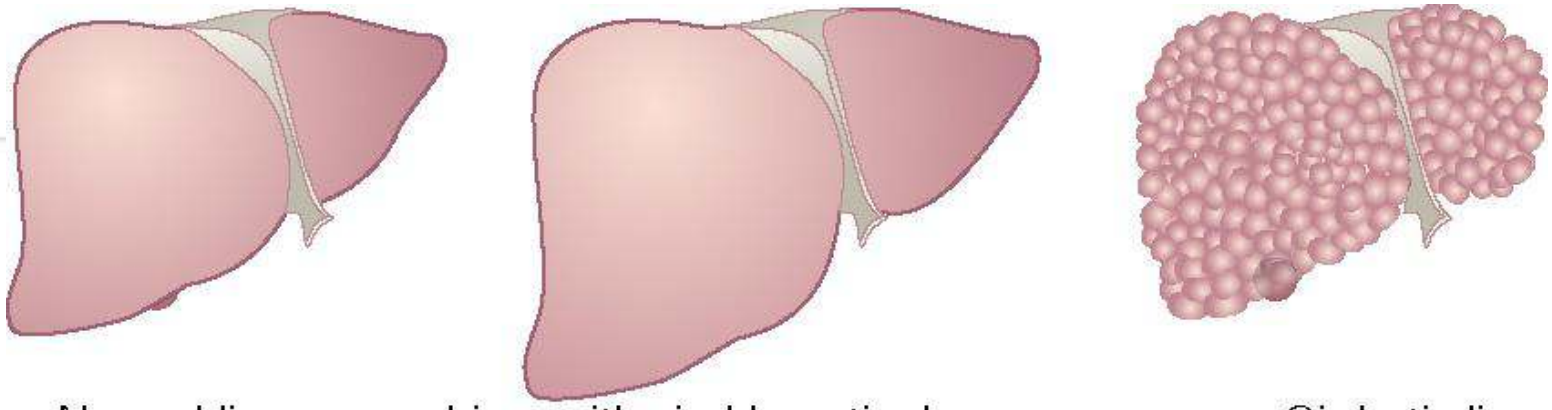


FIGURE 29-4 Clinical manifestations of cirrhosis.

Normal Liver vs. Damaged Liver

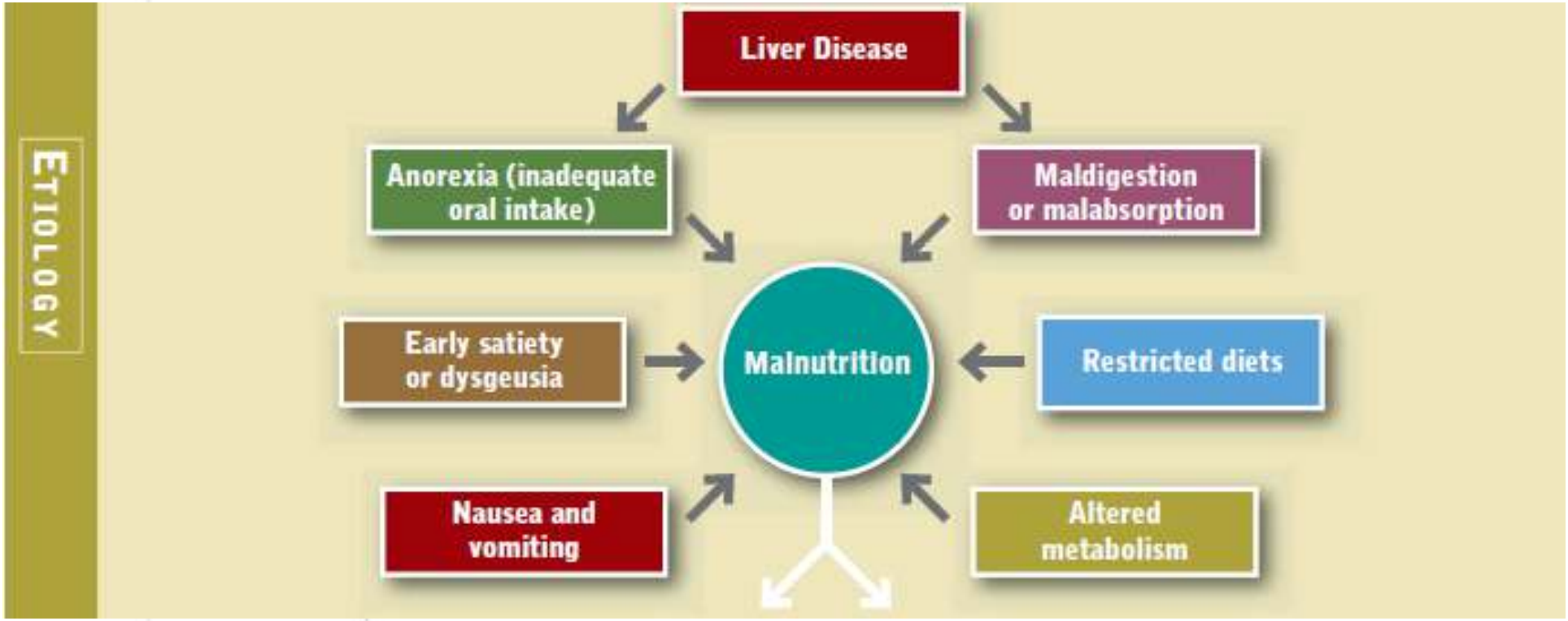


Normal liver

Liver with viral hepatic damage

Cirrhotic liver

Masalah gizi pada Penyakit Hati



PATHOPHYSIOLOGY

Clinical Findings

- Abnormal liver function tests
- Jaundice
- Ascites and edema
- Hepatic encephalopathy
- Portal hypertension and varices
- Vitamin/mineral deficits
- Glucose intolerance or fasting hypoglycemia

Nutrition Assessment

- Serial monitoring of body weight and anthropometry
- Dietary intake
- Subjective global assessment
- Laboratory tests for nutritional deficiencies such as vitamins, magnesium, iron, and others

MANAGEMENT

Medical Management

- Diuretic therapy
- Medication for encephalopathy (e.g., lactulose, rifaximin)
- Management of portal hypertensive bleeding (e.g., pharmacologic therapy, shunts, banding)
- Monitoring of blood glucose

Nutrition Management

- Increased energy intake via small, frequent meals
- Sodium restriction for fluid retention
- Fluid restriction for hyponatremia
- Carbohydrate-controlled diets for hyperglycemia
- Vitamin and mineral supplements
- Oral liquid supplements or enteral (tube) feeding

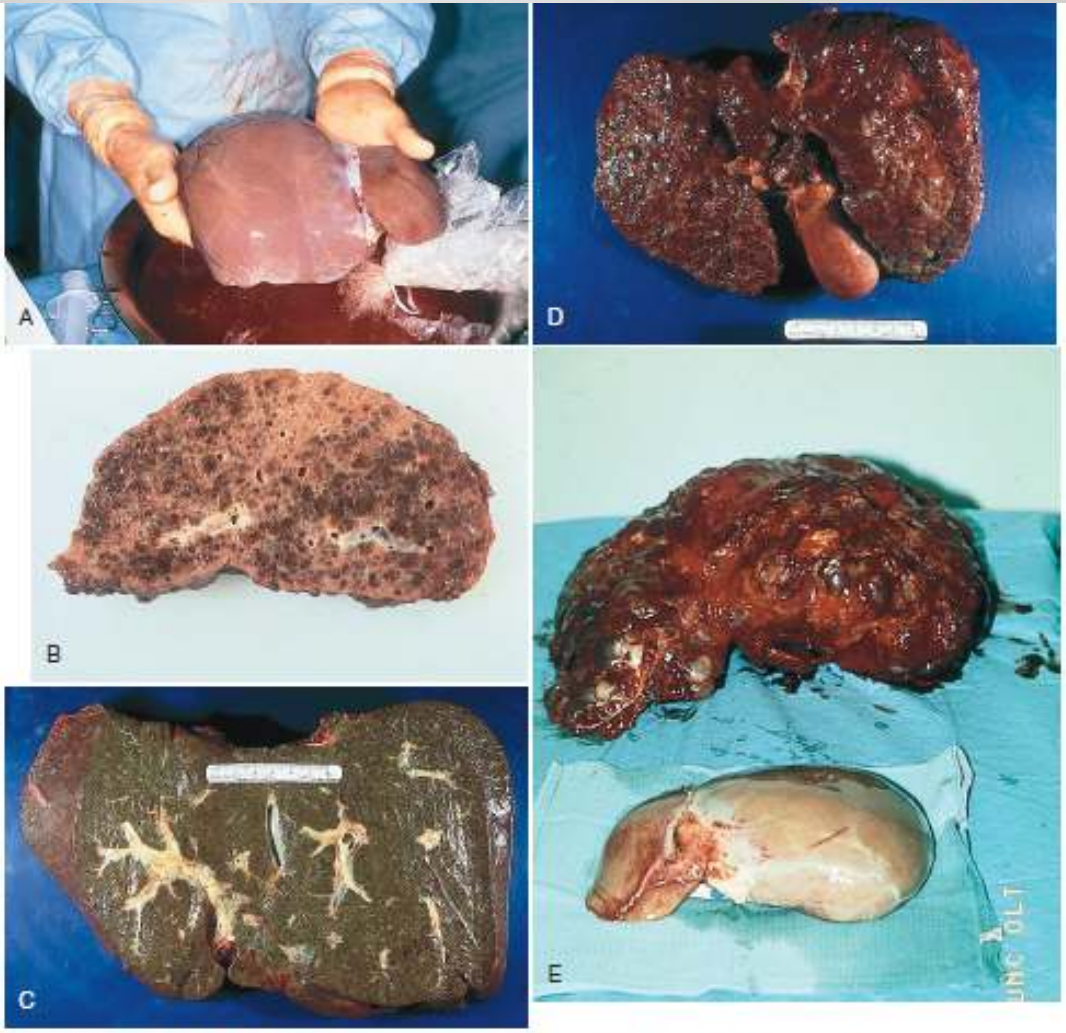
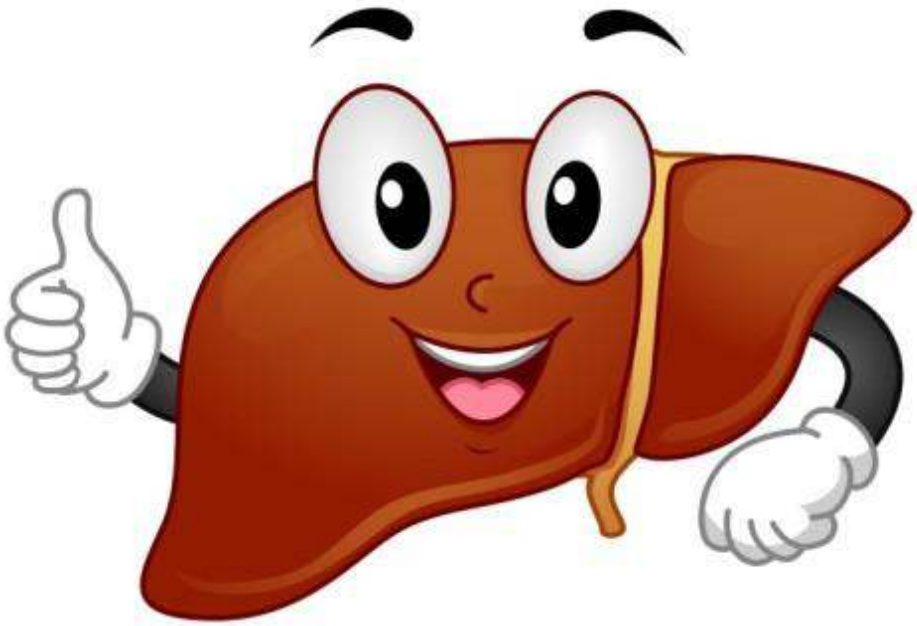


FIGURE 29-1 **A,** Normal liver. **B,** Liver with damage from chronic active hepatitis. **C,** Liver with damage from sclerosing cholangitis. **D,** Liver with damage from primary biliary cirrhosis. **E,** Liver with damage from polycystic liver disease *(background)* and normal liver *(foreground)*. (Courtesy Baylor Simmons Transplant Institute, Baylor University Medical Center, Dallas, TX.)



TERIMA KASIH