

肝臟、膽道系統和胰臟
Diseases of the Liver,
Biliary tract,
and Pancreas

病理學科 劉蓓麗醫師

E-mail: lilyliew@tmu.edu.tw

Tel: 27361661#3143

*Reference: Pathology for the Health-Related
Professions*

大綱及摘要 (1)

- 肝臟系統：正常解剖構造及生理功能
 - 黃疸 (Jaundice)
 - 肝炎 (Hepatitis): 急性，慢性
 - 肝硬化 (Cirrhosis)
 - 藥物及毒性物質肝疾病
 - 酒精性肝疾病
 - 非酒精性肝疾病
 - 先天性肝疾病

- 免疫性肝疾病
- 細菌性，原蟲類及寄生蟲感染
- 原發性肝臟腫瘤：肝癌
- 轉移性惡性腫瘤
- 肝臟移植

大綱及摘要 (2)

- **膽系統：正常解剖構造**
 - 膽結石 (Cholelithiasis)
 - 膽道癌 (Cholangiocarcinoma)
- **胰臟：正常解剖構造及生理功能**
 - 急性胰臟炎 (Acute pancreatitis)
 - 慢性胰臟炎 (Chronic pancreatitis)
 - 胰臟癌 (Pancreatic carcinoma)
 - 糖尿病 (Diabetes mellitus)

肝臟解剖構造及生理功能

- 1500 gram
- Right upper abdomen quadrant
- **Hilus (肝門):**
 1. Hepatic artery (oxygenated blood)
 2. Portal vein (nutrients absorbed from food)
肝門靜脈/循環
 3. Bile ducts
- 體循環: **Hepatic vein**→ **inferior vena cava**(下腔靜脈)
- 肝門循環 **Portal circulation**
- Hepatocytes, bile ductal cells, sinusoids, veins and arteries
- **Functional unit: hepatic lobules (腺泡)**

肝臟主要功能

1. 碳水化合物代謝
2. 脂肪代謝
3. 蛋白質代謝&合成：all major plasma proteins except immunoglobulins
4. 膽汁(bile)合成：main excretory product of liver
5. 儲存
6. 解毒

Important facts

1. **Digestive tract**消化道: portal veins and bile ducts
2. **Encapsulated, self-contained organ**
3. Uptake, processing and excretion of **bilirubin**膽紅素(heme) released from aged RBCs
4. Source of most **plasma proteins**
5. Rich in **enzymes**, released into circulation when liver cell injury
6. **Metabolizes and detoxifies** drugs, hormones, cytokines
7. Certain **viruses** have tropism for liver
8. Liver cells can **regenerate**
9. **Primary liver tumor is common in Asia**
10. Bile can form **gallstones**

Digestive tract: Portal Vein 肝門靜脈

- Low-pressure venous system
- Nutrients from intestines
- No functional communication with systemic blood flow
- Increased pressure in portal system: open the nonfunctional anastomoses between portal and systemic circulation
 - Blood bypassed liver: metabolites and toxic substances
 - Blood lacks essential metabolites formed in liver

Anastomoses between Systemic and Portal Circulation

Caput medusae 蛇女頭 (periumbilical vein)

Esophageal and gastric varices 靜脈曲張

Splenomagaly 脾臟腫大

Hemorrhoid 痔瘡

Portal Hypertension

- Widens the venous channels connecting the portal and systemic circulation
- **Varicosities** (tortuous and dilated veins 血管扭曲及擴張): esophagus, hemorrhoid and umbilical venous
- **Splenomegaly** (脾腫大)
- **Ascites** (腹水)

Major clinical consequence of portal hypertension

- Hepatic encephalopathy
- Esophageal varices
- Splenomegaly
- Ascites
- Malnutrition
- Hemorrhoid
- Testicular atrophy
- Skin: spider angiomas
- Periumbilical caput medusae

Source of most plasma proteins

- Liver diseases result in hypoproteinemia
- Edema: lack of albumin, reduces oncotic capacity of plasma
- Bleeding tendency: decreased production of coagulation factors
- Aspartate aminotransferase (AST)
- Alanine aminotransferase (ALT)
- Alkaline phosphatase: marker of bile duct obstruction

Liver removes metabolites from circulation

- Accumulation of ammonia and neurotoxin in intestine: coma (**hepatic encephalopathy**)
- Disturbance of sex hormone metabolism
- Estrogen: dilated arterioles surrounded by dilated capillaries in skin (**spider nevi** 蜘蛛痣)
testicular atrophy (睪丸萎縮)
gynecomastia (男性女乳症)

黃疸 (Jaundice)

- Yellow discoloration of skin and mucosa
- Symptom (症狀); not a disease
- 生化上的黃疸：
血漿膽紅素(bilirubin) > 1.2mg/dL
- 血漿膽紅素(bilirubin) > 2.5mg/dL : 鞏膜
及脾臟表顯出異常的黃色
- 黃疸起因於膽紅素代謝異常

膽紅素 (bilirubin)

- 膽紅素起源於**血鐵質(heme, hemoglobin)**的破壞，從脾臟的脾靜脈直接進入肝臟的門靜脈
- **未結合性膽紅素（脂溶性）**與蛋白結合，藉由循環到肝臟，在肝臟與尿甘酸（glucuronic acid）結合
- **結合性膽紅素（水溶性）**會排放到膽汁
- 腸道中，細菌會分解產生尿膽色素原（urobilinogen），大部分排到**糞便**
- 20%urobilinogen吸收進入血液，被肝臟再次分泌（**腸肝循環**）

膽紅素代謝異常

Type of jaundice	Major cause
Prehepatic or hemolytic	hemolysis
Hepatic	viral hepatitis, drugs, cirrhosis, tumors
Posthepatic or obstructive	gallstones, cancer of bile ducts

黃疸的分類: Prehepatic Jaundice

- Hemolysis (溶血)
- Hematoma (血腫)
- Gilbert's disease
- Red blood cells → hemoglobin → bilirubin

黃疸的分類: Hepatic Jaundice

- Viral hepatitis (病毒性肝炎)
- Alcoholic liver disease
- Drug-induced liver disease
- Chronic hepatitis due to various causes
- Cirrhosis (肝硬化)
- Tumors

黃疸的分類: Posthepatic Jaundice

- Gallstones in common bile duct
- Carcinoma of the head of the pancreas
- Carcinoma of the common bile duct
- Carcinoma of the gallbladder (late symptom)

肝炎 (Hepatitis)

- 肝臟的發炎疾病稱為“肝炎”
- 病毒性肝炎是肝炎最常見的原因
- Hepatitis A,B,C,D and E
- Epstein-Barr virus (Infectious mononucleosis), Herpesvirus, Cytomegalovirus, HIV
- Children: measles (麻疹), rubella (德國麻疹), varicella (水痘), yellow fever

Human hepatitis A,B,C,D,E

	HAV	HBV	HCV	HDV	HEV
Family	picorna	hepadna	flavi	viroid	Calici
Genome	RNA	DNA	RNA	RNA	RNA
Size	27nm	42nm	30-60nm	35nm	32nm
Viremia	brief	long	long	Like HBV	brief
transmission 傳染途徑	Fecal/ oral	Parenteral /sexual	Parenteral/ sexual	Parenteral/ sexual	Fecal/ oral
Incubation (days)	15-45	40-180	15-150	30-50	14-60

Human hepatitis A,B,C,D,E

	HAV	HBV	HCV	HDV	HEV
Fulminant hepatitis % 猛爆性肝炎	0.1	1	0.1	10	1-2
Chronicity	No	10%	50%	10%	No
HCC 肝癌 association	No	Yes	Yes	No	No
Chronic carrier 帶原者	No	Yes	Yes	Yes	No
Vaccine available 預防疫苗	Yes	Yes	No	No	No

A型肝炎經口糞傳染，不會導致慢性 肝炎

Incubation period (15-45 days)		Fecal HAV
Acute disease (2-12 weeks)	Jaundice, symptoms	IgM-anti-HAV Total anti-HAV antibody
Convalescence and recovery (months)		Total anti-HAV antibody

B型肝炎

- **B型肝炎的感染非經腸胃途徑**
 1. 急性自限性肝炎
 2. 猛爆性肝炎
 3. 慢性肝炎
 4. 無症狀帶原期
 5. 臨床上不明顯的無症狀感染
- 大部分病人中，急性**B**型肝炎感染是自限性的
- 肝內病毒無法消滅時，會造成永久性**B**型肝炎感染
 1. Hepatitis B surface antigen (HBsAg) 表面抗原
 2. Hepatitis B core antigen (HBcAg) 核心抗原
 3. Hepatitis B e antigen (HBeAg) e抗原

Serologic findings in acute hepatitis B infection

Incubation period		Serum transaminases	4-26 weeks (average 8)
Acute disease	Jaundice symptoms	HBeAg, HBV-DNA, HBsAg IgM-anti-HBc, Anti-HBe	4-12 weeks
Convalescence		IgM-anti-HBc, Anti-HBe	4-20 weeks
Recovery		IgG-anti-HBc, IgG-anti-HBc	Years

C型肝炎 (1)

Incubation period (2-26 weeks)	Serum transaminases	
Acute disease (1-3 weeks)	Jaundice, symptoms	HCV-RNA
Recovery (months to years)		Anti-HCV antibody

C型肝炎 (2)

Incubation period (2-26 weeks)	Serum transaminases	
Acute disease (1-3 weeks)	Jaundice, symptoms	HCV-RNA
Recovery (months to years)		HCV-RNA

肝炎

- D型肝炎只可能發生在B型肝炎病毒上
- 臨床上C型肝炎類似B型肝炎感染
- 臨床上E型肝炎類似A型肝炎感染
- 組織學上急性病毒肝炎，在所有型態上是類似的：
 1. Reversible (可逆性) hepatocellular changes
 2. Irreversible hepatocellular changes
 3. Inflammatory infiltrates (發炎細胞浸潤)
 4. Regeneration of hepatocytes (肝細胞再生)

肝硬化 (cirrhosis)

- 肝硬化是肝臟被彌漫性的肝細胞結節取代，且被纖維化(fibrosis)所分隔
- End-stage liver disease
- Liver transplantation
- 肝硬化特徵：
 - 1.長年的肝細胞破壞
 - 2.慢性發炎刺激纖維化
 - 3.肝細胞再生結節

Pathogenesis of cirrhosis

1. Necrosis of liver cells
2. Inflammation
3. Repair by fibrosis
4. Regeneration

- Micronodular < 0.5cm
- Macronodular > 0.5cm

Scarring and regeneration:

- Irregular shape
- Nodular surface

Complications (後遺症) of cirrhosis

- Ascites (腹水)
- Splenomegaly (脾臟腫大)
- Anastomoses between portal and systemic circulation:
 1. Varices (靜脈曲張): massive hemorrhage
 2. Hepatic encephalopathy: ammonia and neurotoxin from intestines
 3. Hepatic coma (肝昏迷)
 4. Hepatorenal syndrome: cardiopulmonary failure, pulmonary edema

腹水(ascites)的病理機轉

- 腹水是體液在腹腔的聚集
 1. **Portal hypertension**: 因為門靜脈淨水壓的升高造成體液的滲出
 2. **Hypoproteinemia (低蛋白血症)**: 因為血漿滲透壓低造成體液的滲出（和肝細胞白蛋白合成的功能衰竭有關）
 3. **Hepatorenal syndrome**: 因為不明機制造成腎臟將水和鈉得留在體內

Pathogenesis of ascites in cirrhosis

```
graph TD; A[Pathogenesis of ascites in cirrhosis] --> B[Decreased albumin production]; A --> C[Renal Hypoperfusion]; A --> D[Portal hypertension]; B --> E[Reduced oncotic pressure];
```

Decreased albumin production

Renal Hypoperfusion

Portal hypertension

Reduced oncotic pressure

Laboratory Findings in Patients with Cirrhosis

- **Liver cell injury:**
 - serum transaminases (ALT and AST) elevated
- **Loss of liver cell function:**
 - Hypoalbuminemia 低蛋白血症
 - Prolonged prothrombin time (bleeding tendency) 凝血因子缺乏造成出血
- **Loss of detoxification (解毒) function**
 - blood ammonia elevated 血氨濃度上升

酒精性肝疾病

- 酒精是西方國家最常見慢性肝臟疾病的成因
- 酒精會引起脂肪肝，酒精性肝炎及肝硬化
- **Steatosis:**
 - fatty change
 - perivenular fibrosis
- **Hepatitis:**
 - liver cell necrosis
 - Inflammation
 - Mallory bodies
 - fatty change
- **Cirrhosis:**
 - Fibrosis
 - Hyperplasia
 - nodules



非酒精性脂肪肝疾病 (Nonalcoholic fatty liver disease, NAFLD)

- 高血壓、高血脂、高膽固醇、糖尿病及脂肪肝疾病是**新陳代謝症候群 (metabolic syndrome)**
- 廣泛性肝臟破壞的統稱: 單純性脂肪肝，肝臟發炎，肝臟纖維化及肝硬化

非酒精性脂肪肝疾病

- 致病機轉：“兩類撞擊”的假說
 1. “第一類撞擊”：脂肪囤積在肝臟細胞，與胰島素抗性（**insulin resistance**）有密切關係
 2. “第二類撞擊”：合併發炎反應
 - 不正常細胞激素（**cytokine**）產生
 - 氧化壓力反應（**oxidative stress**）

先天性肝疾病

- **Gilbert's Disease**: unconjugated hyperbilirubinemia
- **Hemochromatosis**: iron (鐵) absorption
- **Wilson's disease**: copper (銅) metabolism
- **Alpha₁-antitrypsin deficiency**: emphysema of lung and liver cirrhosis

免疫性肝疾病

	Autoimmunoe hepatitis	Primary biliary cirrhosis	Primary sclerosing cholangitis
sex	females	females	males
age	20-30	30-60	20-40
Bile duct lesions	+/-	++	+
Intrahepatic	-	-	++
Extrahepatic			
Ab to Mitochondria	-/+	++	-
Nuclear Ag	++	+/-	-
Smooth muscle	++	-	-
Steroid	++	-	-

肝臟的感染

- 經由三個途徑：
 1. 上行性傳播，由膽道傳入，常見於膽道阻塞
 2. 腹部膿瘍，經門脈血管（門脈膿血症）進入肝臟
 3. 因敗血症造成全身性血液傳染，導致嚴重急性肝衰竭
 4. 直接侵入 direct inoculation (wounds)
- Gram-negative enteric bacteria: E.coli
- Amebic abscess (膿瘍)

肝腫瘤

- 良性肝腫瘤：肝細胞腺瘤 (hepatic adenoma)
- 膽道腺瘤 (bile duct adenoma)
- 肝臟血管瘤 (hemangioma)
- 肝細胞癌 (hepatocellular carcinoma)
- 膽道細胞癌 (cholangiocarcinoma)
- 轉移性腫瘤(經由血液傳播至肝臟)：肺、乳房、結腸和胃

Primary hepatobiliary neoplasms

Tumor	Incidence	Risk factors	Markers
Liver cell adenoma	F:M=9:1 Rare	Oral contraceptive	-
Hepatocellular carcinoma	M:F=5:1 Common in Asia	Cirrhosis, HBC, HCV	AFP
Cholangiocarcinoma	M:F=5:1 Common in China	Opisthorchisinesis Primary sclerosing cholangitis	CEA

肝細胞癌 (Hepatocellular carcinoma, HCC)

- Male: female=5:1
- Hepatitis B and hepatitis C infections
- Diffuse infiltrative
- Solitary mass
- Multiple nodules

肝細胞癌

- Alpha-fetoprotein (AFP): useful for early diagnosis
- Weight loss, loss of appetite, nausea, portal hypertension, splenomegaly
- Budd-Chiari syndrome: tumor obstruct hepatic vein, intravenous thrombosis
腫瘤細胞出現在靜脈造成栓塞

肝細胞癌

- Paraneoplastic syndrome:
 1. Secrete insulin-like growth factors (hypoglycemia)
 2. Erythrocytosis
 3. Hyperestrinism
 4. Hypercholesterolemia
 5. hypercalcemia

肝臟移植

- 肝臟移植容易造成排斥和原生病症的原發
- Immune response: corticosteroids and immunosuppressive cytotoxic drugs
- Destruction of bile ducts and intrahepatic blood vessels
- Nosocomial (病院的) infection: cytomegalovirus, herpesvirus, fungal infection

膽結石 (Gallstones, Cholelithiasis)

- 膽結石可能會阻塞膽道且會促進引起膽囊癌症
- 膽結石可能引起急性膽囊炎
- 慢性膽囊炎和膽結石有關
- 總膽管的阻斷引起阻塞性黃疸

膽結石 (Gallstones, Cholelithiasis)

1. 膽固醇結石 (cholesterol stone) 本質於膽汁內膽固醇溶解度的變化
 - **Four Fs: female, forty, fertile, fat (cholesterol stones)**
2. 色素性結石 (pigmentary stone) 來自於肝臟膽紅素分泌的增加

Types of Gallstones

	cholesterol	black	brown
Components	Cholesterol	Calcium bilirubin, calcium soaps, cholesterol	Calcium bilirubin, calcium soaps, glycoproteins
Location	Gallbladder	Gallbladder	Bile ducts
Incidence	75%	20%	5% (Far East)
Shape/pattern	Solitary, round	Multiple, feceted	Multiple, irregular shape
Radiopaque	30%	>50%	10%
Risk factors	Female Obese Fertile >40 y/0	hemolysis cirrhosis	infection

Four contributing factors for cholelithiasis

1. Biliary lipid
2. Supersaturation: mixed micelles, bile salts, lecithin, cholesterol
3. Gallbladder hypomotility and cholesterol nucleation
4. Accretion: mucus hypersecretion, gallbladder hypomotility, calcium salts

Clinical Features

- Cholecystitis (inflammation of gallbladder)
- Acute cholecystitis: gangrene, rupture, cholecystoenteric fistula, gallstone ileus
- Chronic cholecystitis: porcelain gallbladder (瓷器的)

Complications of gallstones

- **Cholecystitis**
 - Secondary infection of ulcer
 - Gallstone
 - Decubital ulcer
 - Carcinoma
 - Cholecystoenteric fistula
 - Obstruction
 - Pancreatitis
- **Secondary obstruction**
 - Cholangitis and liver abscess
 - Biliary cirrhosis
 - Obstructive jaundice

Carcinoma of Biliary Tract

- Cholangiocarcinoma: intrahepatic biliary tract
- Carcinoma of gallbladder: 和膽結石有關
- Carcinoma of extrahepatic bile duct

胰臟的正常解剖構造及生理功能

- Retroperitoneum (後腹腔) of upper abdomen
- Pancreas: head, body and tail
- Pancreatic duct and ductules
- Pancreatic acini
- Islets of Langerhans

正常解剖構造及生理功能

- **Exocrine (外分泌) and endocrine (內分泌)**
- **Exocrine (98%): acini, ductules and ducts**
 - amylase, lipase, peptidases
 - pancreatic juice: controlled by vagus nerve
 - bicarbonate, cholecystokinin and secretin
- **Endocrine: islets of Langerhans (藍氏小島)**
 - insulin, glucagon, somatostatin

Overview of major diseases of pancreas

1. Part of digestive tract
 - pancreatic juice; malabsorption and diarrhea
2. Symptoms are basic anatomic facts
 - Obstructive jaundice, duodenal obstruction and retroperitoneal nerves invasion
3. Pancreatic juice contains inactive proenzymes:
activated in intestines
 - Enzymatic destruction

Overview of major diseases of pancreas

4. **Pancreatic enzymes**: trace amount in blood
5. **Poor prognosis of pancreatic cancer**
6. **Endocrine tumors**: slow dividing cells with less aggressive
7. **Insulin (胰島素)**: most important hormone
 - Metabolism of carbohydrates and lipids
 - Diabetes mellitus

胰臟炎

- Sterile chemical inflammation
- Tissue destruction: digestive enzymes released from damaged exocrine cells
 - Acute pancreatitis
 - Chronic pancreatitis

急性胰臟炎

- 組織的酵素性壞死 (necrosis)
- Autodigestion: premature activation of proenzymes within pancreas cause tissue lysis

Causes of acute pancreatitis

1. Common (95%):

Alcohol

Bile stones

Unnknown (15%)

2. Rare (5%):

Trauma

Surgery (resection of pancreas)

Drug-induced (diuretics, oral contraceptives)

Metabolic (hyperlipidemia); Infection (mumps)

Pathogenesis of acute pancreatitis

- **Bile stones**
- **Alcohol**
- **Overeating increased demand**
- Viruses
- Drugs
- Trauma, surgery
- **Acinus: necrosis, leakage of enzymes**
- **Enzymatic fat tissue necrosis**
- **Vessel wall necrosis: hemorrhage, enzymes in bloodstream**

急性胰臟炎: Pathogenesis

- Obstruction of **main pancreatic duct** is important cause of pancreatitis
- Reflux of bile into pancreas
- Mechanical disruption
- Chemical injury
- Overstimulation of pancreatic cells

急性胰臟炎

- Tissue damage mediated by pancreatic digestive enzymes
 1. Activation of **trypsinogen to trypsin**: tissue necrosis
 2. **Elastase**: blood vessels
 3. **Lipase**: fat necrosis
- Pseudocysts (假性囊腫), dystrophic calcification (不良鈣化), calcium soaps
- 後遺症: Peritonitis, Abscess, Chronic pancreatitis

急性胰臟炎的臨床症狀

- Sudden onset
- Abdominal pain and distension, nausea and vomiting
- Syncope and shock
- Peritonitis (腹膜炎)
- Leukocytosis (白血球上昇), amylase↑, lipase ↑
- No effective treatment
- High recurrence rate

慢性胰臟炎

- Irregular fibrosis
- Progressive, irreversible
- Male: female= 3:1
- Insidious onset (狡猾的症狀或惡化)
- **Alcohol abuse**
- 20% presented with no risk factors or preexisting disease: **idiopathic cause** (不明原因)

慢性胰臟炎: Pathology

- Fibrotic and firm
- Dilated main pancreatic duct
- Stones (+)
- Fibrosis, pseudocyst, calcification

慢性胰臟炎: Clinical Features

- Pain: epigastric and back
- Exocrine pancreatic insufficiency: malabsorption and steatorrhea
- Endocrine insufficiency: diabetes

胰臟：小結論

- 急性胰臟炎，導致組織的酵素性壞死
- 慢性胰臟炎，主要起因於慢性酒精濫用
- 慢性胰臟萎縮，發生於惡腫性纖維化時
- 良性胰臟腫瘤是不常見的

胰臟癌

- >95% pancreatic tumor are malignant epithelial neoplasms: **adenocarcinoma**
- Solid (60%): pancreatic head
- Diffuse (25%)
- Cystic tumors are rare
- Derived from **pancreatic ducts: exocrine** part
- Functionally silent
- Enzymes (-)
- Hormones (-)

胰臟癌

- Risk factors: smoking, chronic pancreatitis
- Disease of old age
- Male: female= 3:1
- 60% located in head of pancreas
- Metastasis: lymph node, lungs, bone
- Weight loss, loss of appetite, nausea, vomiting, jaundice
- Surgical resection
- 5-year survival rate is <5%

胰臟癌：小結論

胰臟癌盛行率逐漸升高：抽菸

1. 阻塞性黃疸
2. 局部侵犯
3. 淋巴結轉移
4. 血行性轉移
5. 症狀：體重減輕、食慾不振、上腹部持續性疼痛、移行性靜脈血栓（Trousseau's syndrome）

內分泌性胰臟細胞

Islets of Langerhans

1. Alpha cells (20%): glucagon
2. Beta cells (70%): insulin
 - Metabolism of carbohydrates, lipids and amino acids
3. Delta cells (10%): somatostatin

內分泌性胰臟腫瘤

- **Islet cell tumors**: endocrine cells in islets of Langerhans
- **Insulinomas**, gastrinomas (Zollinger-Ellison syndrome), glucagonomas, somatostatinomas, vipomas
- Benign or low-grade malignant

內分泌性胰臟腫瘤

- Better prognosis
- Hormonally active
- Multiple, associated with tumors of other organs:
multiple endocrine neoplasia syndrome type I
(MEN I)

糖尿病的分類

Primary DM	Secondary DM	Special form
Type 1 (insulin-dependent)	Pancreatic diseases Chronic pancreatitis Tumors	Gestational
Type 2 (non-insulin-dependent)	Endocrine diseases Acromegaly Cushing's syndrome Pheochromocytoma	Impaired glucose tolerance
	Drugs: Corticosteroids; Diuretics; Antihypertension	
	Insulin receptor deficiency	
	Genetic syndromes Hemochromatosis Hyperlipidemia	

第一型vs.第二型糖尿病

第一型	第二型
兒童/青少年	中年晚期/老年期
瘦	胖
酮酸中毒: 常見	罕見
嚴重胰島素缺乏	胰島素相對缺乏; 週邊器官抗性
胰島素細胞抗體 (+)	胰島素細胞抗體 (-)
自體免疫機制	非自體免疫機制
遺傳: HLA-DR	多基因遺傳

糖尿病 Diabetes Mellitus

- **第一型糖尿病**：一種器官專一性自體免疫疾病
- **第二型糖尿病**：週邊組織對胰島素產生抗性而造成
- 糖尿病的罹病率和死亡率，主要肇因於組織結構的併發症
- 糖尿病患者特別容易遭到**感染**
- 非常嚴重的**粥狀動脈硬化**

Pathogenesis (1)

Insulin: carbohydrates, lipid, amino acids metabolism

1. Absolute deficiency of insulin: islet cell destruction cause lack of beta cells
2. Relative deficiency of insulin: demand for insulin > supply
3. Interference with insulin binding to target tissues: tissue resistance (組織抗性)
 - insulin receptors
 - antibodies to insulin or insulin receptors

Pathogenesis (2)

4. Hyperglycemia, glycolysis, glycogenesis, lipogenesis
5. Diabetes has a genetic predisposition: type 2
6. Diabetes develops under the influence of some environmental factors: viral infection, seasonal

Complication

- **Cardiovascular system**

1. Atherosclerosis
2. Gangrene (壞死)

- **Kidneys**

1. Glomerulosclerosis
2. Polynephritis
3. Papillary necrosis

Eyes:

1. 視網膜病變
2. 黃斑病變
3. 白內障
4. 青光眼

Nervous system

1. Microangiopathy:
focal ischemia
2. Peripheral neuropathy

糖尿病

- 微細血管疾病是糖尿病的一項重要特徵，產生許多病理併發症
- 末梢神經病變是糖尿病患者，足部難癒性潰瘍的重要成因
- 糖尿病腎病變是糖尿病的一個主要死因

Clinical Features

- Polyuria 多尿
- Polydipsia 多渴(excessive thirst)
- Polyphagia 多吃
- Bacterial infection