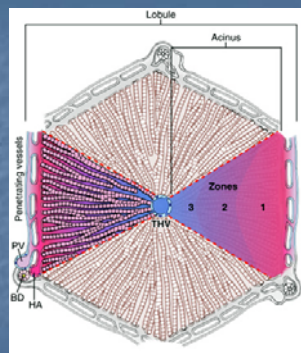


## Disorders of the Liver and Pancreas

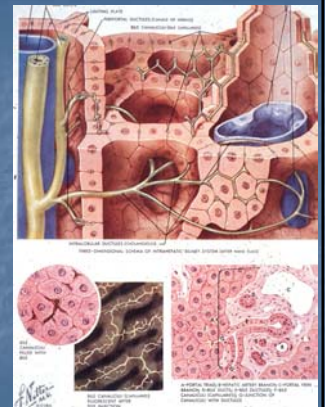
### Liver Lobule

- Hexagonal plates
- Sinusoids
- Triads
  - Bile duct branch
  - Arteriole
  - Venuole
- Blood flows from periphery to
- Central vein
- Space of Dissé



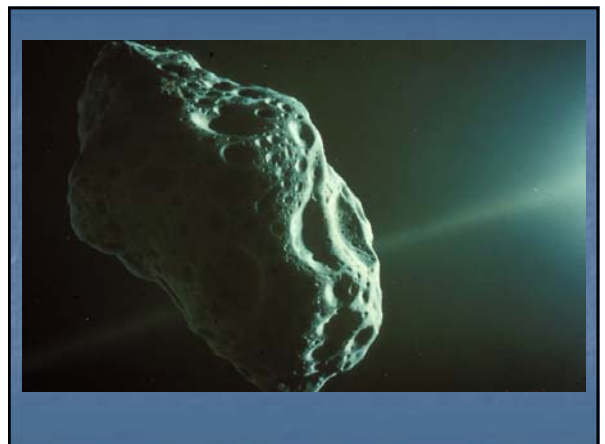
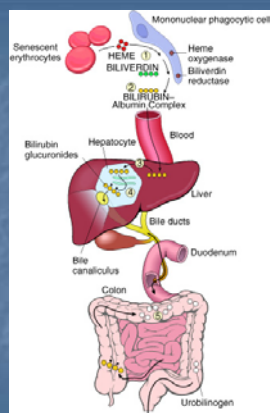
### Lobular Microanatomy

- Hepatocytes
- Canaliculi
- Triad
  - Arteriole
  - Venuole
  - Bile Duct Branch



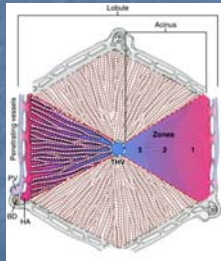
### Bile Formation

- Hemoglobin breakdown
- Conversion in liver to water soluble form
  - Bilirubin
  - Serum levels help diagnose liver disease
- Excretion in bile
- Some is reabsorbed



## Zonal Pattern of Injury

- Peripheral
- Middle
- Central
- Triadal
  - Limiting plate
- Piecemeal necrosis

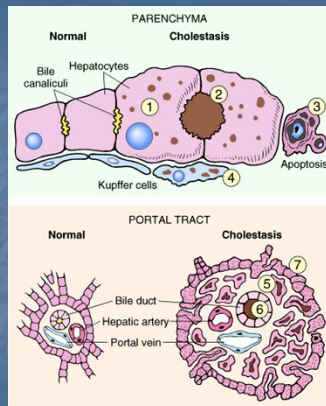


## Liver Injury, The Basics

- Lots of stuff injures the liver.
- It's the great detoxifier
- Chronic injury
  - Fibrosis
  - Regeneration
    - Providing the underlying framework remains

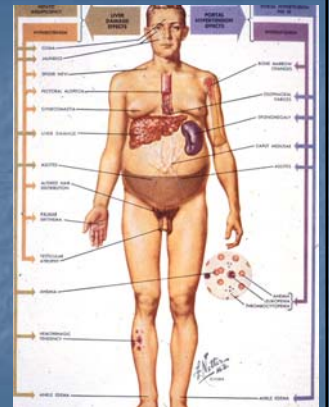
## Cholestasis

- Slowed bile excretion
- Intracellular
  - Drugs
  - Viral infection
- By means of ducts
  - Drugs
  - Obstruction



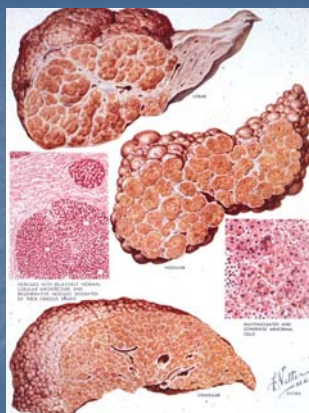
## Cirrhosis

- Many things may lead to cirrhosis
- Common features
  - Irreversible
  - Chronic inflammation
  - Scarring (fibrosis)
  - Parenchymal loss
  - Regenerative nodules
  - Altered vascularity
- Symptoms
  - Ascites
  - Gynecomastia
  - Esophageal varices
  - Splenomegaly
  - Caput medusae



## Cirrhosis

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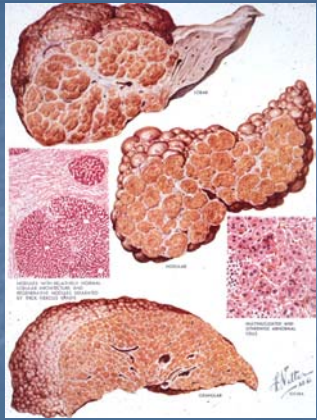
## Cirrhosis

- Irreversible
- Scarring
- Botched regeneration
- Vascular rearrangements
  - Caput medusae ->
- Ascites ->
- Low albumin
- Venous portal hypertension



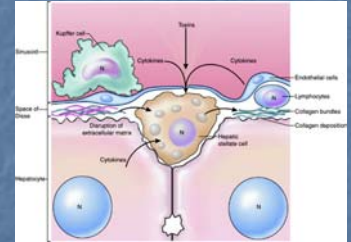
## Common Etiologies

- Inherited
- Pigmentary
- Post necrotic
- Chronic viral
- Nutritional



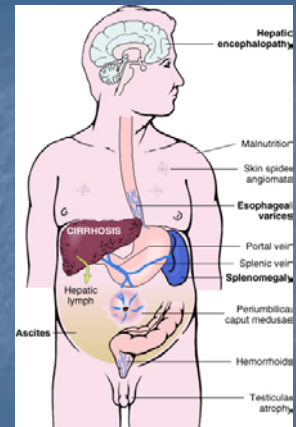
## Cirrhosis

- Stellate cell becomes real important
- Normally stores vitamin A
- Lymphocytes turn him into a collagen making machine



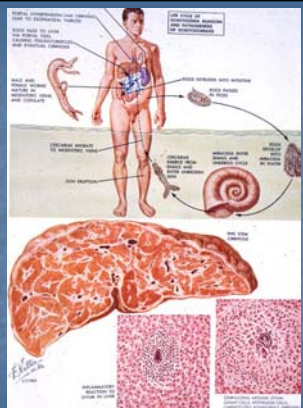
## Sequence of Events

- Liver cell injury
- Cycle of chronic inflammation
  - Destruction of underlying architecture
  - Fibrosis
  - Attempts to regenerate
  - Vascular reorganization leading to shunting
  - Repeat cycle
- Progressive
- Irreversible



## Parasitic

- There are several
- Schistosomiasis
- Clonorchis sinensis



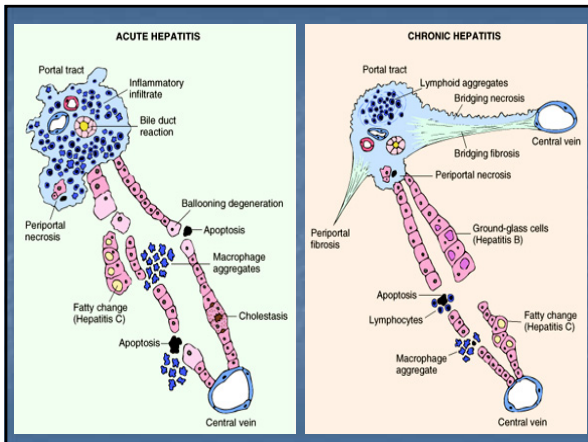


## Inflammation of Liver

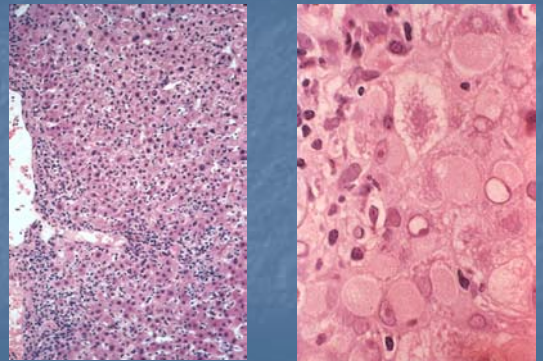
- Very common, lots of things do it.
- Toxins and drugs
- Bacteria
  - Cholangitis
  - Abscesses
- Viruses
  - EBV
  - CMV
  - Hepatic specific
- Parasites
- Autoimmune

## Viral Hepatitis

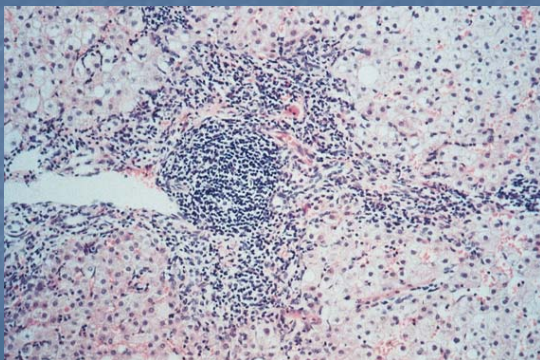
- Generally taken to mean hepatic specific viruses.
- Histologic features common to most
- Acute
  - Necrosis of random liver cells
    - Councilman bodies = bright pink dead cells
  - Diffuse liver cell swelling
  - Bile stasis
  - Portal (triadal) inflammation
- Chronic pattern = persistence or relapse for 6 months
  - Chronic and acute inflammation
  - Piecemeal necrosis
  - Bridging necrosis
  - cirrhosis



## Acute Viral Hepatitis

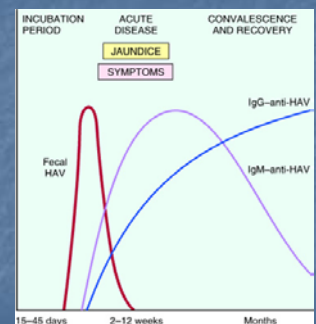


## Chronic or Persistent Hepatitis



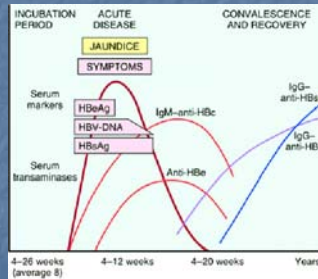
## Hepatitis A

- 'Infectious hepatitis'
- Food handlers
- Virus in stool
- Seafood
- Self limiting
- No chronic state
  - No cirrhosis
- No carrier state
- History and serology
  - IgM
  - IgG
  - Maybe virus



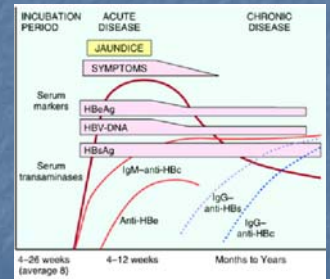
## Hepatitis B

- 'Serum hepatitis'
- Sexually transmitted
- Blood borne
- Longer incubation
- Common in Asia
- Most get over it fine
- Immunologic damage
- Less common
  - Chronic progressive
  - Fulminant failure and death
  - Cirrhosis
  - Chronic carrier state

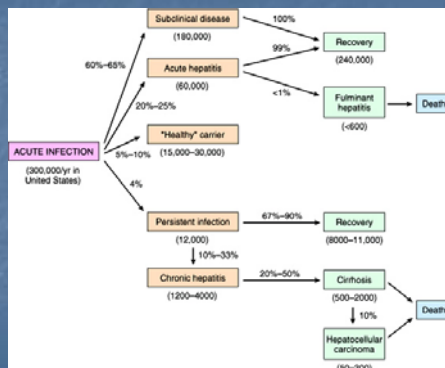


## Chronic Hepatitis B

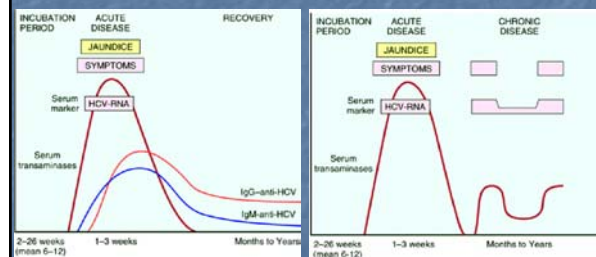
- Infrequently a person develops chronic infection with B.
- Leads to cirrhosis



## Hepatitis B Outcomes



## Hepatitis C

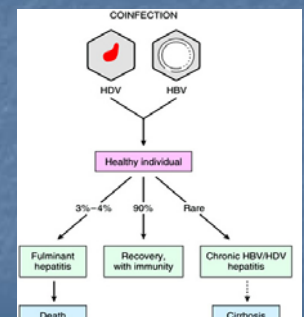


## Hepatitis C

- Very high rate of persistence
- Long incubation period
- Cirrhosis

## Delta Agent

- Incomplete virus
- Needs hepatitis B to replicate
- The two together cause terrible disease.
- Fulminant loss of liver
- Can become infected later if you are a carrier of hepatitis B



## Hepatitis Outcomes

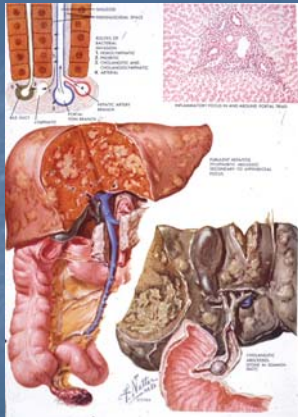
- Asymptomatic infection
- Acute hepatitis like a bad case of the flu
- Overt Jaundice
- Carrier state
- Fulminant liver death
- Chronicity, +/- cirrhosis

## Autoimmune Hepatitis

- Women
- Chronic hepatitis
- No viral markers
- May lead to cirrhosis

## Abscesses

- Bacterial
- Parasitic
- Blood borne
- Ascends ducts



## Drug and Toxin

- Too many to list
- Direct hepatocyte toxicity
- Biliary paralysis
- Conversion to a truly toxic agent

## Reye's Syndrome

- Young kids
- Follows flu
- Got aspirin
- Liver and brain
- Fulminant liver failure

## Alcoholic Liver Disease

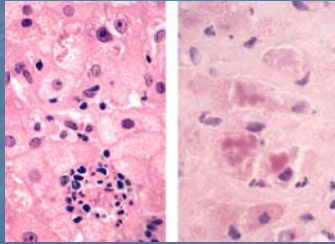
- Acute and chronic
- Acute hepatitis
- Fatty liver ->
- Cirrhosis





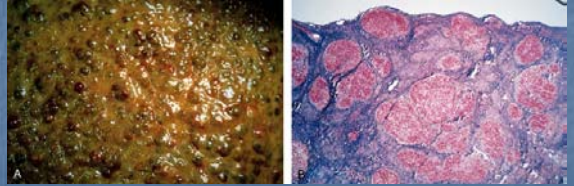
## Acute Alcoholic Hepatitis

- Liver cell necrosis
- Balloon degeneration
- Neutrophils
- Mallory bodies



## Alcoholic Cirrhosis

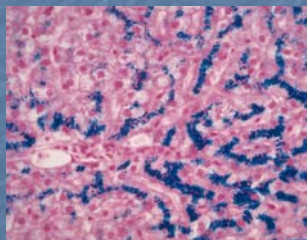
- About 15-20% of alcoholics
- Micronodular pattern, so called 'hobnails'
- Increased portal pressures



## Other Types of Cirrhosis

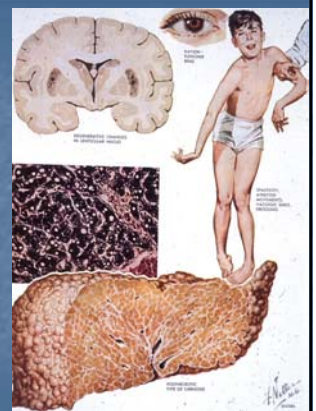
### Pigmentary

- Iron
- Oxidative injury
- Scarring
- Congenital problem with excessive absorption



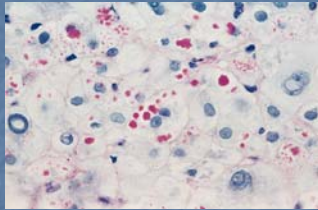
### Wilson's Disease

- Copper metabolism
- Absence of transport protein
- Builds up in various organs
- Cirrhosis
- Brain degeneration
- Corneal ring



## Alpha-1 Anti-trypsin Deficiency

- Neutralizes proteases and elastases
- Made in the liver
- Can't finish the process
- Constipated cells fill up with partially completed anti-trypsin
- Causes cell death and scarring
- Emphysema

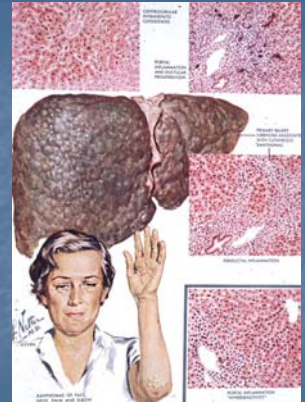


## Intrahepatic Biliary Disease

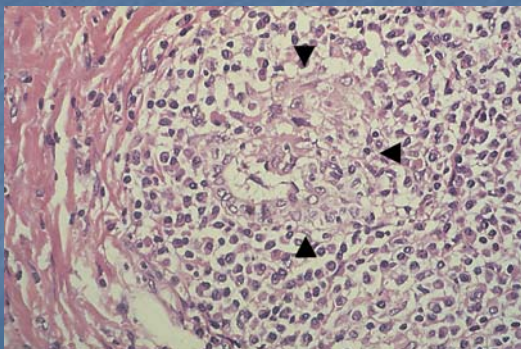
- Drug related
  - Bile stasis
  - Inflammation
  - Scarring
- Primary conditions of the biliary tree
  - Autoimmune, often leading to cirrhosis
  - Sometimes associated with other conditions

## Primary Biliary Cirrhosis

- Women
- Granulomatous destruction of medium sized bile ducts
  - High serum cholesterol
  - Xanthomas
- Cirrhosis
- Antimitochondrial antibodies
- Sicca syndrome
  - Dry eyes & mouth
  - Scleroderma
  - Rheumatoid arthritis
  - All autoimmune in nature

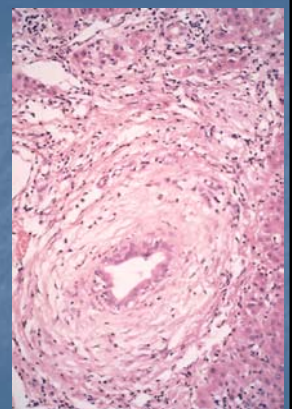


## Primary Biliary Cirrhosis



## Primary Sclerosing Cholangitis

- Concentric fibrosis of smaller bile ducts
  - Onionskin
- Seen with ulcerative colitis
- No antibodies
- No other problems, like Sicca syndrome

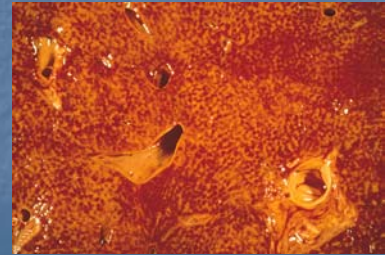






## Vascular Related

- Congestion
- Infarcts
- Cirrhosis altered vascularity of liver

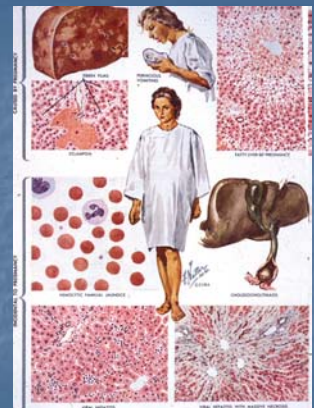


## Hepatic Infarct



## Pregnancy Related

- HELLP syndrome
  - Hepatic enzymes
  - Low platelets
- Eclampsia
  - High blood pressure
  - Fatty liver
  - May be life threatening



## Eclampsia



## Tumors of the Liver

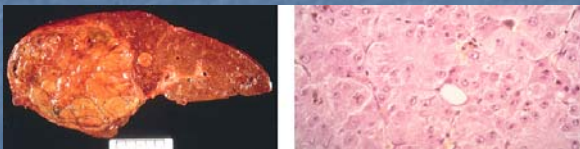
- Hyperplasia vs. true tumor
  - Estrogens
- Benign vs. malignant
- Primary vs. metastatic
  - Bowel
  - Lung
  - Kidney
  - Breast

## Metastatic Cancer



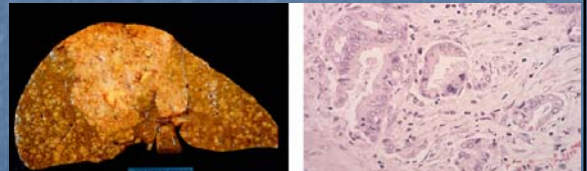
## Hepatocellular Carcinoma

- Malignant hepatocytes
- Associated with
  - Hepatitis B
  - Cirrhosis
- May be multiple foci



## Cholangiocarcinoma

- Comes from bile duct epithelium
- Adenocarcinoma
- Much desmoplasia
- Not associated with the stuff seen in hepatocellular cancer

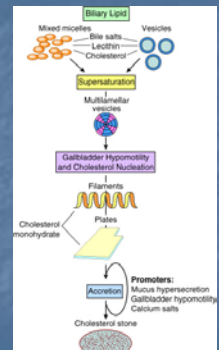
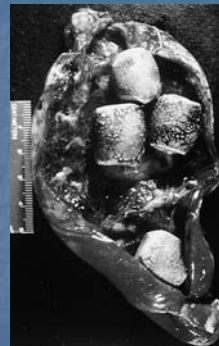


## Gallstones

- Ethnicity
- Age
- Sex
- Fatty foods
- Cholesterol and mixed stones
- Pigmentary stones
- Obstruction
  - Painful
  - Infection



## Gallstones

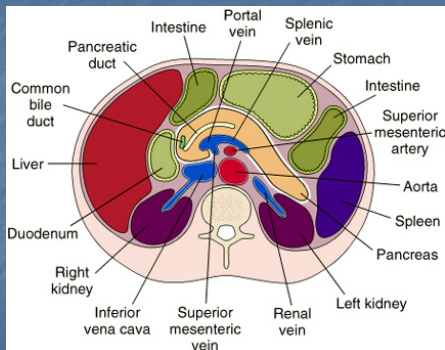


## Cancer of Gallbladder

- Chronic irritation of gallstone
- Chronic cholecystitis
- Presumed oxidative damage
- Cancer

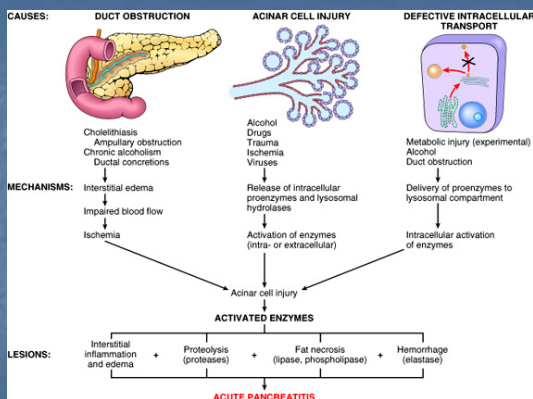


## Pancreas



## Acute Pancreatitis

- Autodigestion
  - Acute inflammation
  - Enzyme activation
  - Fat necrosis with soaponification
  - Hemorrhage
- Causes
  - Obstruction
    - Stone
    - Tumor
  - Alcohol
- Complications
  - Pseudocyst
  - Shock

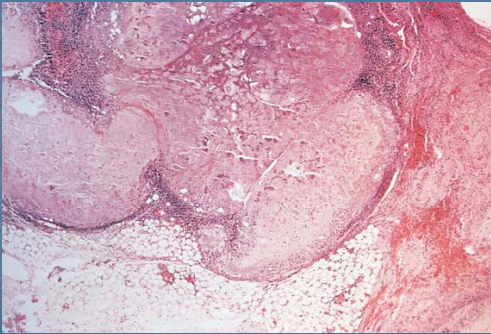


## Acute Pancreatitis





## Soaponification

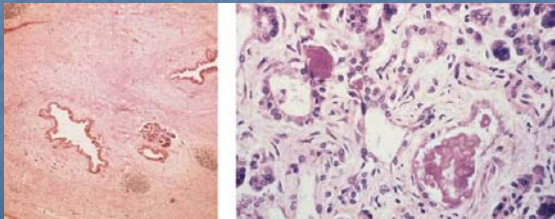


## Pancreatic Pseudocyst



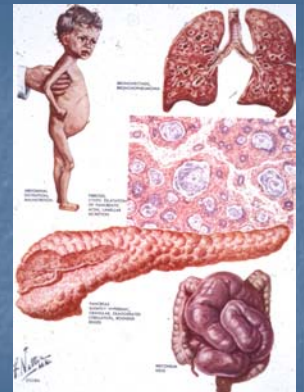
## Chronic Pancreatitis

- Extensive fibrosis
- Calcifications
- Cystic fibrosis



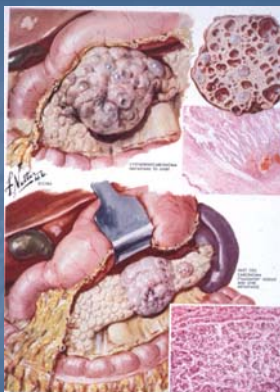
## Cystic Fibrosis

- Inherited problem of chloride pump
- Thick mucus
- Clogs
  - Bowel
  - Pancreas
    - Fibrosis
    - Malabsorption
  - Bronchi



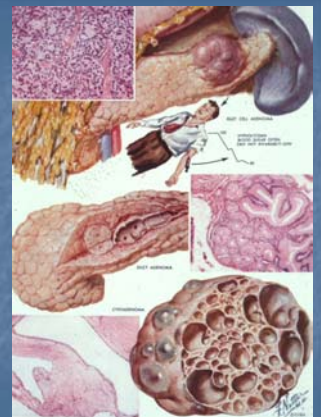
## Pancreatic Cancer

- Often advanced at the time of discovery.
- Adenocarcinoma
- From ductal epithelium
- Spreads to liver
- Not hormonally active
- Painless jaundice

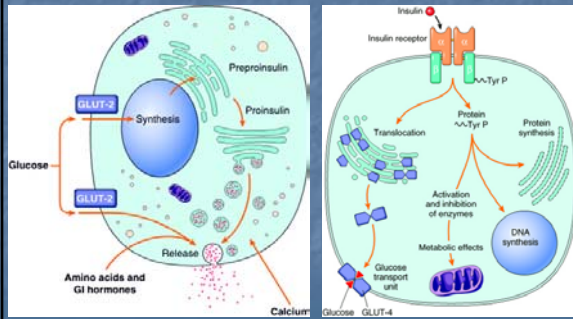


## Islet Cell Tumors

- Insulin secreting
  - Hypoglycemic episodes
- Gastrinoma
  - Zollinger-Ellison
- Glucagonomas
- VIPomas

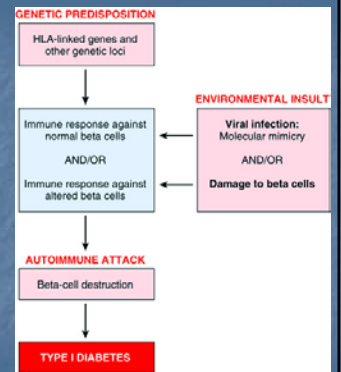


## Insulin Secretion and Peripheral Utilization



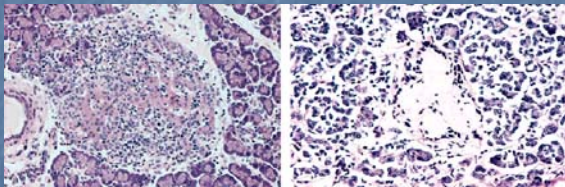
## Type I Diabetes

- Lack of insulin
- Trigger causes autoimmune destruction of beta cells.
- Ketosis prone



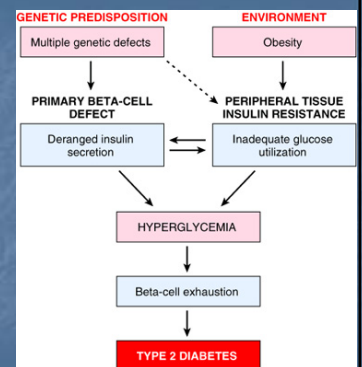
## Type I Diabetes

- Trigger leads to autoimmune destruction of islets



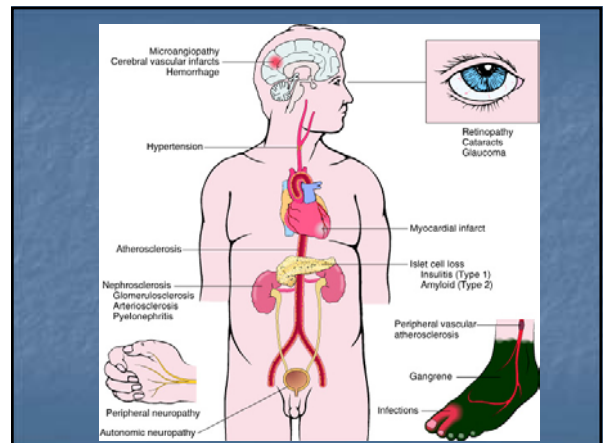
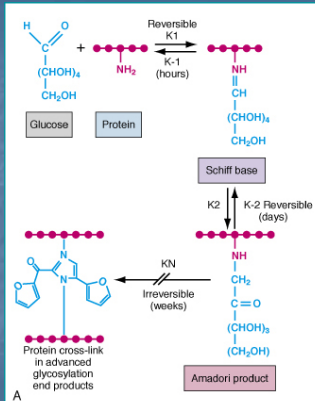
## Type II Diabetes

- Insulin release problem
- Peripheral resistance
- Non-ketosis prone



## Glycosylated Proteins

- Small vessel vascular disease
- This is what diabetes becomes



## Diabetic Vascular Changes

