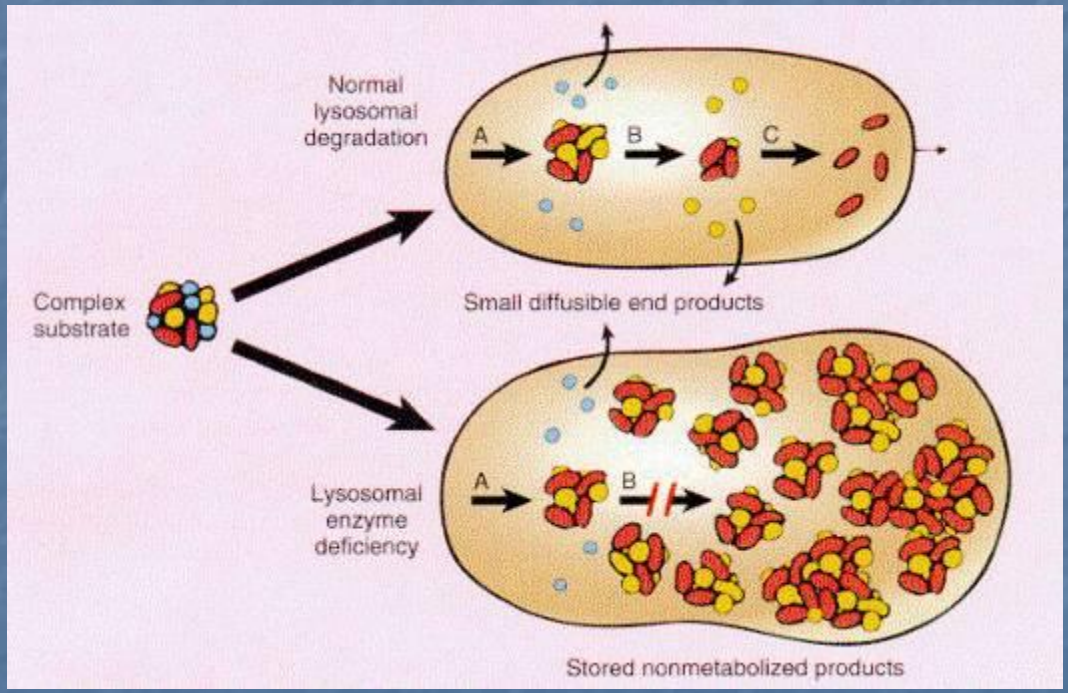
Bone Marrow Disorders of Nonhematopoietic Elements

January 5, 2004

- I. Storage disorders
- II. Noninfectious granulomas
- III. Disorders of bone marrow stroma
- IV. Metabolic bone disease
- V. Metastatic tumors

I. Lipid Storage Disorders

- Hereditary lysosomal enzyme deficiency
  - Autosomal recessive
- Partially degraded lipids accumulate in macrophages
  - Liver, spleen, bone marrow, etc.
    - Organomegaly, cytopenias

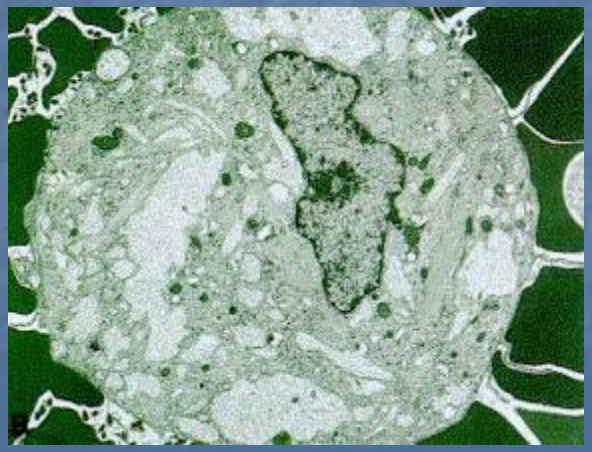


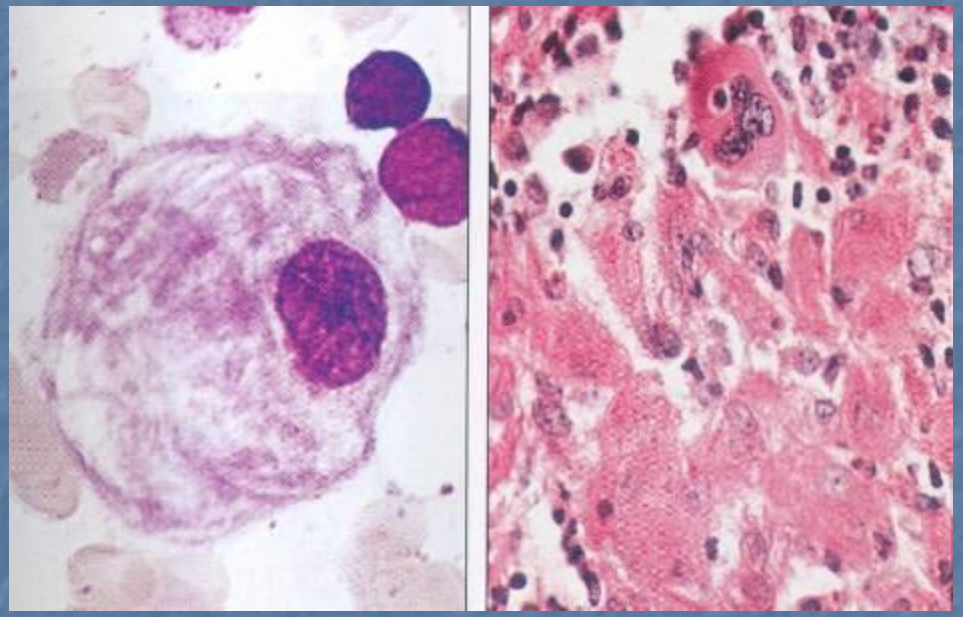
Gaucher's Disease

- Enzyme deficiency= Glucocerebrosidase
- Accumulate= Glucocerebroside
- 3 clinical forms, all AR
  - Type I- adult
  - Type II- acute infantile, neuronopathic
  - Type III- subacute juvenile, neuronopathic

Gaucher's Disease

- Gaucher cell
  - "Wrinkled cigarette paper"
  - PAS positive



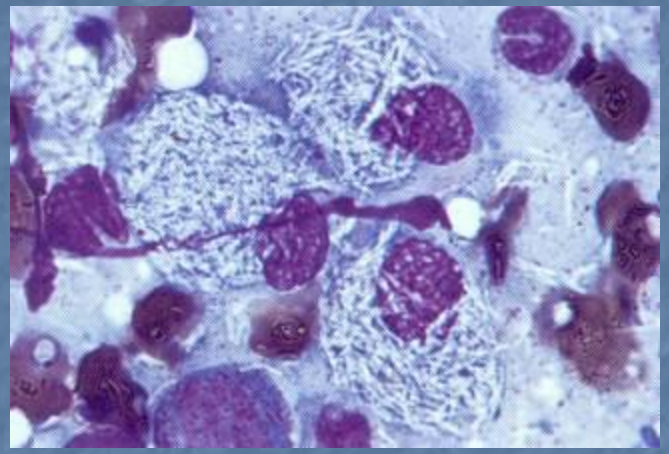


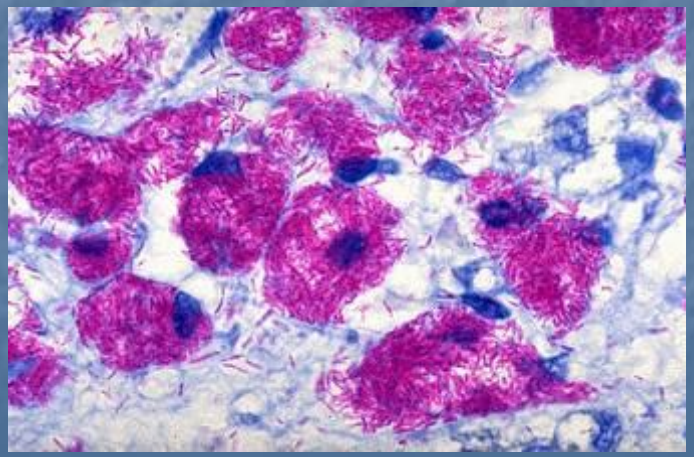
Pseudo-Gaucher Cell

- Indistinguishable from true Gaucher cell
- Conditions with high cell membrane turnover
  - CML, Hemoglobinopathies, Myeloma
  - Increased burden of glucocerebroside

Pseudo-Gaucher Cell

- MAI infection
- Macrophages packed with organisms
  - Negatively staining organisms mimics striations of Gaucher cells.



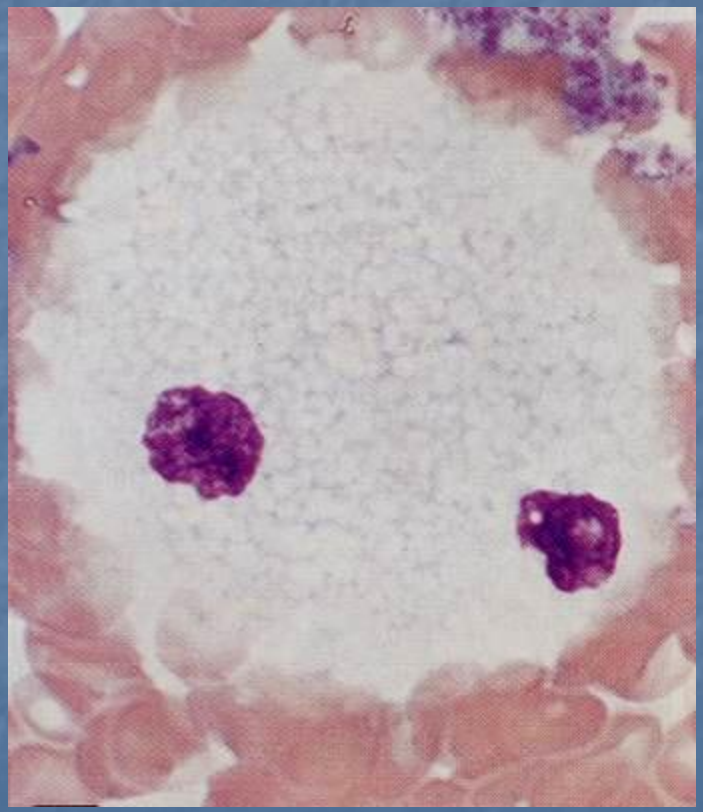


Niemann-Pick Disease

- Enzyme deficiency= Sphingomyelinase
- Accumulate= Sphingomyelin
- 3 clinical forms, all AR
  - Type A- early onset
  - Type B- adult, no cerebral involvement
  - Type C- late onset

Niemann-Pick Disease

- Foamy macrophages
  - "Bubbly" appearance
  - Weak PAS+
  - Oil Red O and Sudan black positive
- Sea blue histiocytes

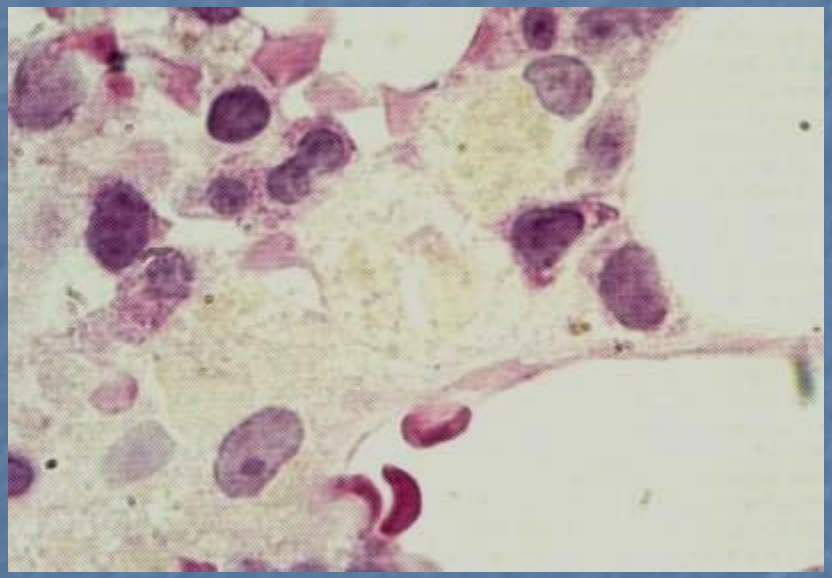


Sea Blue Histiocytes

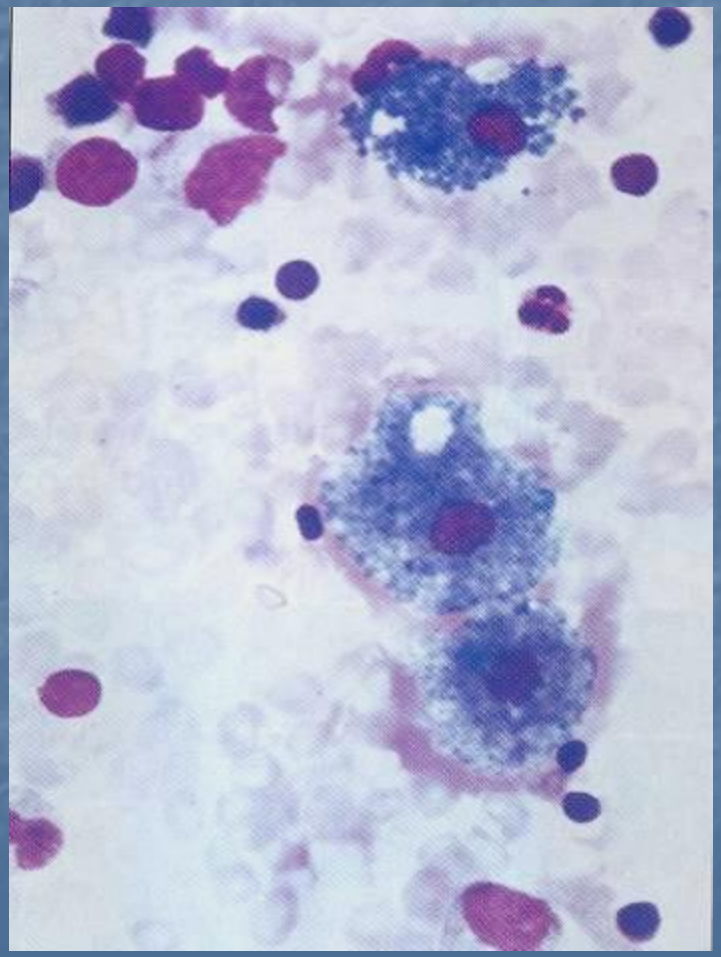
- Macrophages contain ceroid
  - Lipofuscin-like pigment
  - H&E, yellow-brown
  - Geimsa, bright blue green
  - PAS positive
- High turnover states- CML, ITP, SCD
- Lipidoses and hyperlipidemia

Sea Blue Histiocytes

H & E



Geimsa

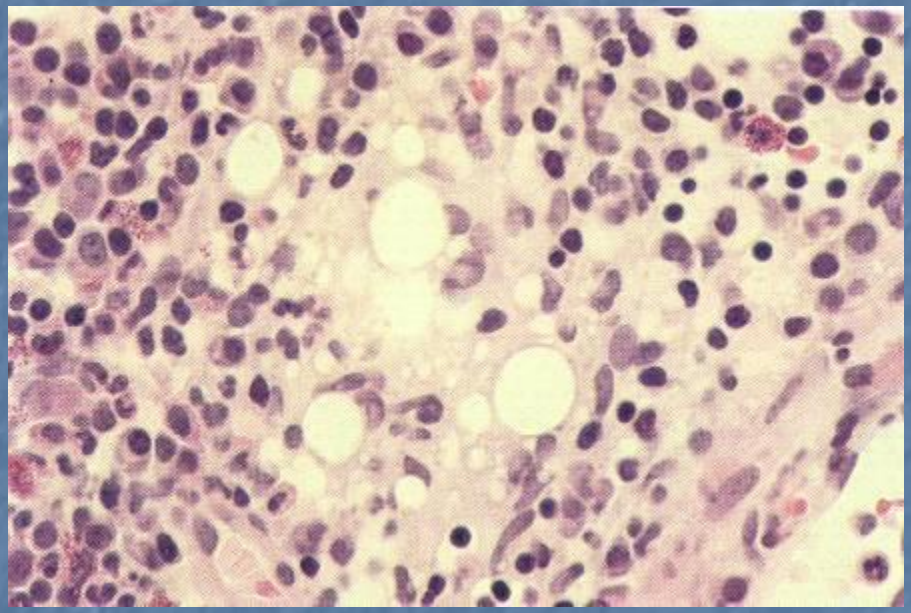


II. Noninfectious Granulomas

- Lipogranuloma
- Sarcoidosis
- Reactive (sarcoid-like) granuloma

Lipogranuloma

- Focal aggregate of macrophages with lipid vacuoles
- +/-Inflammatory cells
- Rare MNGC

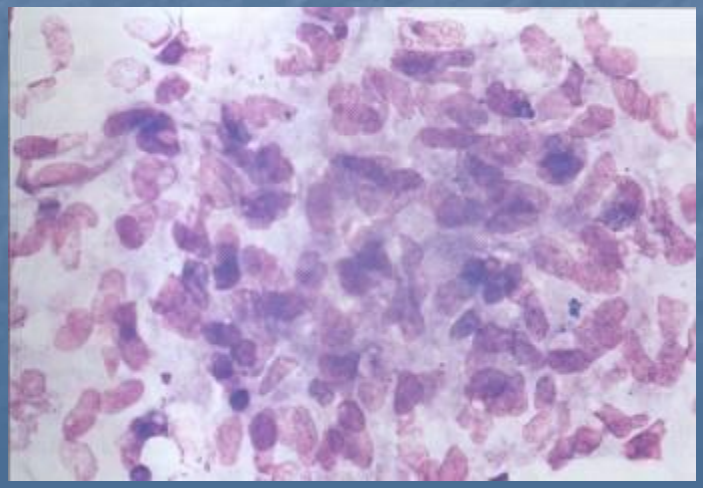


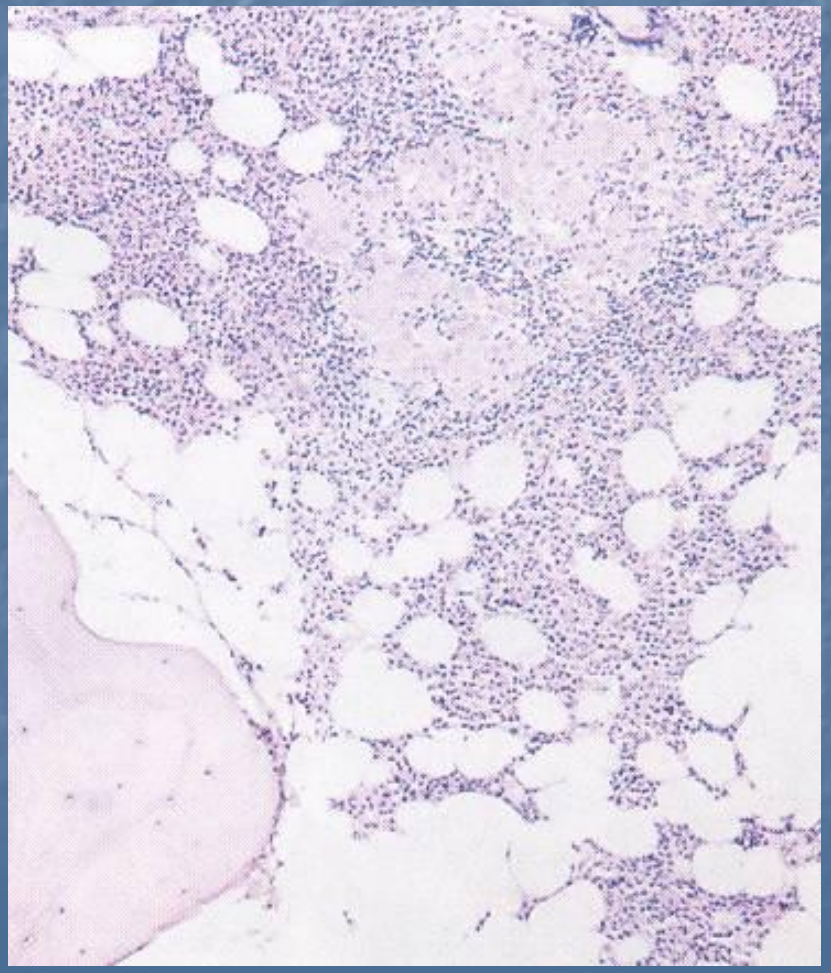
Sarcoidosis

- Epitheloid granulomas in lung and other organs
  - Bone marrow involvement 17%
  - LAD, Spleenomegaly, lymphopenia

Sarcoidosis

- Epitheloid histiocytes
  - Small, noncaseating
  - "Naked" granulomas
- MNGC





Reactive (Sarcoid-like) Granuloma

Table 24.1 Etiology of Bone Marrow Granulomas

Noninfectious Bone Marrow Granulomas	Infectious Bone Marrow Granulomas
Sarcoidosis	Mycobacterial and fungal infections
	Mycobacterium tuberculosis
	Mycobacterium avium-intracellulare
Drugs	*Bacillus* of Calmette and Guerin
Procainamide	*Mycobacterium leprae*
Diphenylhydantoin	*Histoplasma capsulatum*
Allopurinol	*Cryptococcus neoformans*
Phenylbutazone	*Coccidioides immitis*
Chlorpropamide	*Saccharomyces cerevesiae*
Ibuprofen	*Aspergillus*
	Bacterial, rickettsial, and mycoplasmal infections
Autoimmune and hypersensitivity disorders	Brucellosis
Rheumatoid arthritis	Tularemia
Systemic lupus erythematosus	Rocky Mountain spotted fever
Hypersensitivity pneumonitis	Q-fever
Primary biliary cirrhosis	*Mycoplasma pneumoniae*
Crohn's disease	Protozoan infections
	Toxoplasma gondii
Neoplasms	*Leishmania donovani*
Hodgkin's disease	Viral infections
Non-Hodgkin's lymphoma	Infectious mononucleosis
Leukemia	Cytomegalovirus
Metastatic carcinoma	Viral hepatitis

III. Disorders of Bone Marrow Stroma

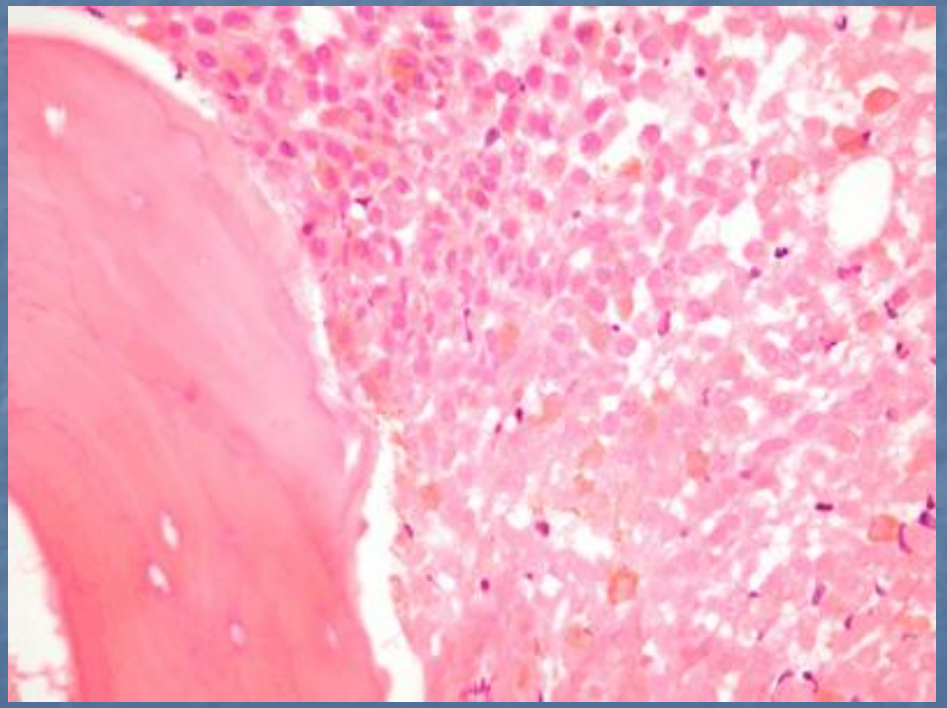
- Bone marrow infarction
- Serous fat atrophy

Bone Marrow Infarction

- Coagulative necrosis
- Associated with neoplastic process, vasocculsive disorders and hemoglobinopathies

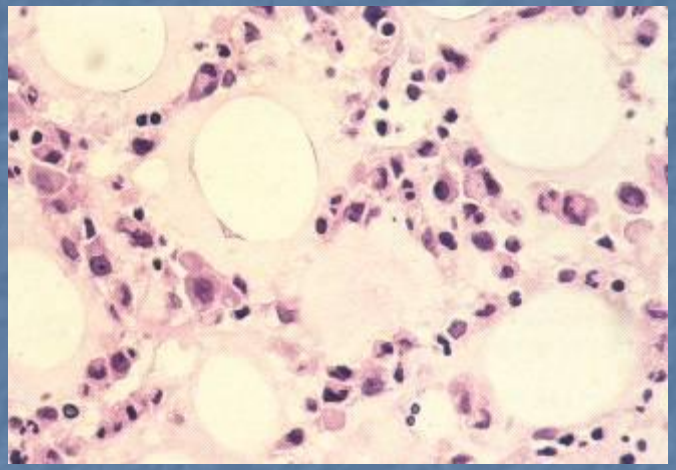
Bone Marrow Infarction

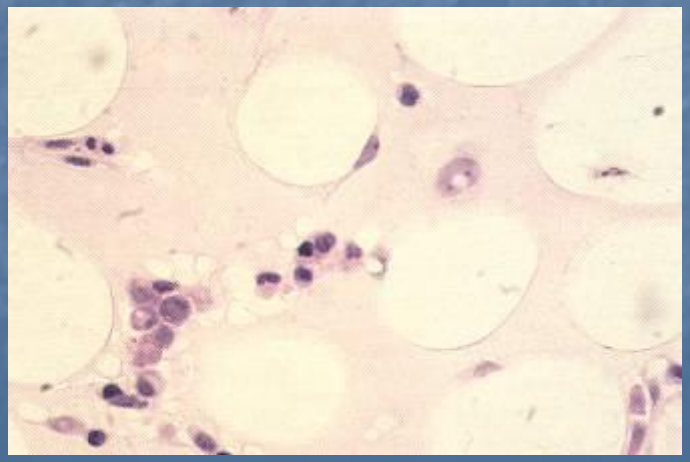
- Homogenously staining
- Ghost cells



Serous Fat Atrophy

- AKA gelatinous transformation
- Associated with starvation and wasting diseases
- Homogenous extracellular substance with watery appearance



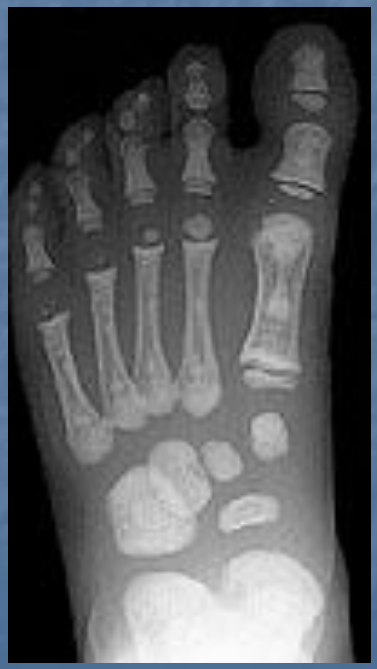


IV. Metabolic Bone Disease

- Osteopetrosis
  - (Albers-Schonberg or marble bone disease)
- Osteomalacia
- Renal osteodystrophy
- Paget's disease
  - (Osteitis deformans)

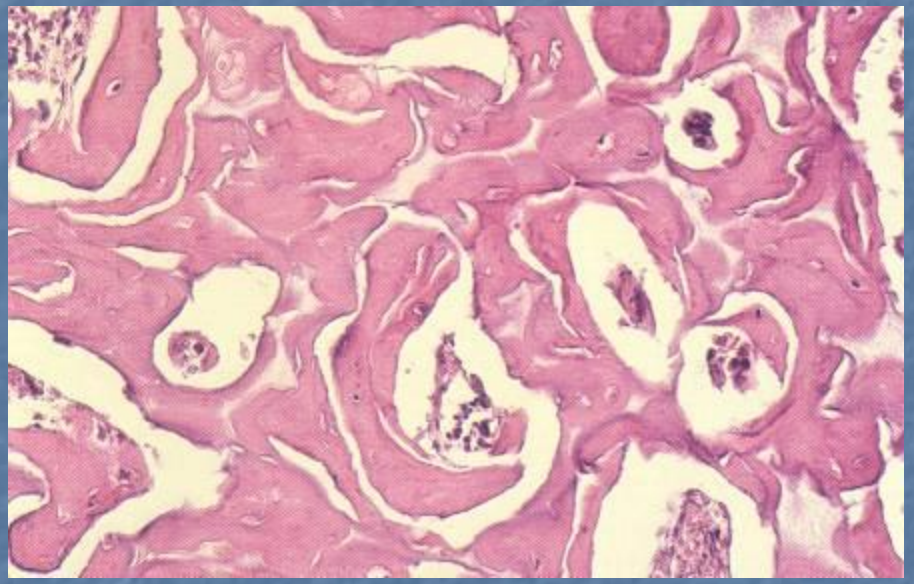
Osteopetrosis

- Functional defect in osteoclasts
  - Abnormal accumulation of dense bone
- AR- severe, infancy
  - Hematopoietic failure
- AD- frequently asymptomatic



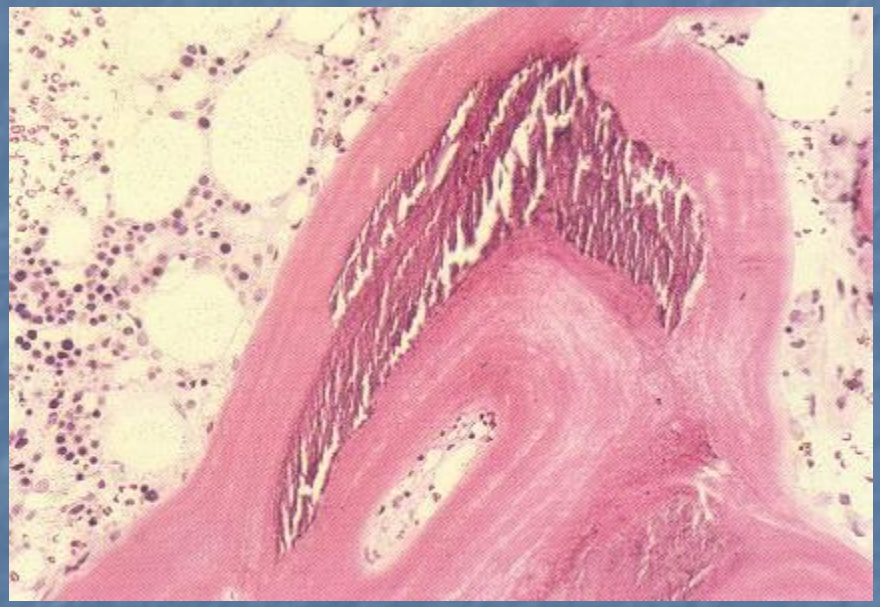
Osteopetrosis

- Dense bone
- Persistence of cartilaginous cores



Osteomalacia

- Defective mineralization of bone
  - Vitamin D deficiency
- Hyperosteoidosis
  - Increased unmineralized osteoid

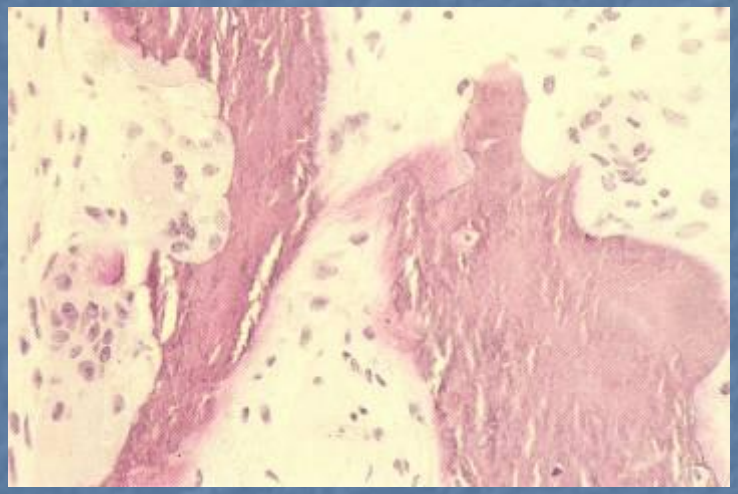


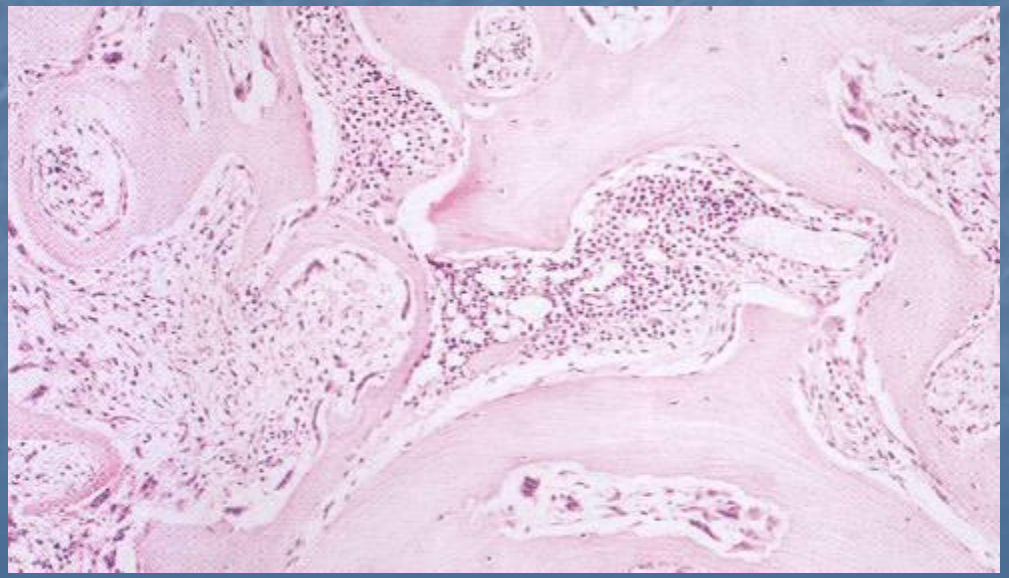
Renal Osteodystrophy

- Chronic renal insufficiency
  - Deficiency of active vitamin D
    - Hyperosteoidosis
  - 2^{o} hyperparathyroidism
    - Increased osteoclast activity- irregular scalloping of bony trabeculae and peritrabecular fibrosis
    - Osteitis fibrosa cystica

Renal Osteodystrophy

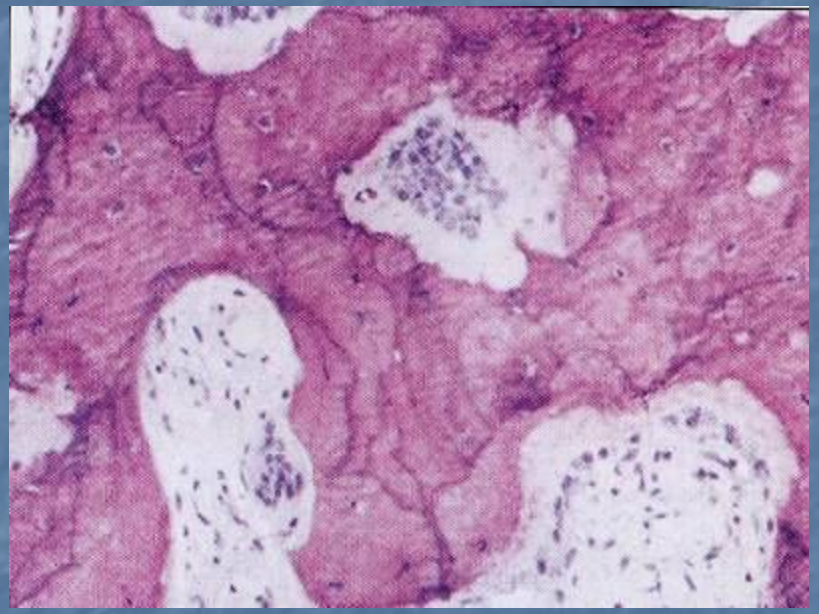
- "Scalloping" of bony trabeculae
- Peritrabecular fibrosis





Paget's Disease

- Disordered bone remodeling
  - Thickened trabeculae
  - Irregular cement lines "mosaic" pattern
  - Osteoblasts and osteoclasts prominent

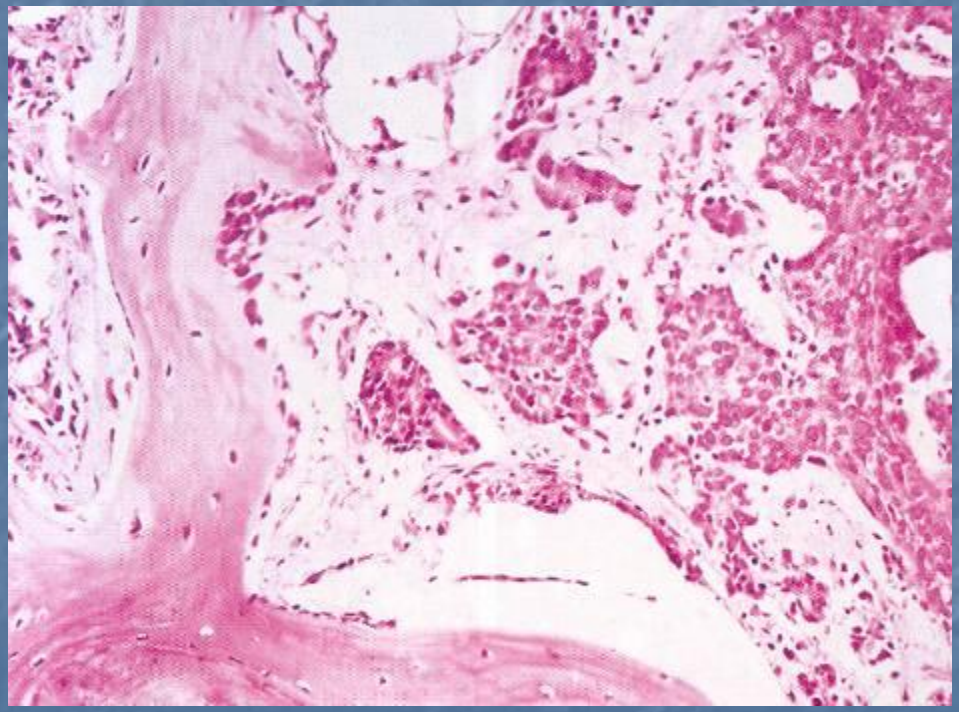


V. Metastatic Tumors

- Adults
  - Breast, prostate, lung and GI carcinoma
- Pediatric
  - Neuroblastoma
- Clues: unexplained fibrosis or necrosis

Metastatic Tumors

Prostate Carcinoma



Artifact