Universitas Kristen Indonesia
Fakultas Kedokteran

SURAT KEPUTUSAN
No. : 181/UKI.F5.D/HKP.3.5.6/2021
tentang

PENUGASAN TENAGA AKADEMIK DALAM MEMBERIKAN KULIAH PAKAR PIMPINAN FAKULTAS KEDOKTERAN UNIVERSITAS KRISTEN INDONESIA

MENIMBANG : Bahwa untuk kelancaran proses belajar mengajar dan meningkatkan mutu pendidi di FKUKI diperlukan penugasan tenaga akademik FKUKI untuk memberi Kuliah Pakar

MENGINGAT :
1. Peraturan Pemerintah No. 60 tahun 1999 tentang Pendidikan Tinggi
2. Surat Keputusan Dekan FKUKI No. 53/SK/FKUKI/11.2006 tanggal November 2006 tentang Pemberlakuan Kurikulum Berbasis Kompetensi (K di FKUKI
3. Surat Keputusan Rektor UKI No. 90/UKI.R/SK/SDM.8/2018 tent pengangkatan Dekan Fakultas Kedokteran UKI
4. Surat keputusan pengangkatan sebagai tenaga akademik

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Semester	genap 2020/2021
Kelas	A : 0,21 SKS
	B : 0,21 SKS
SKS	0,42 SKS

2. Apabila dikemudian hari ternyata terdapat kekeliruan dalam Surat Keputus akan diperbaiki sebagaimana mestinya

Asli Surat Keputusan ini disampaikan kepada yang bersangkutan untuk diketahui

Ditetapkan di : Jakarta
Pada tanggal : 15 April 202
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Bones, Joints and Soft Tissue Pathology

Fajar L. Gultom
Departemen Patologi Anatomik FK UKI
Mei 2021

11 SISTEM MUSKULOSKELETAL

No	Daftar Penyakit	Tingkat Kemampuan
Tulang dan Sendi		
1	Artritis, osteoarthritis	3A
2	Fraktur terbuka, tertutup	3B
3	Fraktur klavikula	3A
4	Fraktur patologis,	2
5	Fraktur dan dislokasi tulang belakang	2
6	Dislokasi pada sendi ekstremitas	2
7	Osteogenesis imperfekta	1
8	Ricketsia, osteomalasia	1
9	Osteoporosis	
10	Akondroplasia	
11	Displasia fibrosa	
12	Tenosinovitis supuratif	
13	Tumor tulang primer, sekunder	
14	Osteosarkoma	
15	Sarcoma Ewing	
16	Kista ganglion	
17	Trauma sendi	3A
18	Kelainan bentuk tulang belakang (skoliosis, kifosis, lordosis)	2
19	Spondilitis, spondilodisitis	2
20	Teratoma sakrokoksigeal	2
21	Spondilolistesis	1
22	Spondilolisis	1
23	Lesi pada ligamentosa panggul	1
24	Displasia panggul	2
25	Nekrosis kaput femoris	1
26	Tendinitis Achilles	1
27	Ruptur tendon Achilles	3A
28	Lesi meniskus, medial, dan lateral	3A
29	Instabilitas sendi tumit	2
30	Malformasi kongenital (genovarum, genovalgum, *club foot, pes planus*)	2
31	*Claw foot, drop foot*	2
32	*Claw hand, drop hand*	2

Otot dan Jaringan Lunak		
33	Ulkus pada tungkai	4A
34	Osteomielitis	3B
35	Rhabdomiosarkoma	1
36	Leiomioma, leiomiosarkoma, liposarkoma	1
37	Lipoma	4A
38	Fibromatosis, fibroma, fibrosarkoma	1

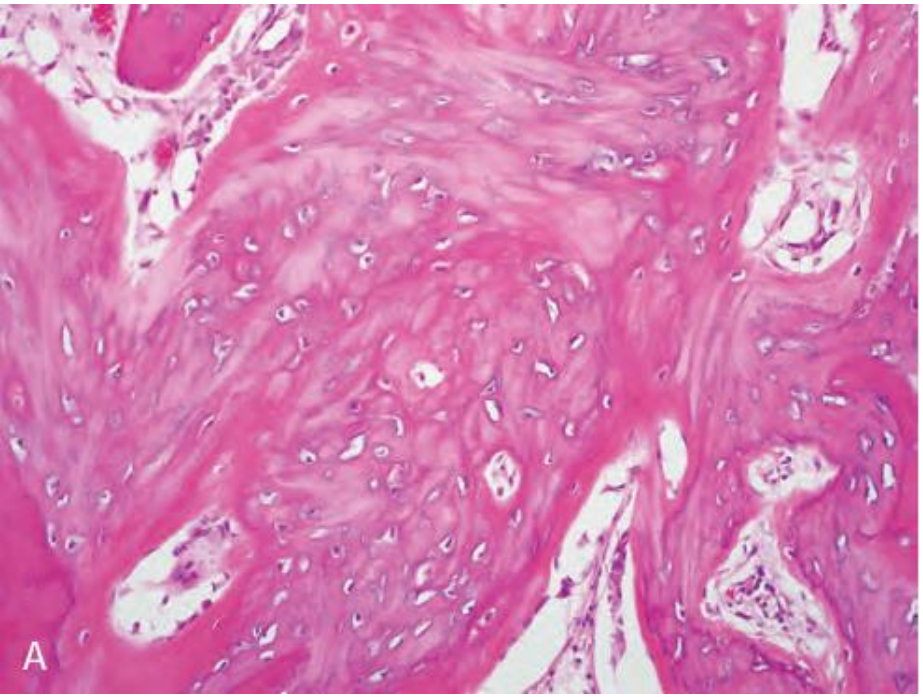
Bone

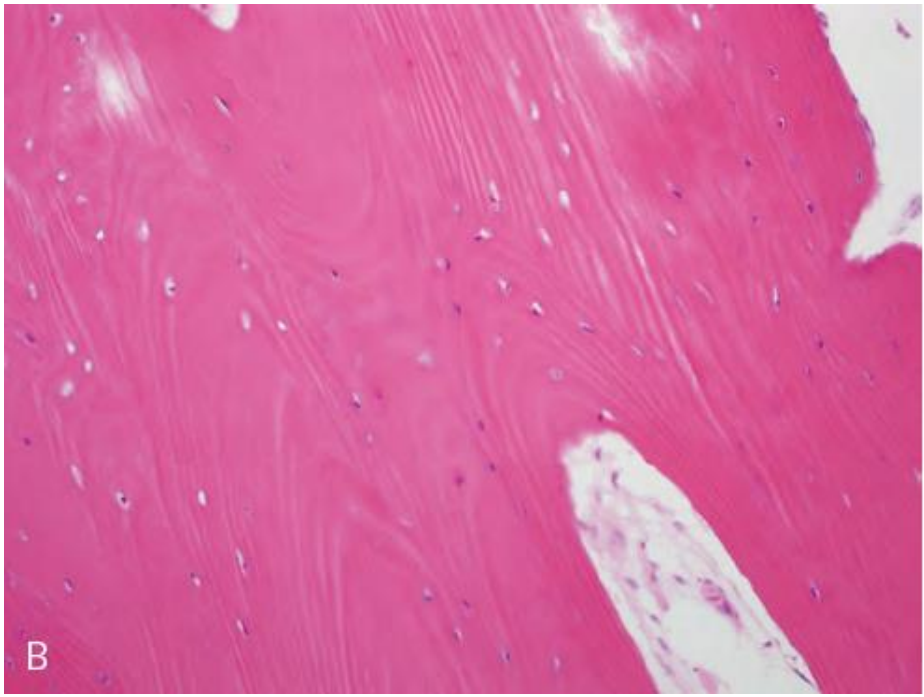
- Adult: 206 bones, 12% BW.
- Functions:
  - Mechanical support
  - Transmission force
  - Protection of viscera
  - Mineral homeostasis
  - *Niche* production of blood cells
- Extracellular matrix and specialized cells

Matrix

- Organic component – osteoid (35%) – type I collagen.
- Mineral component (65%).
- Hardness → hydroxyapatite – repository calcium (99%) and phosphorus (85%).
- 2 forms: woven bone – lamellar bone.

Two Histologic Forms





WOVEN VS LAMELLAR

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Table 26-1 Proteins of Bone Matrix

Osteoblast-Derived Proteins
Type I collagen
Calcium-binding proteins
Osteonectin, bone sialoprotein
Cell adhesion proteins
Osteopontin, fibronectin, thrombospondin
Cytokines
IL-1, IL-6, RANKL
Enzymes
Collagenase, alkaline phosphatase
Growth factors
IGF-1, TGF-β, PDGF
Proteins involved in mineralization
Osteocalcin
Proteins Concentrated from Serum
Albumin
β_2-microglobulin

IGF, linsulin-like growth factor; *TGF,* transforming growth factor; *PDGF,* platelet-derived growth factor; *IL,* interleukin; *RANKL,* receptor activator of nuclear factor-κB ligand.

Robbins, Pathologic Basis of Disease 9th Ed, 2015

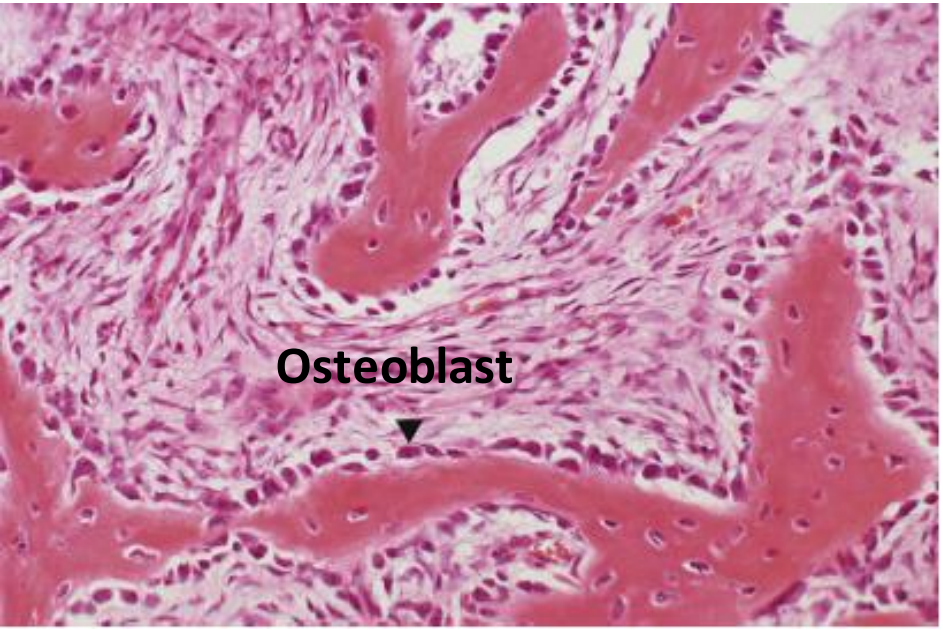
Cells

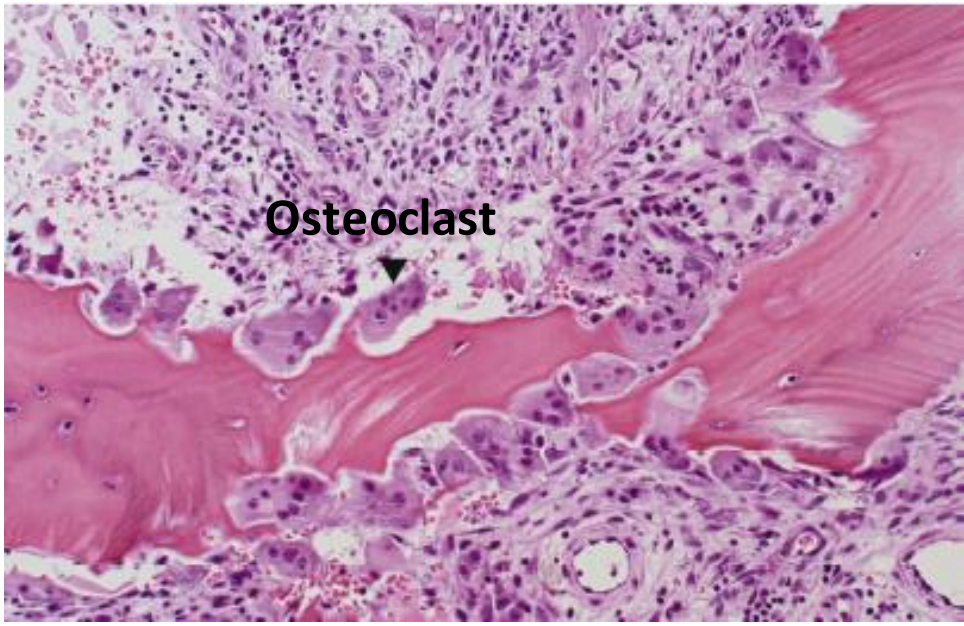
- Osteoblasts
  - Located on surface
  - Synthesize, transport and assemble matrix
  - Regulate mineralization
- Osteocytes

  Control calcium and phosphat level
- Osteoclasts

  Monocytes → Multinucleated macrophages → bone resorption

Modelling - Remodelling

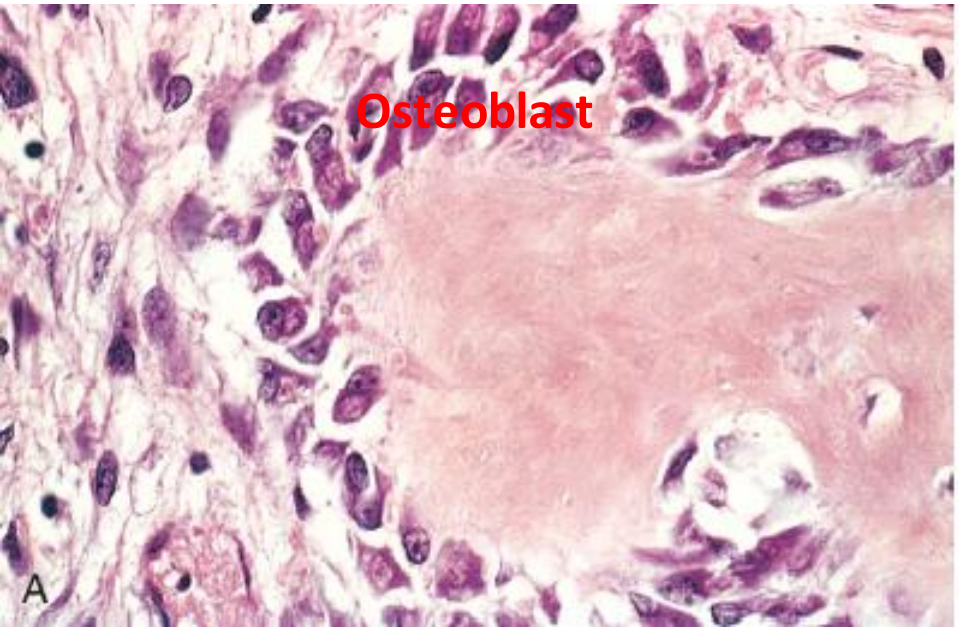


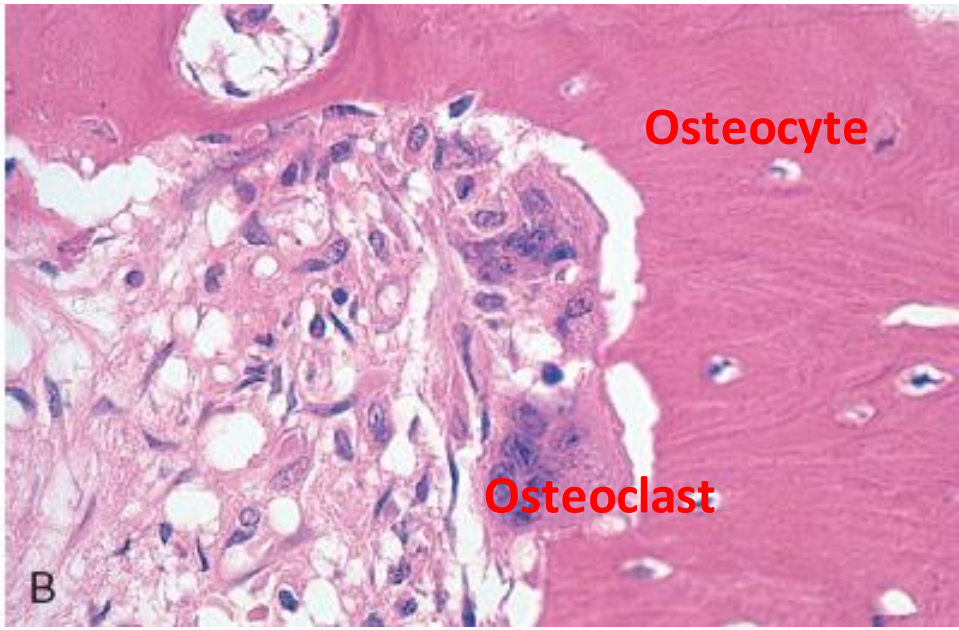


Robbins, Pathologic Basis of Disease 9th Ed, 2015

Remodelling

- Dynamic – NOT static
- Homeostasis production – resorption





Robbins, Pathologic Basis of Disease 9th Ed, 2015

Homeostasis and Remodelling

1. Transmembrane receptor RANK (receptor activator for NF-kB).
2. RANK ligand (RANKL) expressed on osteoblast and marrow stromal cells.
3. Osteoprotegerin (OPG), a secreted “decoy“ receptor made by osteoblast

Osteoclast Regulation

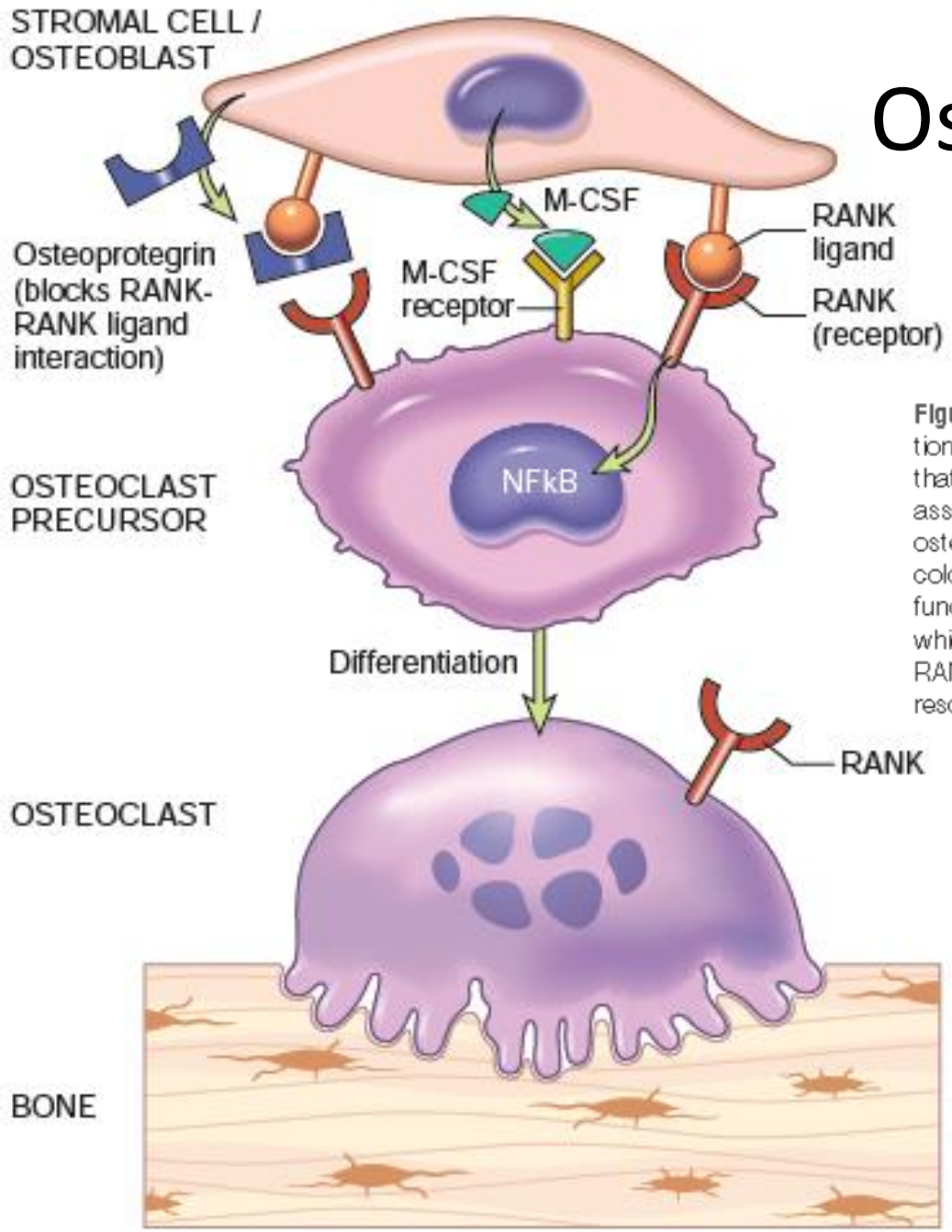


Figure 26-4 Paracrine molecular mechanisms that regulate osteoclast formation and function. Osteoclasts are derived from the same mononuclear cells that differentiate into macrophages. Osteoblast/stromal cell membrane-associated RANKL binds to its receptor RANK located on the cell surface of osteoclast precursors. This interaction in the background of macrophage colony-stimulating factor (M-CSF) causes the precursor cells to produce functional osteoclasts. Stromal cells also secrete osteoprotegerin (OPG), which acts as a "decoy" receptor for RANKL, preventing it from binding the RANK receptor on osteoclast precursors. Consequently, OPG prevents bone resorption by inhibiting osteoclast differentiation.

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Bone Cells and Related Activities

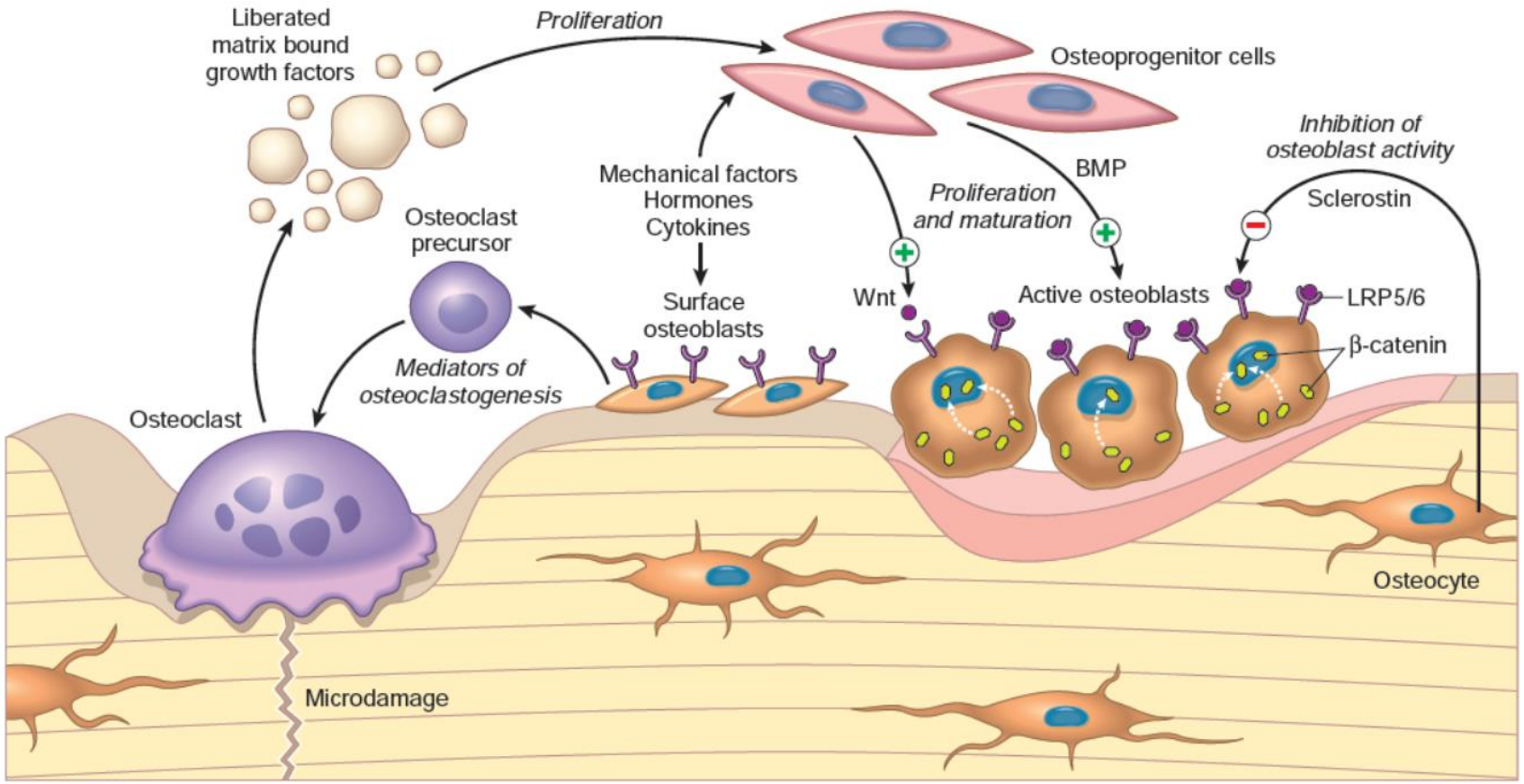


Figure 26-5 Bone cells and their interrelated activities. Hormones, cytokines, growth factors, and signal-transducing molecules are instrumental in their formation and maturation, and allow communication between osteoblasts and osteoclasts. Bone resorption and formation in remodeling are coupled processes that are controlled by systemic factors and local cytokines, some of which are deposited in the bone matrix. BMP, bone morphogenic protein; LRP5/6, LDL receptor related proteins 5 and 6.

- **Parathyroid hormone, IL-1, glucocorticoid promote osteoclast differentiation**
- **Growth factor (BMP), sex hormones favour OPG expression**

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Acquired Disorder

- Osteopenia → decreased bone mass
- Osteoporosis → osteopenia + risk #
- Pagets disease
- Rickets – Osteomalasia: vit D def/ abnormal metabolism → impairment mineralization
- Hyperparatyhroidism
- Renal Osteodystrophy
- Fracture
- Osteomyelitis

Osteoporosis

- Bone mass <<
- Fragile – fracture
- Primary – menopause, senile
- Secondary – metabolic disorder
- Peak bone mass → young adulthood
- Bone loss 0,5%/yr – **inevitable**
- Prevention n Treatment: exercise, calcium n vit D intake, pharmacologic th/ (**bisphosphonate**)

Table 26-4 Categories of Generalized Osteoporosis

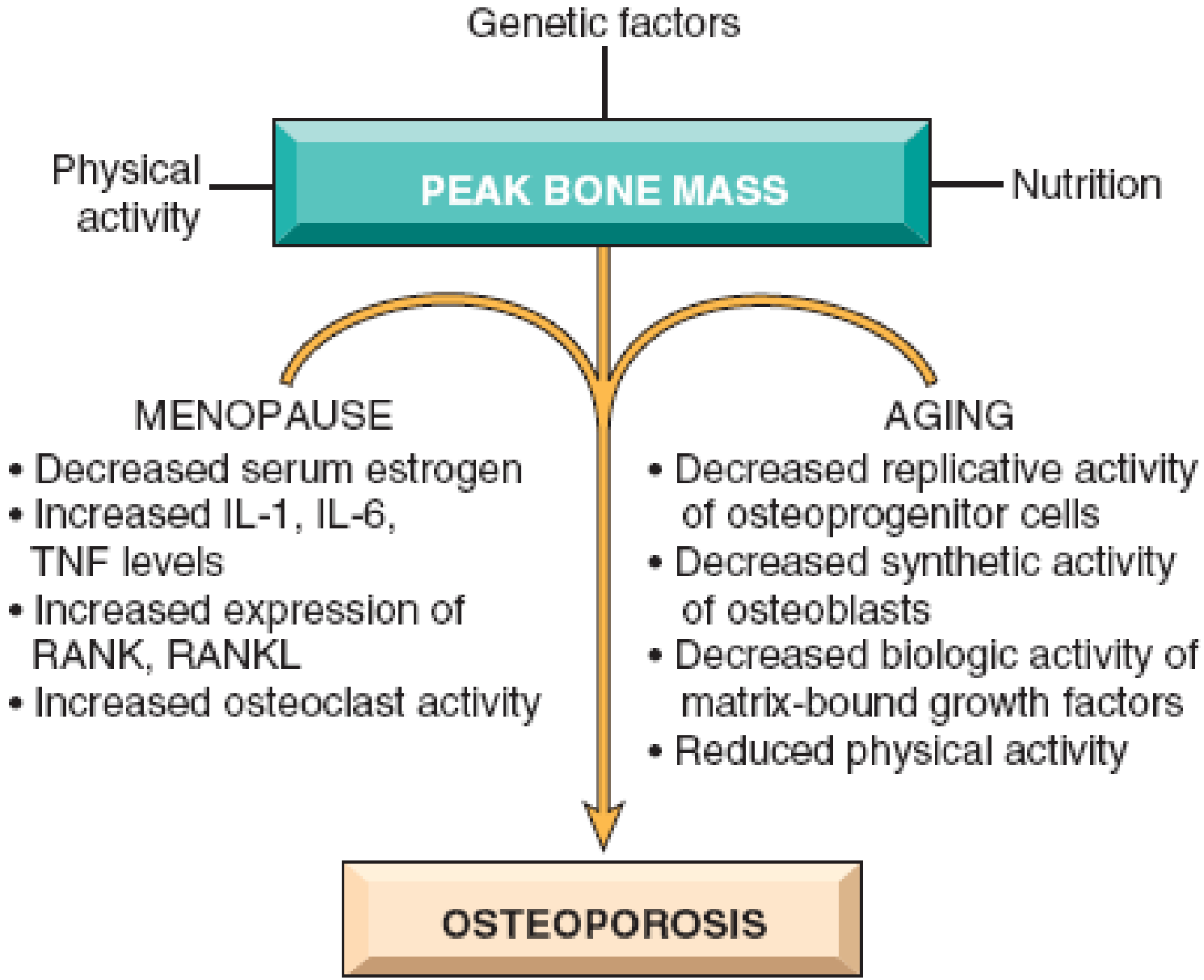
Primary
Idiopathic
Postmenopausal
Senile
Secondary
Endocrine Disorders
Addison disease
Diabetes, type 1
Hyperparathyroidism
Hyperthyroidism
Hypothyroidism
Pituitary tumors
Neoplasia
Carcinomatosis
Multiple myeloma
Gastrointestinal
Hepatic insufficiency
Malabsorption
Malnutrition
Vitamin C, D deficiencies
Drugs
Alcohol
Anticoagulants
Anticonvulsants
Chemotherapy
Corticosteroids
Miscellaneous
Anemia
Homocystinuria
Immobilization
Osteogenesis imperfecta
Pulmonary disease

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Osteoporosis

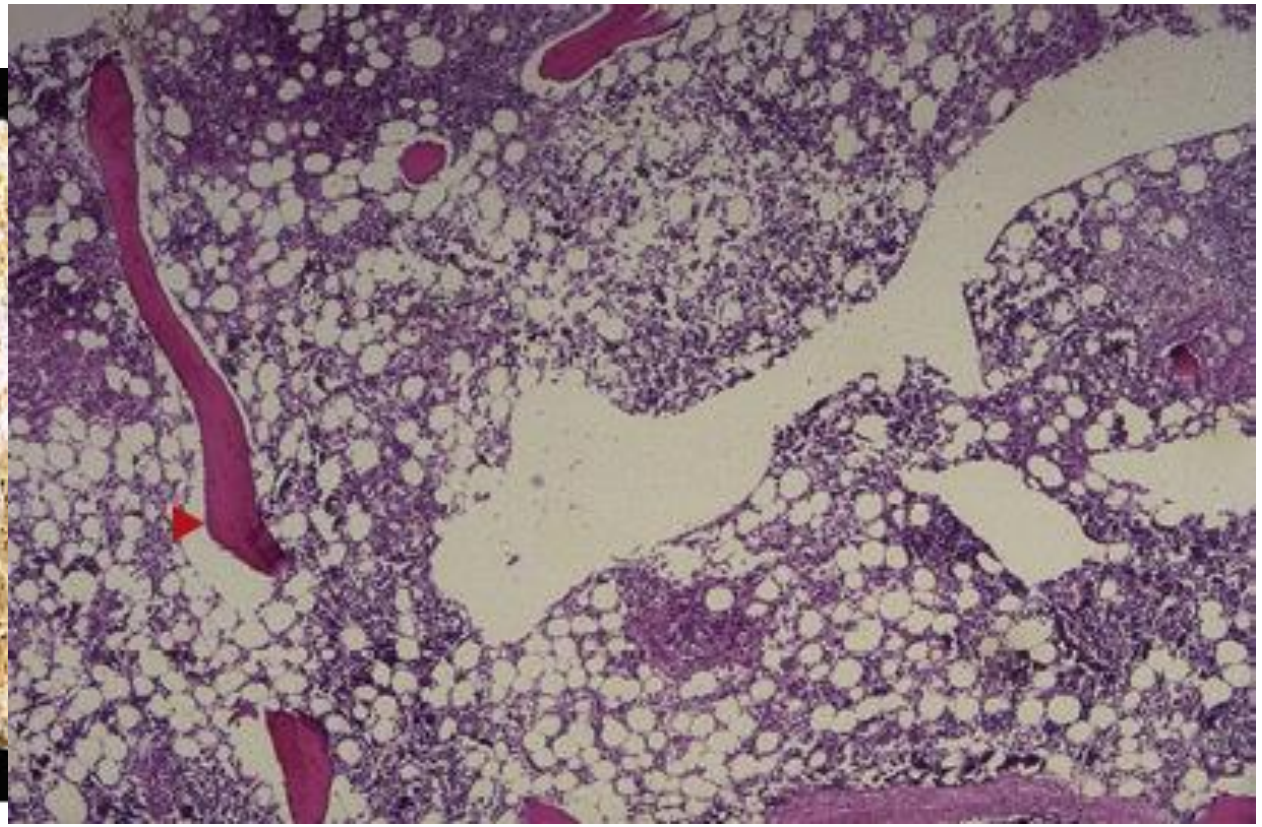
Pathogenesis:

- Age-related changes
  - Osteoblast reduced proliferative n biosynthetic
- Reduced physical activity
  - Mechanical force stimulate remodelling
  - Astronauts vs athlete
- Genetic factors: LRP5 gene
- Calcium nutritional state
- Hormonal influences: estrogen def



Robbins, Pathologic Basis of Disease 9th Ed, 2015

Osteoporosis



Robbins and Cotrans atlas pathology 3th ed, 2015

Fracture

- Loss of bone integrity – mechanical injury or diminished bone strength.
- Simple →
- Compound →
- Comminuted →
- Displaced →
- Stress →
- Greenstick →
- Pathologic →

Healing

- Remarkable repair capacity
- Hematoma →
- Soft tissue callus – pro callus →
- Bony callus →

Healing

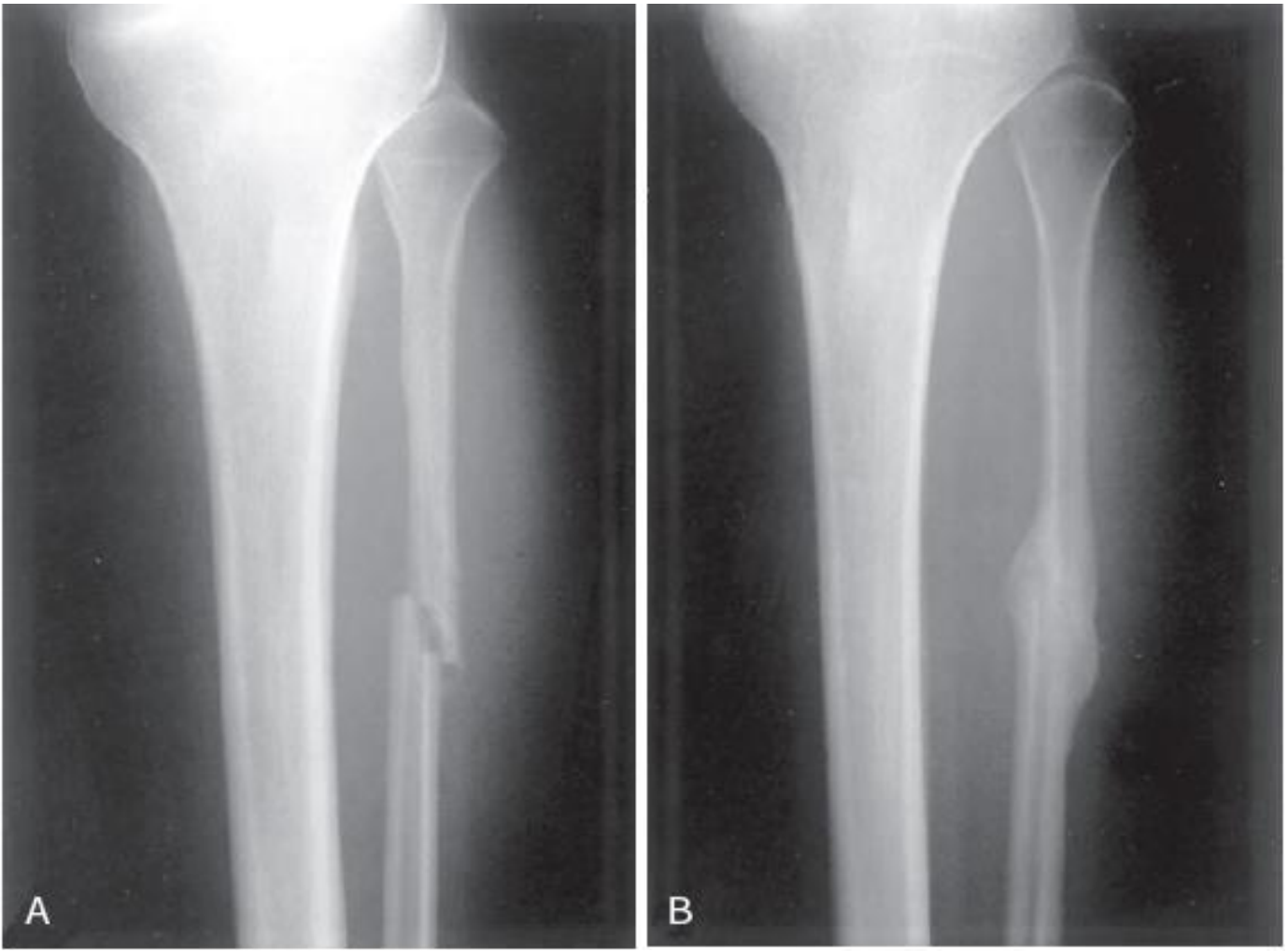


Figure 26-18 A, Recent fracture of the fibula. **B,** Marked callus formation 6 weeks later. (Courtesy Dr. Barbara Weissman, Brigham and Women's Hospital, Boston, Mass.)

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Healing

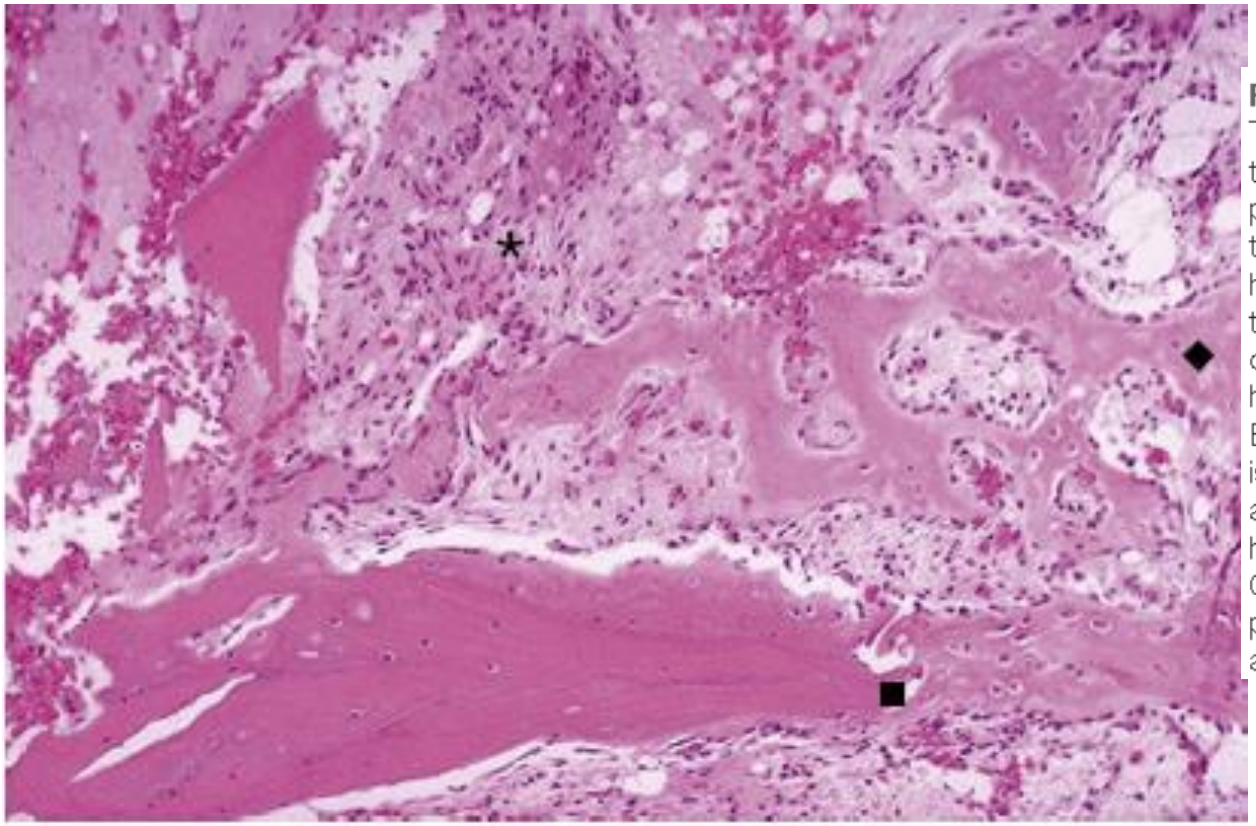


Figure 17-7 Fracture callus, microscopic The region of fracture shows disrupted bony trabeculae (■) at the left and bottom. The paler pink new woven bone (◆) is forming in response to the injury at the right and top in areas of hemorrhage with early granulation tissue (★). In the region of fracture, the new woven bone is called *callus*. After 6 to 8 weeks, enough healing has occurred to support weight and movement. Eventually, over months to years, this new bone is remodeled into more regular lamellar bone that attains the original shape and strength. Fracture healing is more complete in children than adults. Orthopedic procedures to stabilize fractures and provide proper alignment with plates and screws are often performed.

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Osteomyelitis

- Inflammation: bone and marrow.
- Primary or secondary.
- Virus, parasite, fungi, **bacteria (pyogenic, mycobacteria).**
- Mechanism: Hematogen, Extension, Direct extension.
- Children: hematogen
- Adults: open #, surgical procedures, diabetic foot

Osteomyelitis

Acute phase

- Bacteria proliferate – neutrophil
- Bone cells and marrow necrosis → sequestrum
- Periosteum rupture – drainase sinus

Chronic phase

- Chronic inflammatory cells – cytokines – osteoclastic bone resorption, fibrous tissue, reactive bone – involucrum.

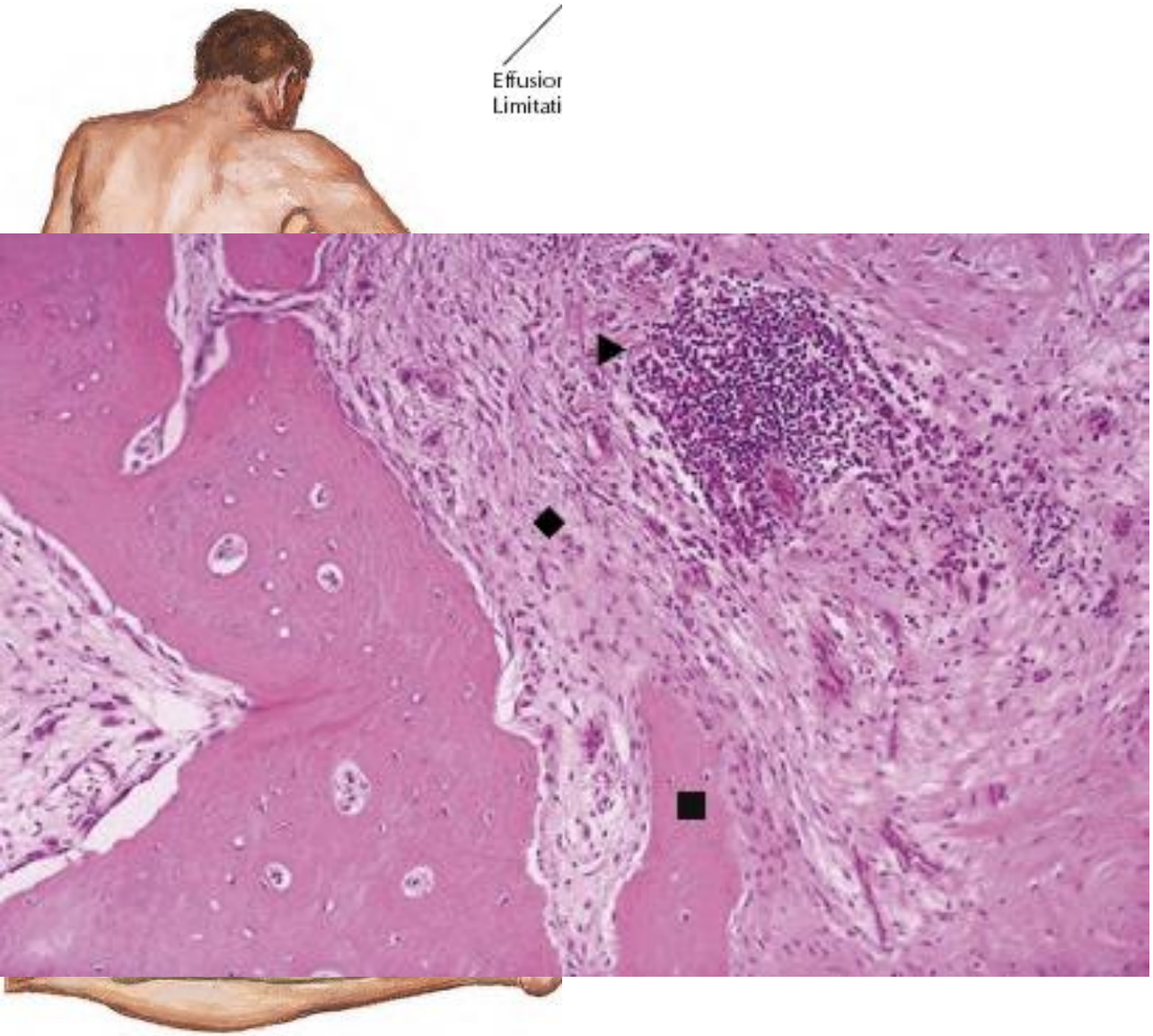
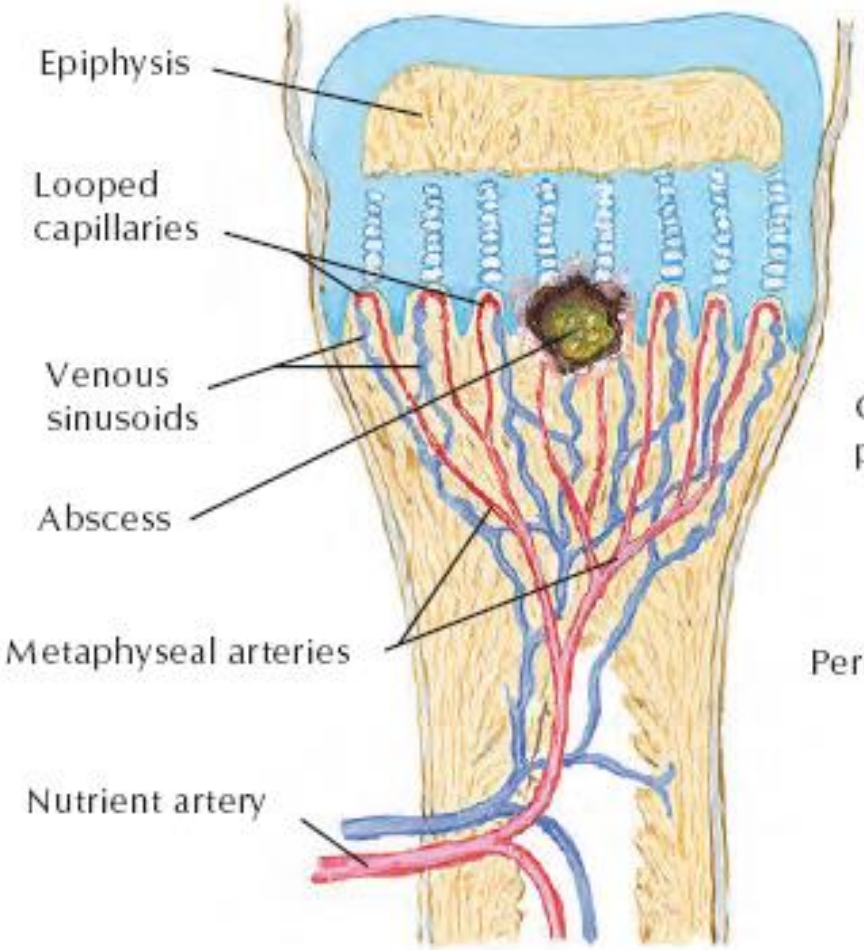


Figure 17-26 Osteomyelitis, microscopic Shown here in the marrow is fibrosis (◆) accompanied by chronic inflammatory cell infiltrates (▶). The bony trabeculae have become disorganized, and the bone is devitalized (■). Osteomyelitis is difficult to treat and may require surgical drainage and antibiotic therapy. The most common causative organism is *Staphylococcus aureus*. Neonates may have *Haemophilus influenzae* and group B streptococcal bone infections. Patients with sickle cell anemia are at risk for *Salmonella* osteomyelitis. Patients with urinary tract infections and injection drug users are at risk for osteomyelitis with *Escherichia coli* and *Pseudomonas* and *Klebsiella* species.

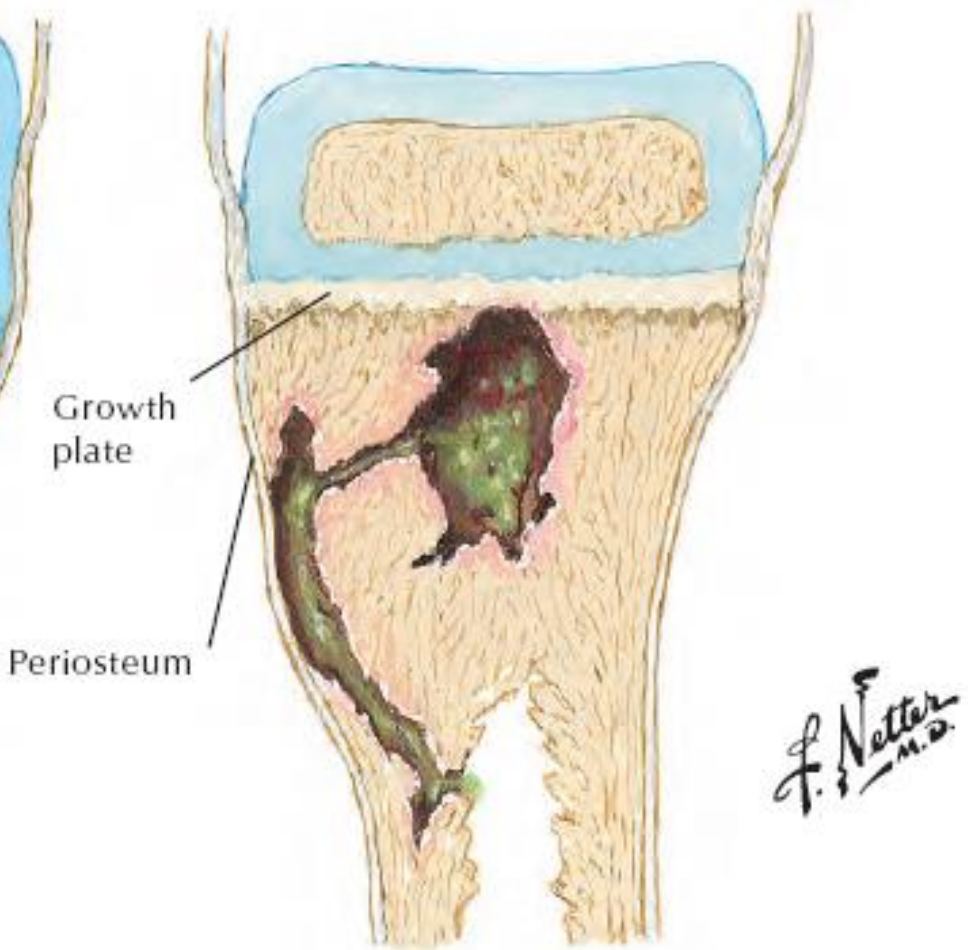
Blood culture and bone aspiration or open biopsy required to establish diagnosis and identify organism for choice of antibiotic therapy

Netter's Illustrated human pathology. 2014

Pathogenesis

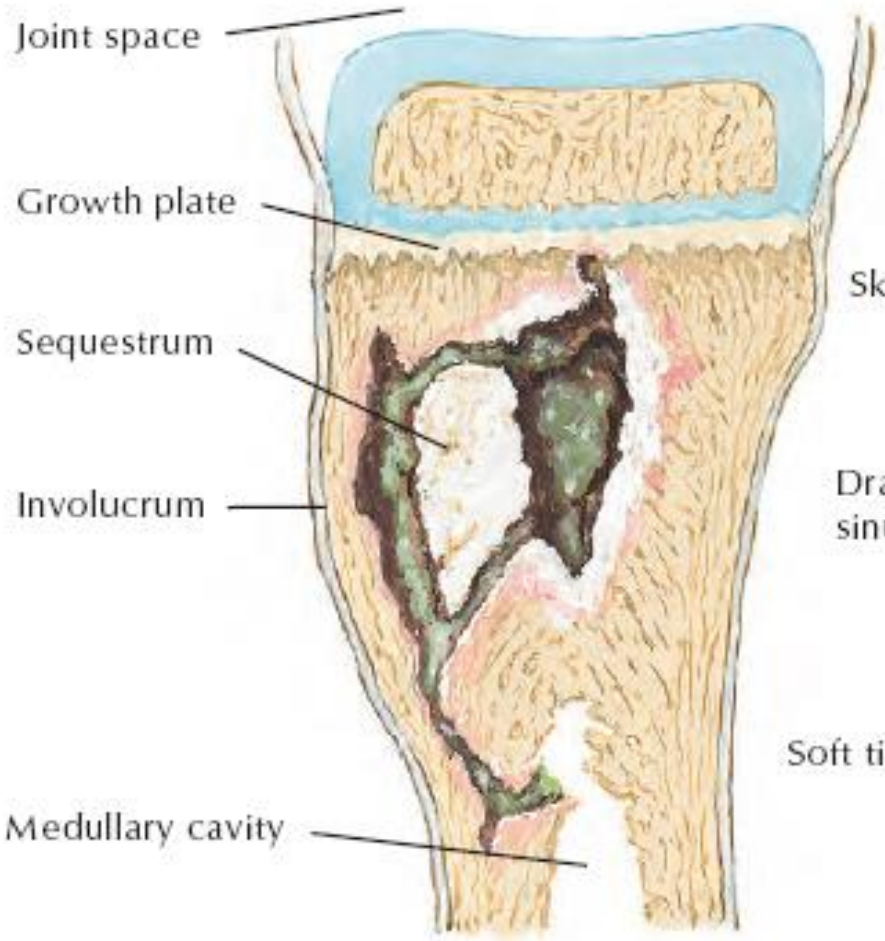


Terminal branches of metaphyseal arteries form loops at growth plate and enter irregular afferent venous sinusoids. Blood flow slowed and turbulent, predisposing to bacterial seeding. In addition, lining cells have little or no phagocytic activity. Area is catch basin for bacteria, and abscess may form.

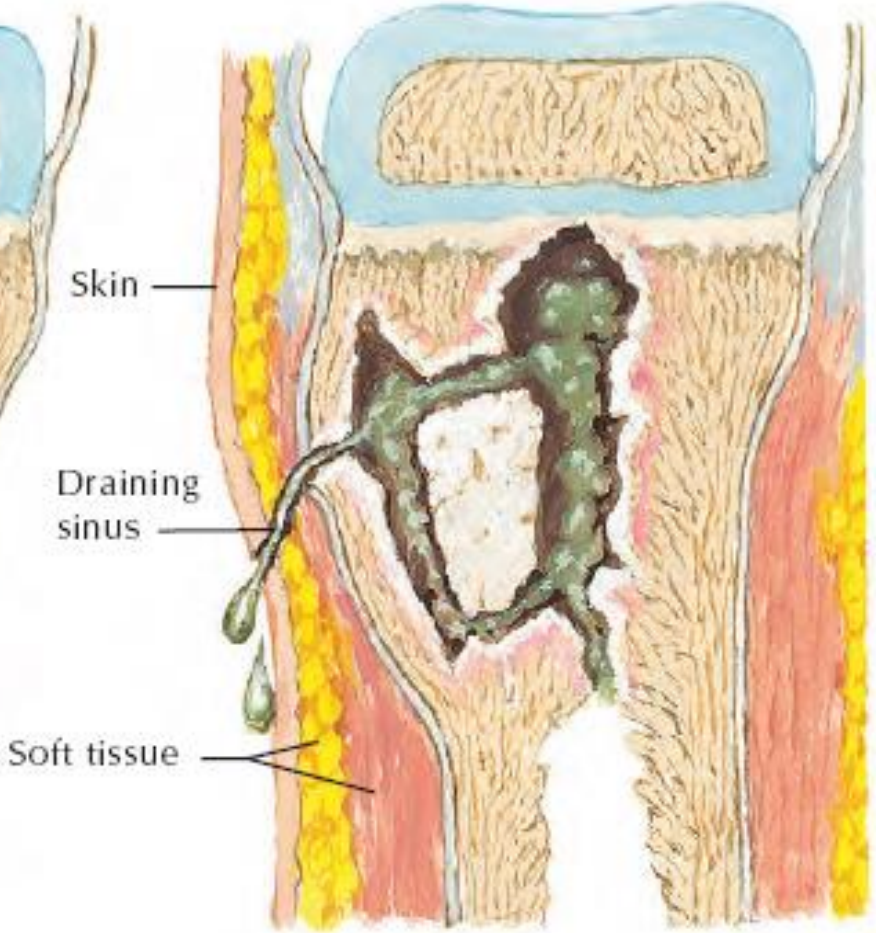


Abscess, limited by growth plate, spreads transversely along Volkmann canals and elevates periosteum; extends subperiosteally and may invade shaft. In infants under 1 year of age, some metaphyseal arterial branches pass through growth plate, and infection may invade epiphysis and joint.

Netter's Illustrated human pathology. 2014



As abscess spreads, segment of devitalized bone (sequestrum) remains within it. Elevated periosteum may also lay down bone to form encasing shell (involucrum). Occasionally, abscess walled off by fibrosis and bone sclerosis to form Brodie abscess.



Infectious process may erode periosteum and form sinus through soft tissues and skin to drain externally. Process influenced by virulence of organism, resistance of host, administration of antibiotics, and fibrotic and sclerotic responses.

Netter's Illustrated human pathology. 2014

Bone Tumor

Table 26-6 Classification of Major Primary Tumors Involving Bones

Category and fraction (%)	Behavior	Tumor type	Common locations	Age (yr)	Morphology
Hematopoietic (20)	Malignant	Myeloma Lymphoma	Vertebrae, pelvis	50-60	Malignant plasma cells or lymphocytes replacing marrow space
Cartilage forming (30)	Benign	Osteochondroma	Metaphysis of long bones	10-30	Bony excrescence with cartilage cap
		Chondroma	Small bones of hands and feet	30-50	Circumscribed hyaline cartilage nodule in medulla
		Chondroblastoma	Epiphysis of long bones	10-20	Circumscribed, pericellular calcification
		Chondromyxoid fibroma	Tibia, pelvis	20-30	Collagenous to myxoid matrix, stellate cells
	Malignant	Chondrosarcoma (conventional)	Pelvis, shoulder	40-60	Extends from medulla through cortex into soft tissue, chondrocytes with increased cellularity and atypia
Bone forming (26)	Benign	Osteoid osteoma	Metaphysis of long bones	10-20	Cortical, interlacing microtrabeculae of woven bone
		Osteoblastoma	Vertebral column	10-20	Posterior elements of vertebra, histology similar to osteoid osteoma
	Malignant	Osteosarcoma	Metaphysis of distal femur, proximal tibia	10-20	Extends from medulla to lift periosteum, malignant cells producing woven bone
Unknown origin (15)	Benign	Giant cell tumor	Epiphysis of long bones	20-40	Destroys medulla and cortex, sheets of osteoclasts
		Aneurysmal bone cyst	Proximal tibia, distal femur, vertebra	10-20	Vertebral body, hemorrhagic spaces separated by cellular, fibrous septae
	Malignant	Ewing sarcoma	Diaphysis of long bones	10-20	Sheets of primitive small round cells
		Adamantinoma	Tibia	30-40	Cortical, fibrous , bone matrix with epithelial islands
Notochordal (4)	Malignant	Chordoma	Clivus, sacrum	30-60	Destroys medulla and cortex, foamy cells in myxoid matrix

Adapted from Unni KK, Inwards CY: Dahlin's Bone Tumors, 6th ed. Philadelphia, Lippincott-Williams & Wilkins, 2010, p 5; by permission of Mayo Foundation.

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Bone Tumor

- According to the normal cell or matrix produced.
- Mostly benign.
- Bone forming: Osteoblastoma, Osteosarcoma
- Cartilage forming: Osteochondroma, Chondroma, Chondrosarcoma.
- Ewing Sarcoma family tumors: t(11;22).

Osteosarcoma

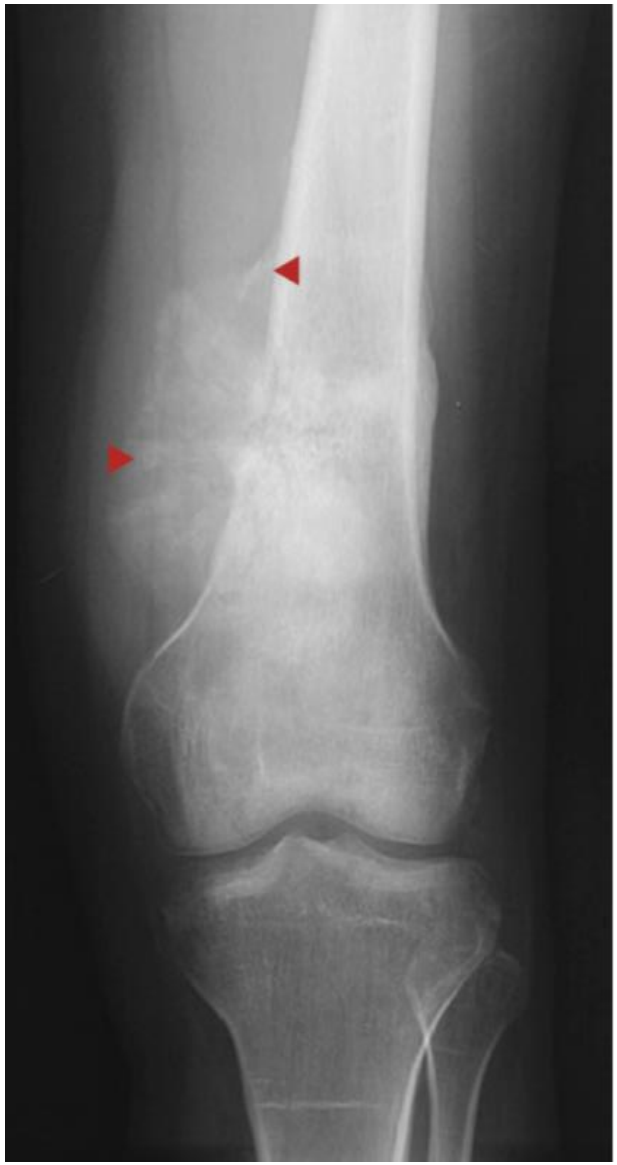


Figure 17-36 Osteosarcoma, radiograph
This malignancy (▼) involves the metaphyseal region of the distal femur. Long bones are more often affected in young individuals, probably because bone growth with mitotic activity increases risk for genetic mutations. This tumor erodes and destroys the bone cortex, extending into soft tissue where irregular reactive bone formation with calcification is visible as brighter areas in the normally dull-gray soft tissues. The periosteum here is lifted off (▲) to form a Codman triangle.

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Osteosarcoma

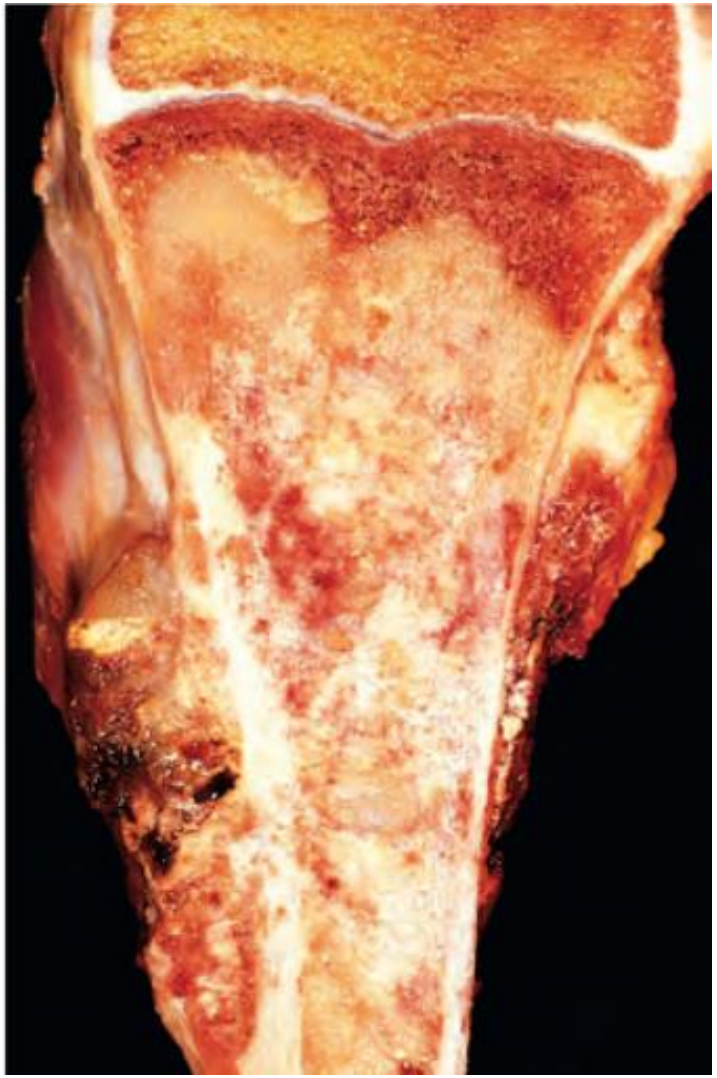
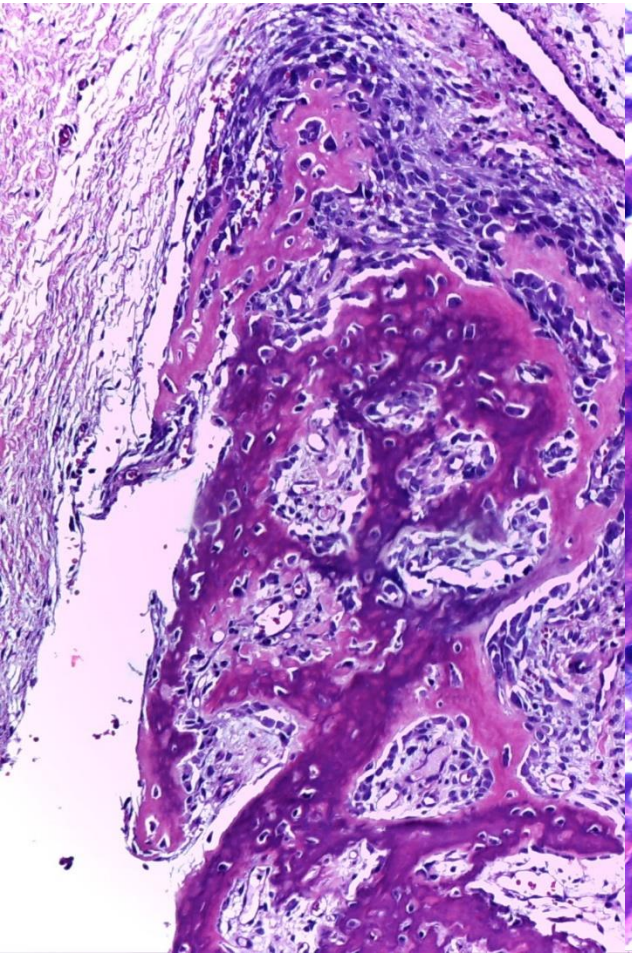
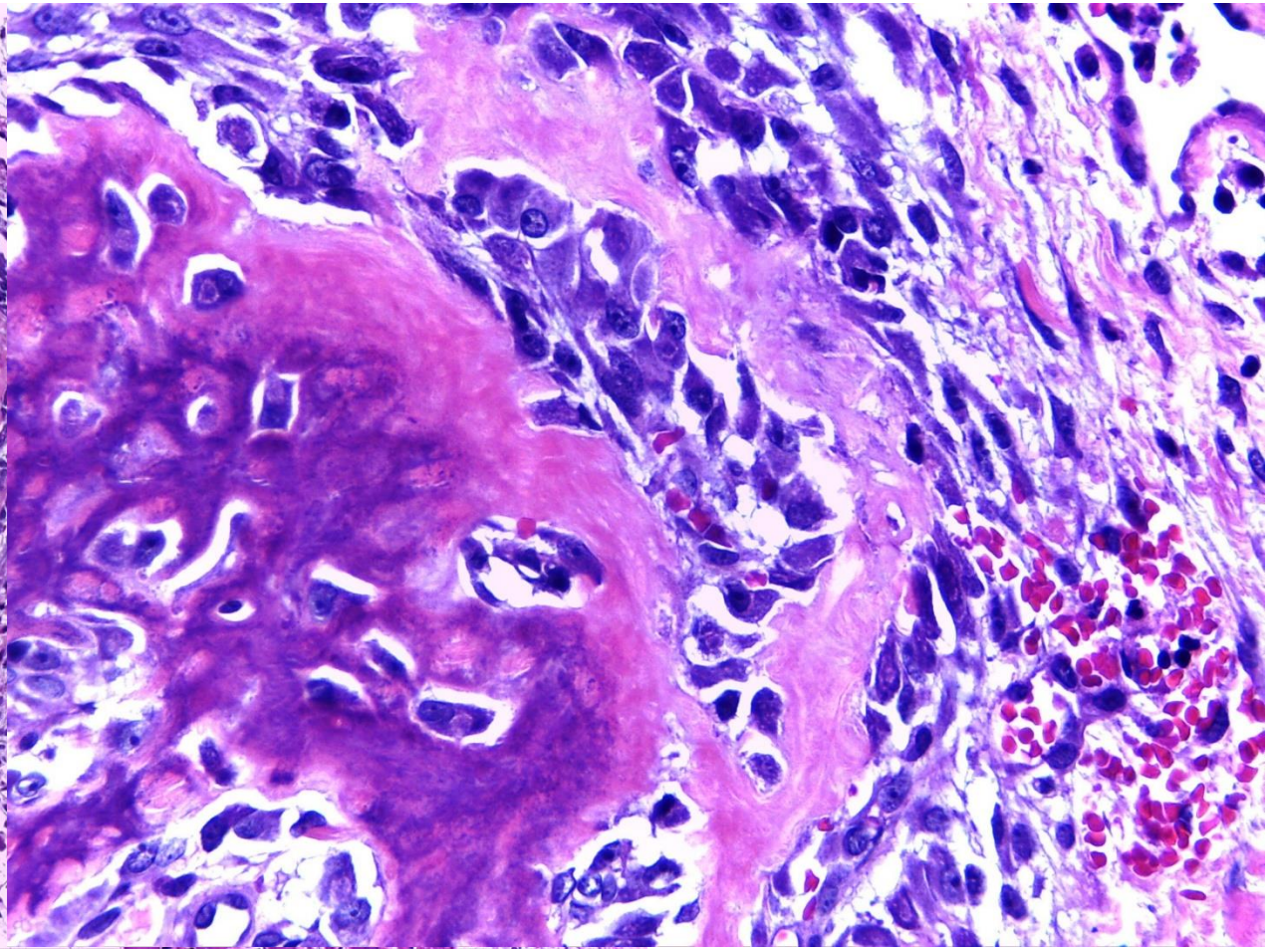


Figure 26-24 Osteosarcoma of the proximal tibia. The tan-white tumor fills most of the medullary cavity of the metaphysis and proximal diaphysis. It has infiltrated through the cortex, lifted the periosteum, and formed soft tissue masses on both sides of the bone.

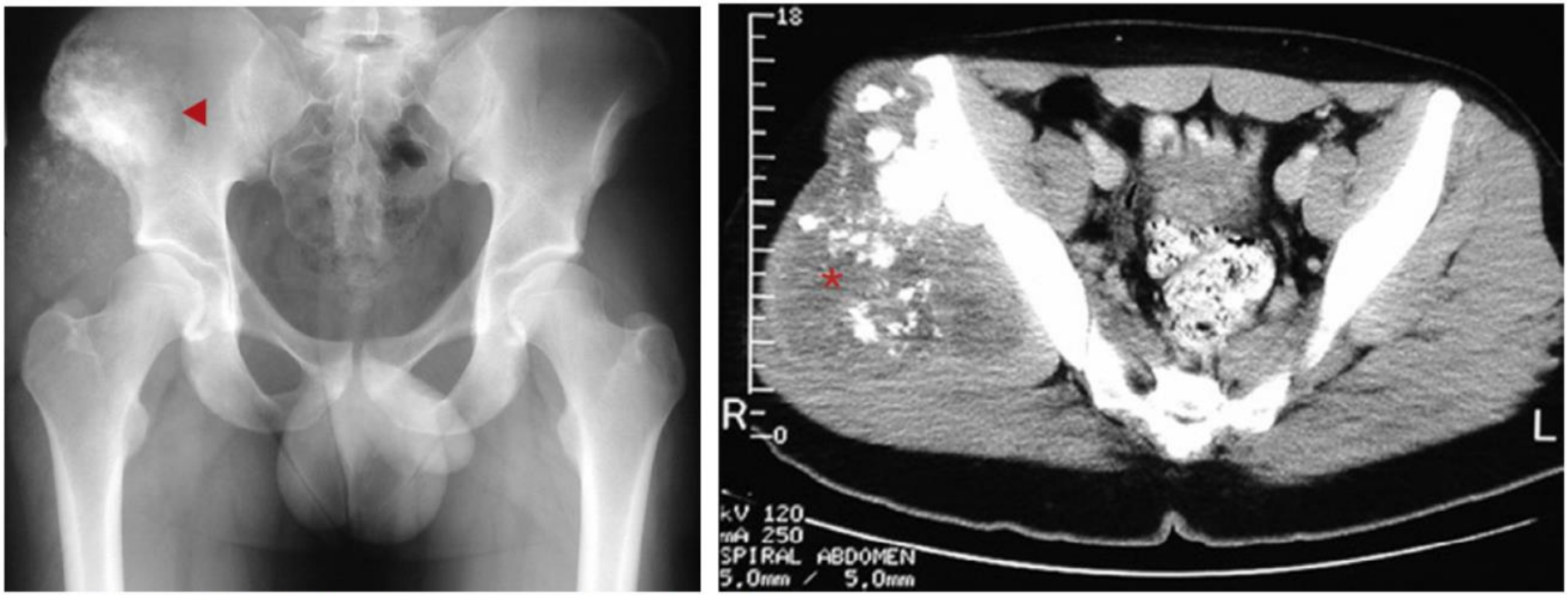
Robbins, Pathologic Basis of Disease 9th Ed, 2015

Osteosarkoma





Chondrosarcoma



Figures 17-46 and 17-47 Chondrosarcoma, radiograph and CT image
In the *left panel*, a chondrosarcoma (◀) arising in the right iliac wing and extending to soft tissues exhibits irregular brightness. In the *right panel*, the CT scan shows extensive soft-tissue involvement (✱) with brightly calcified areas. These appearances reflect the heterogeneous tissue composition of these tumors. They cause local pain. Metastases from high-grade tumors typically occur in the lungs.

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Chondrosarcoma

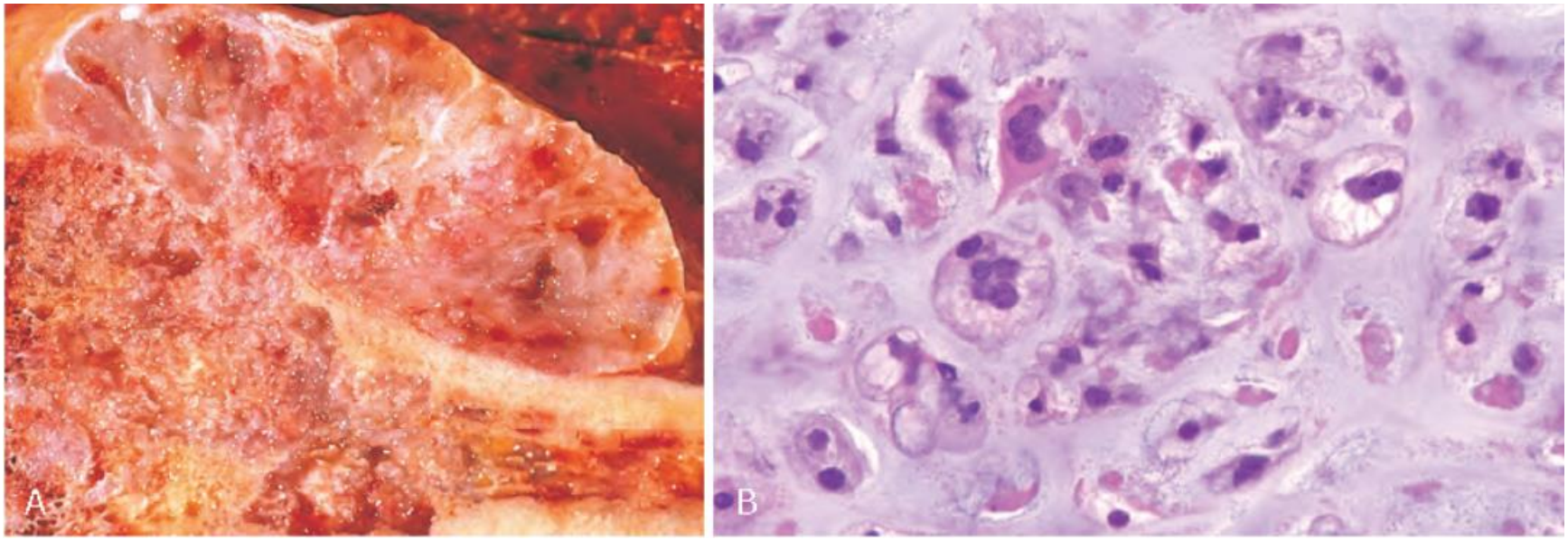
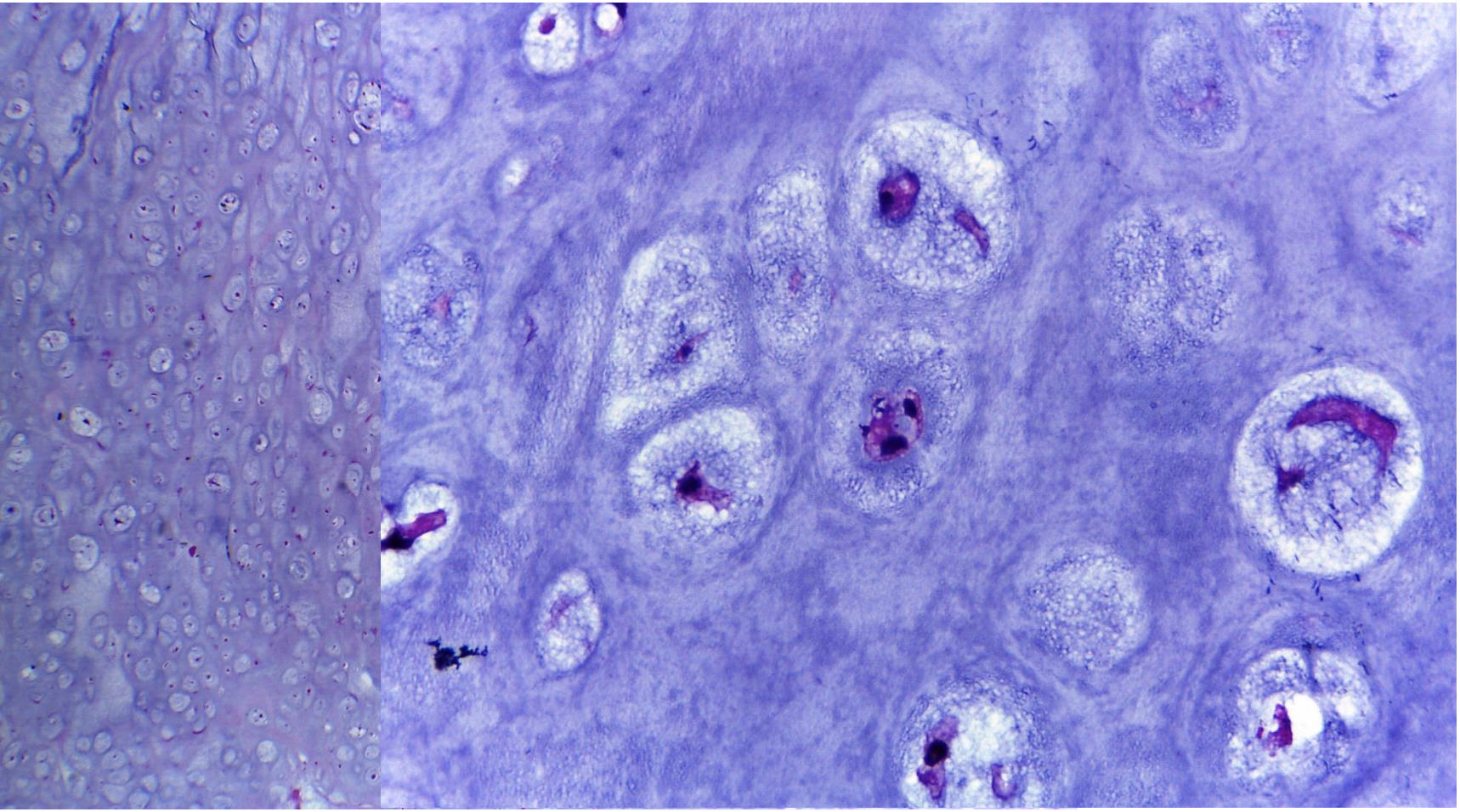


Figure 26-30 Chondrosarcoma. **A,** Nodules of hyaline and myxoid cartilage permeating throughout the medullary cavity, growing through the cortex, and forming a relatively well-circumscribed soft tissue mass. **B,** Anaplastic chondrocytes amid hyaline cartilage matrix in a grade 3 chondrosarcoma.

Robbins, Pathologic Basis of Disease 9th Ed, 2015

Chondrosarcoma



Joints

- Solid – nonsynovial – synarthroses
  - Fibrous synarthroses: cranial sutures
  - Cartilaginous synarthroses: manubrium sternal, pubic
- Cavitated – synovial
  - Joint space – ROM
  - Synoviocytes:

    Type A (macrophage)

    Type B (similar to fibroblast, synthesize hyaluronic acid)

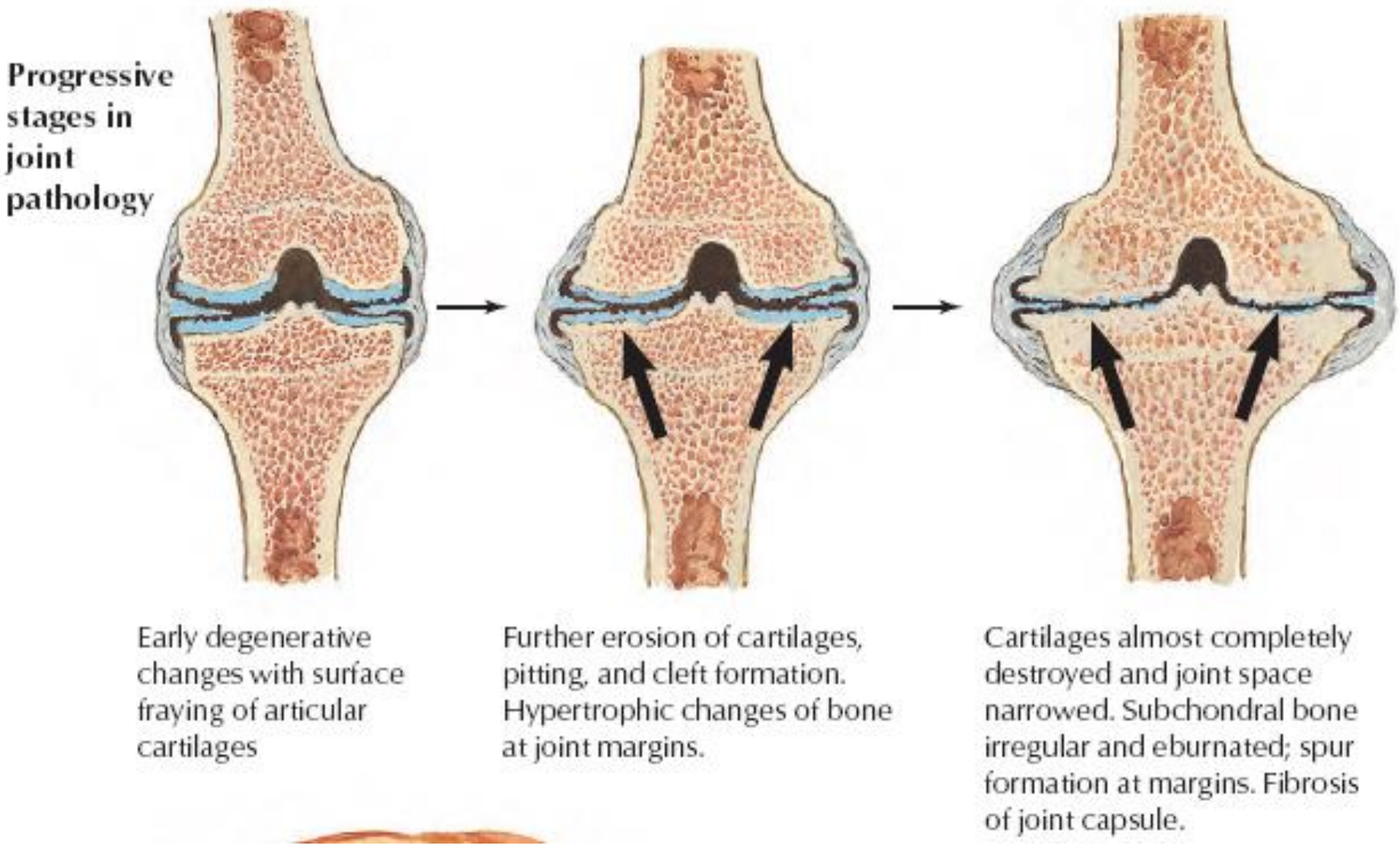
Osteoarthritis

- Degenerative joint disease
- Frequent, aging > 65 yrs
- Hands, knees, hips and spines
- Matrix breakdown exceeds synthesis
- Deep, pain exacerbated by use, morning stiffness, crepitus, limitation ROM

Osteoarthritis

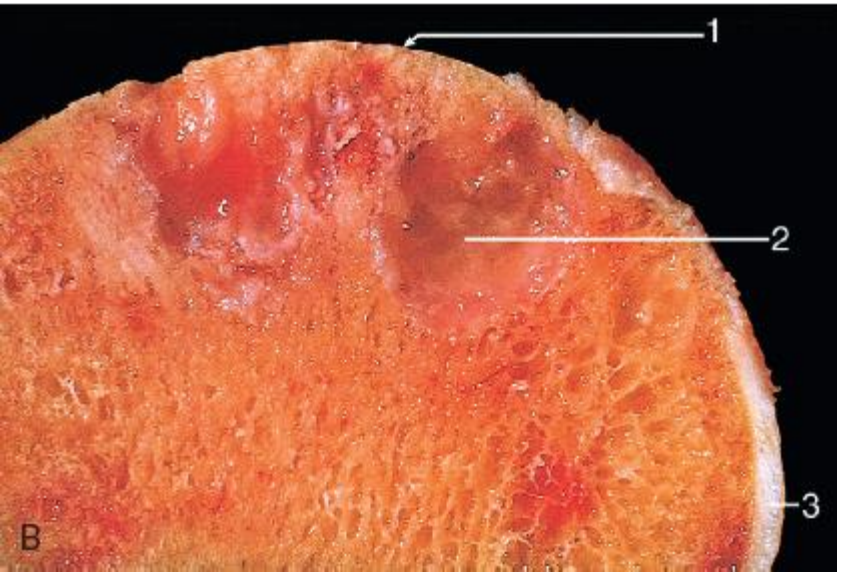
- Normal articular cartilago function:
  - Friction-free movement → synovial fluid
  - Weight-bearing joints – absorb shock n weight
- Cartilago – elastic (proteoglycan + type II collagen → chondrocyte)
- Three phases: (1) Chondrocyte injury, (2) Early OA, (3) Late OA

Osteoarthritis



Netter's Illustrated human pathology. 2014

Osteoarthritis



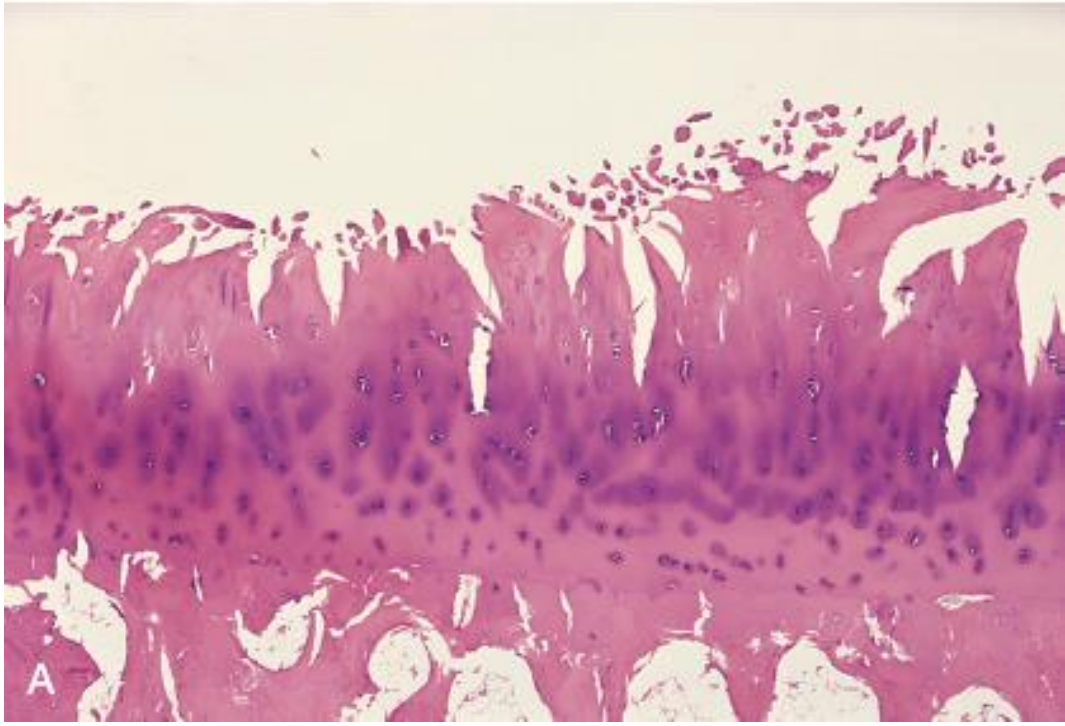


Figure 26-39 Osteoarthritis. **A,** Histologic demonstration of the characteristic fibrillation of the articular cartilage. **B,** Eburnated articular surface exposing subchondral bone (1), subchondral cyst (2) and residual articular cartilage (3).

Robbins basic pathology 9th ed, 2013

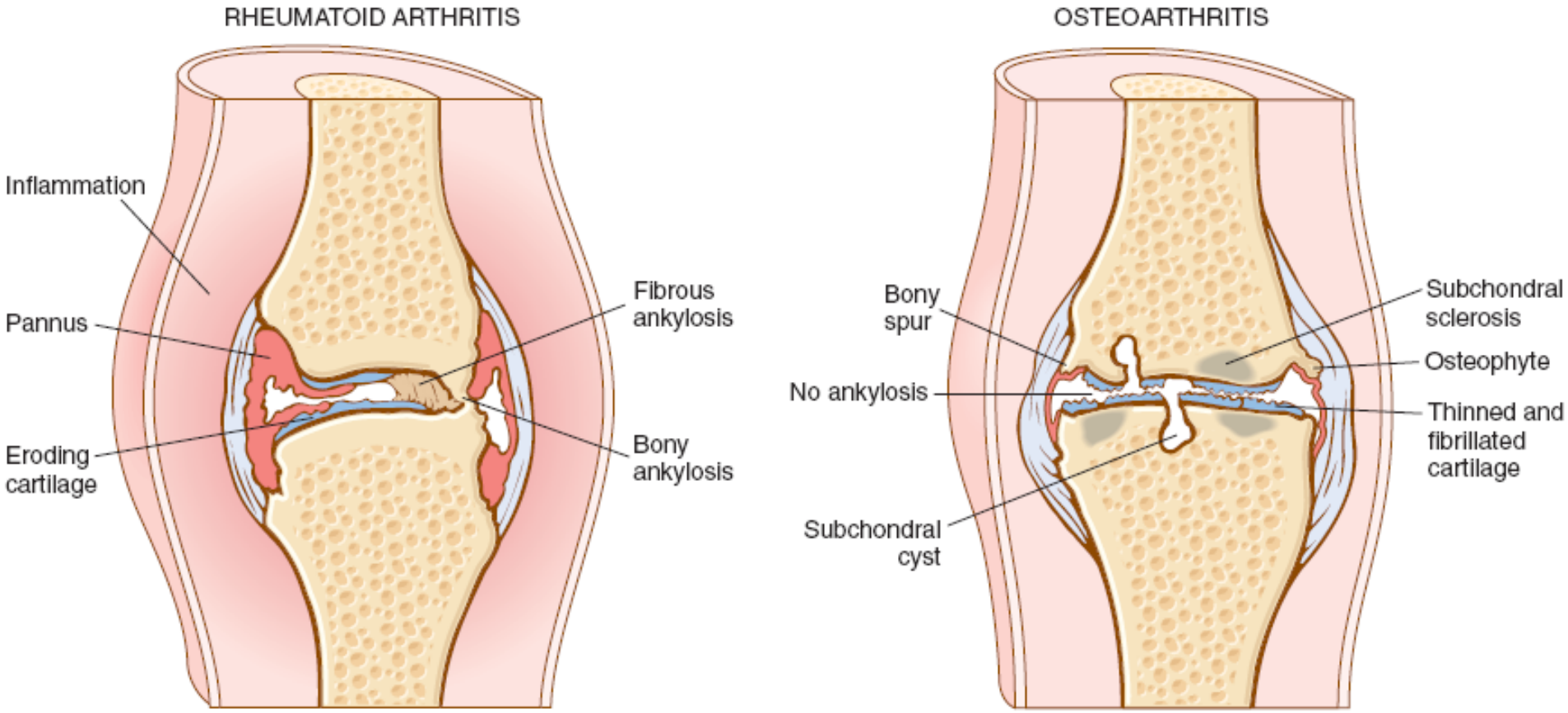


Figure 20–17 Comparison of the morphologic features of rheumatoid arthritis (RA) and osteoarthritis.

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Gout Arthritis

- Transient acute arthritis → crystallization of monosodium urate (MSU) within and around joints
- Primary Gout (90%) or secondary Gout (10%)

Table 26-7 Classification of Gout

Clinical Category	Uric Acid Production	Uric Acid Excretion
Primary Gout (90%)		
Unknown enzyme defects (85%-90%)	↑ (majority) ↑↑ (minority) Normal	Normal ↑ ↓
Known enzyme defects (e.g., partial HGPRT deficiency)	↑	Normal
Secondary Gout (10%)		
Increased nucleic acid turnover (e.g., leukemia)	↑↑	↑
Chronic renal disease	Normal	↓
Congenital (e.g., Lesch-Nyhan syndrome HGPRT deficiency)	↑↑	↑

HGPRT, Hypoxanthine guanine phosphoribosyl transferase.

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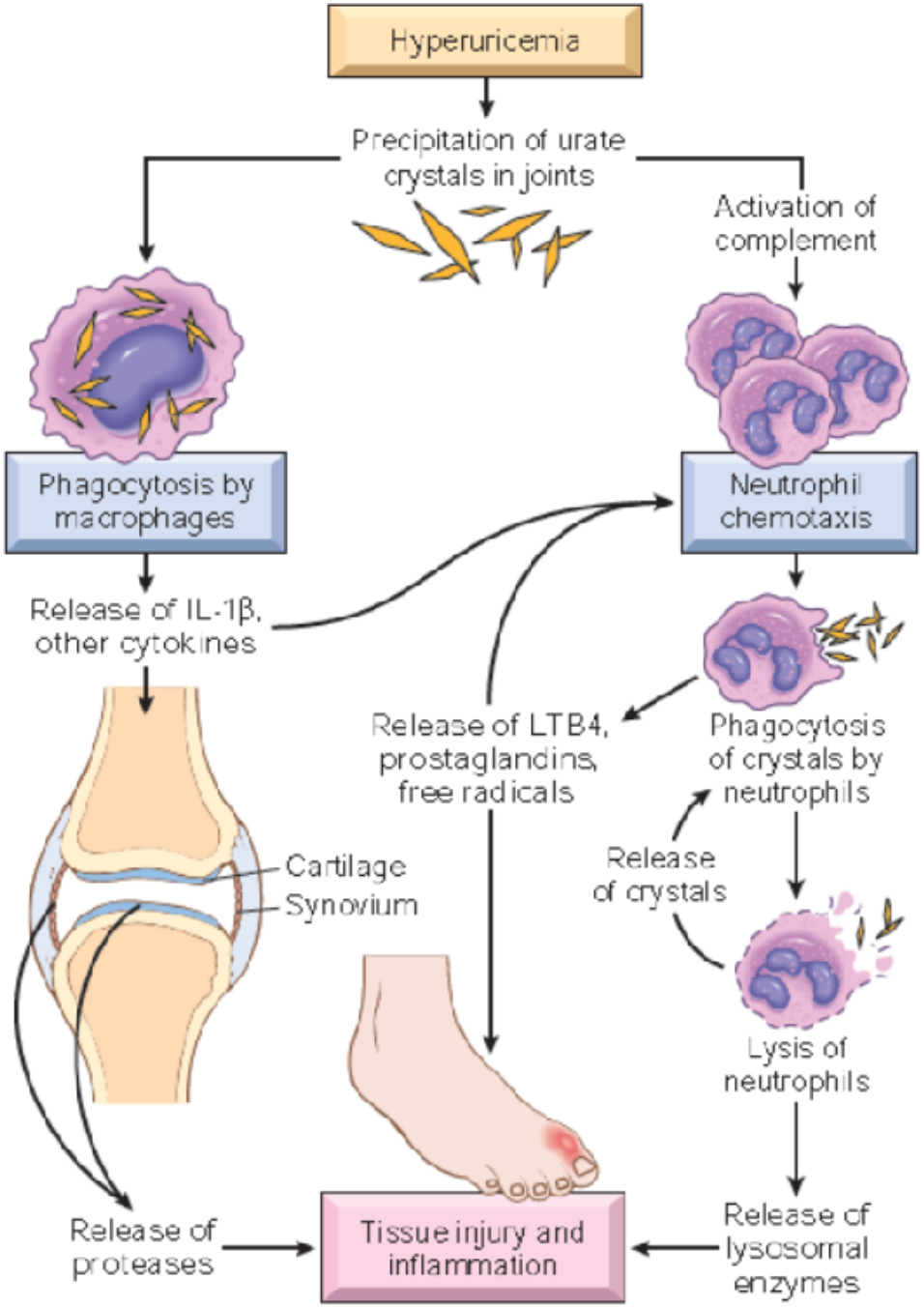

Figure 26-46 Pathogenesis of acute gouty arthritis. LTB4, Leukotriene B4; IL-1β, interleukin 1β.

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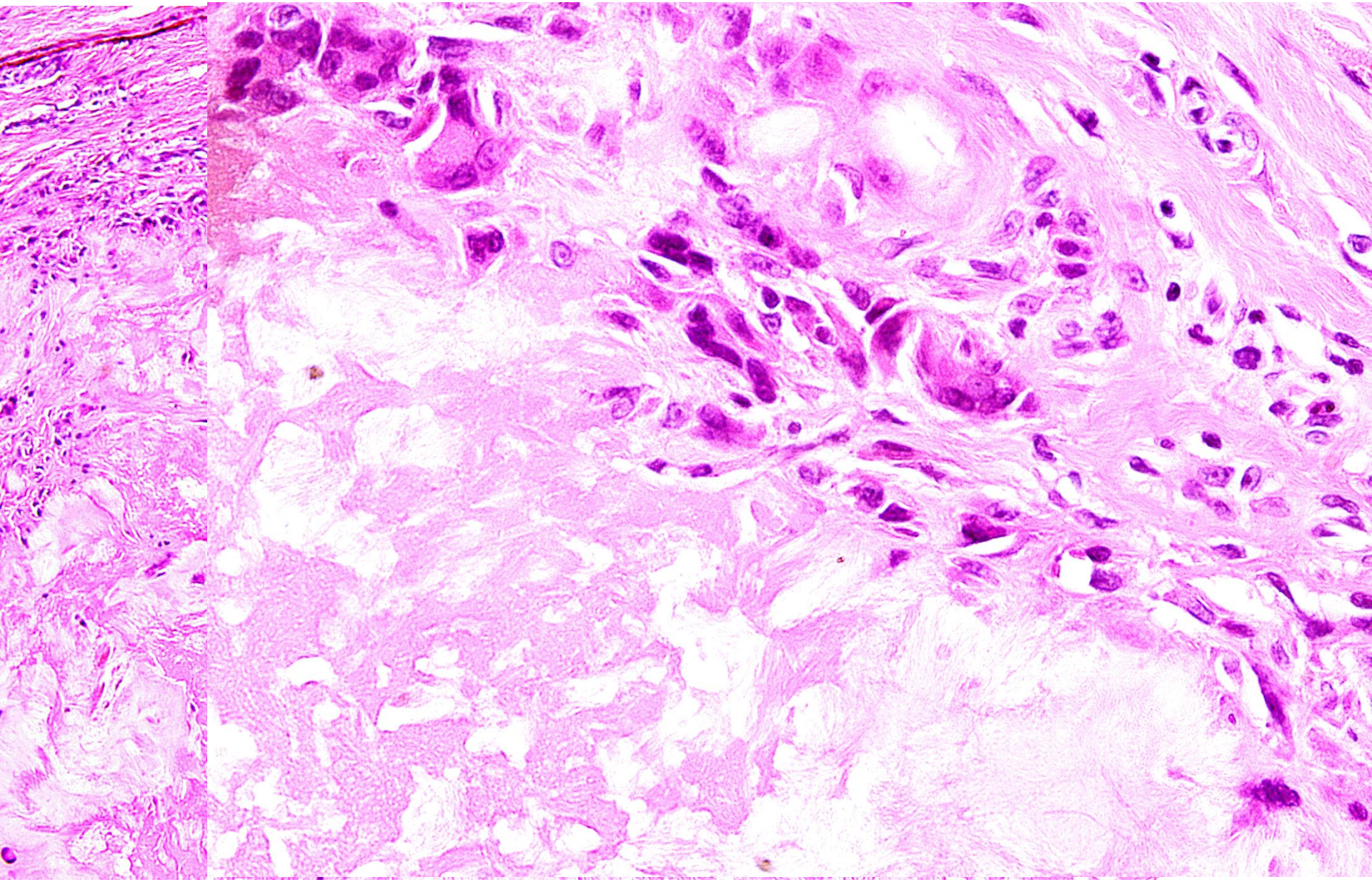


Soft Tissue

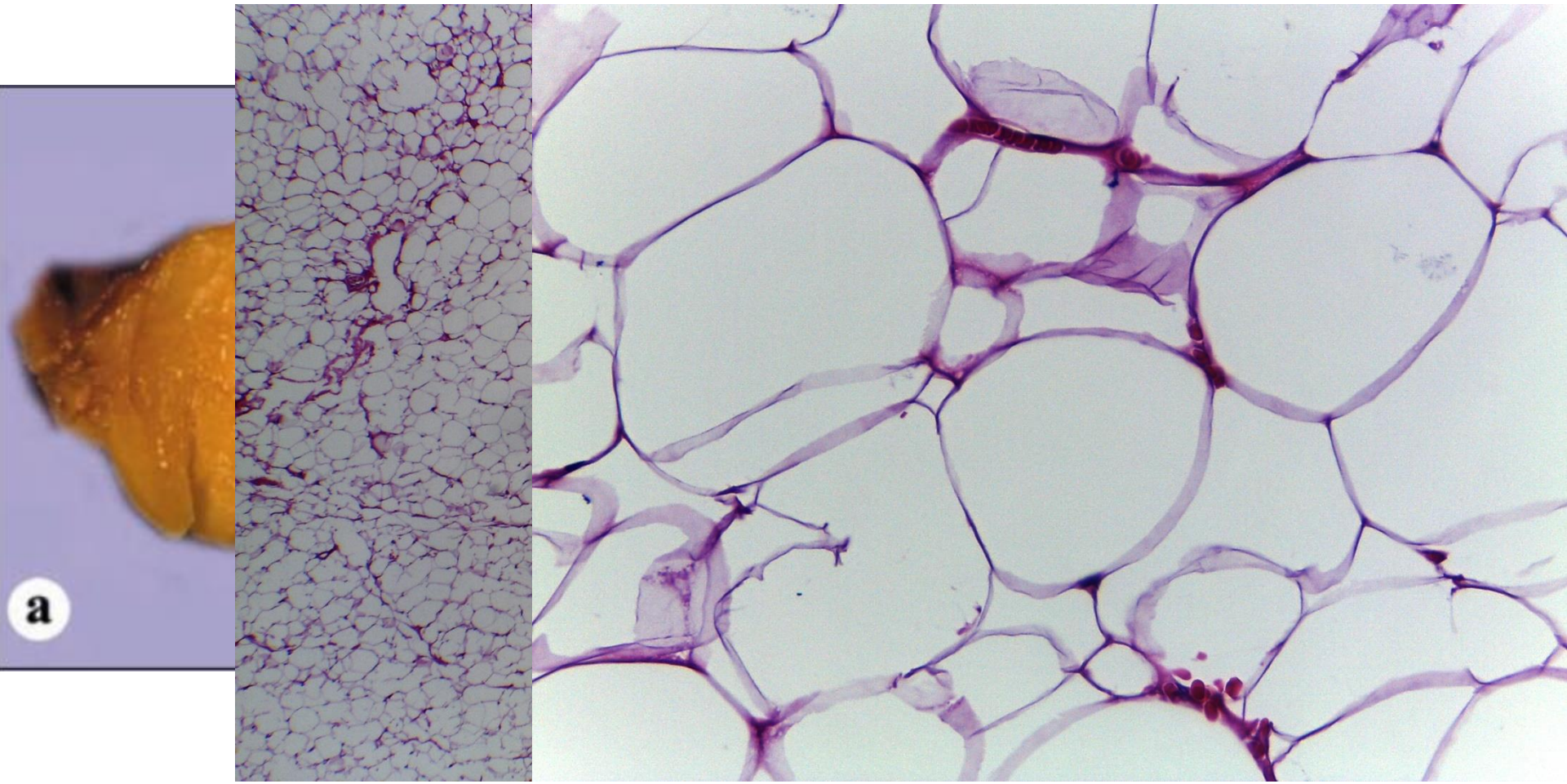
Table 26-9 Soft Tissue Tumors

Category	Behavior	Tumor Type	Common Locations	Age (yr)	Morphology
Adipose	Benign	Lipoma	Superficial extremity, trunk	40-60	Mature adipose tissue
	Malignant	Well-differentiated Liposarcoma	Deep extremity, retroperitoneum	50-60	Adipose tissue with scattered atypical spindle cells
		Myxoid liposarcoma	Thigh, leg	30s	Myxoid matrix, "chicken wire" vessels, round cells, lipoblasts
Fibrous	Benign	Nodular fasciitis	Arm, forearm	20-30	Tissue culture growth, extravasated erythrocytes,
		Deep fibromatosis	Abdominal wall	30-40	Dense collagen, long, unidirectional fascicles
Skeletal muscle	Benign	Rhabdomyoma	Head and neck	0-60	Polygonal rhabdomyoblasts, "spider" cells
	Malignant	Alveolar rhabdomyosarcoma	Extremities, sinuses	5-15	Uniform round discohesive cells between septae
		Embryonal rhabdomyosarcoma	Genitourinary tract	1-5	Primitive spindle cells, "strap" cells
Smooth muscle	Benign	Leiomyoma	Extremity	20s	Uniform, plump eosinophilic cells in fascicles
	Malignant	Leiomyosarcoma	Thigh, retroperitoneum	40-60	Pleomorphic eosinophilic cells
Vascular	Benign	Hemangioma	Head and neck	0-10	Circumscribed mass of capillary or venous channels
	Malignant	Angiosarcoma	Skin, deep lower extremity	50-80	Infiltrating capillary channels
Nerve sheath	Benign	Schwannoma	Head and neck	20-50	Encapsulated, fibrillar stroma, nuclear palisading
		Neurofibroma	Wide, cutaneous, subcutis	10-20+	Myxoid, ropy collagen, loose fascicles, mast cells
	Malignant	Malignant peripheral nerve sheath tumor	Extremities, shoulder girdle	20-50	Tight fascicles, atypia, mitotic activity, necrosis
Uncertain histotype	Benign	Solitary fibrous tumor	Pelvis, pleura	20-70	Branching ectatic vessels,
	Malignant	Synovial sarcoma	Thigh, leg	15-40	Tight fascicles of uniform basophilic spindle cells, Pseudoglandular structures
		Undifferentiated pleomorphic sarcoma	Thigh	40-70	High grade anaplastic polygonal, round or spindle cells Bizarre nuclei, atypical mitoses, necrosis
		Alveolar soft part sarcoma	Trunk, extremities	15-35	Multiple nodules of eosinophilic round cells, septae
		Clear cell sarcoma	Tendons, extremities	20-40	Sheets of pale or clear spindle cells, wreath-like giant cells

Lipoma

- Benign tumor of fat
- Most common soft tissue tumor of adulthood
- Soft, mobile, painless → simple excision
- Well encapsulated mature adipocytes

Lipoma



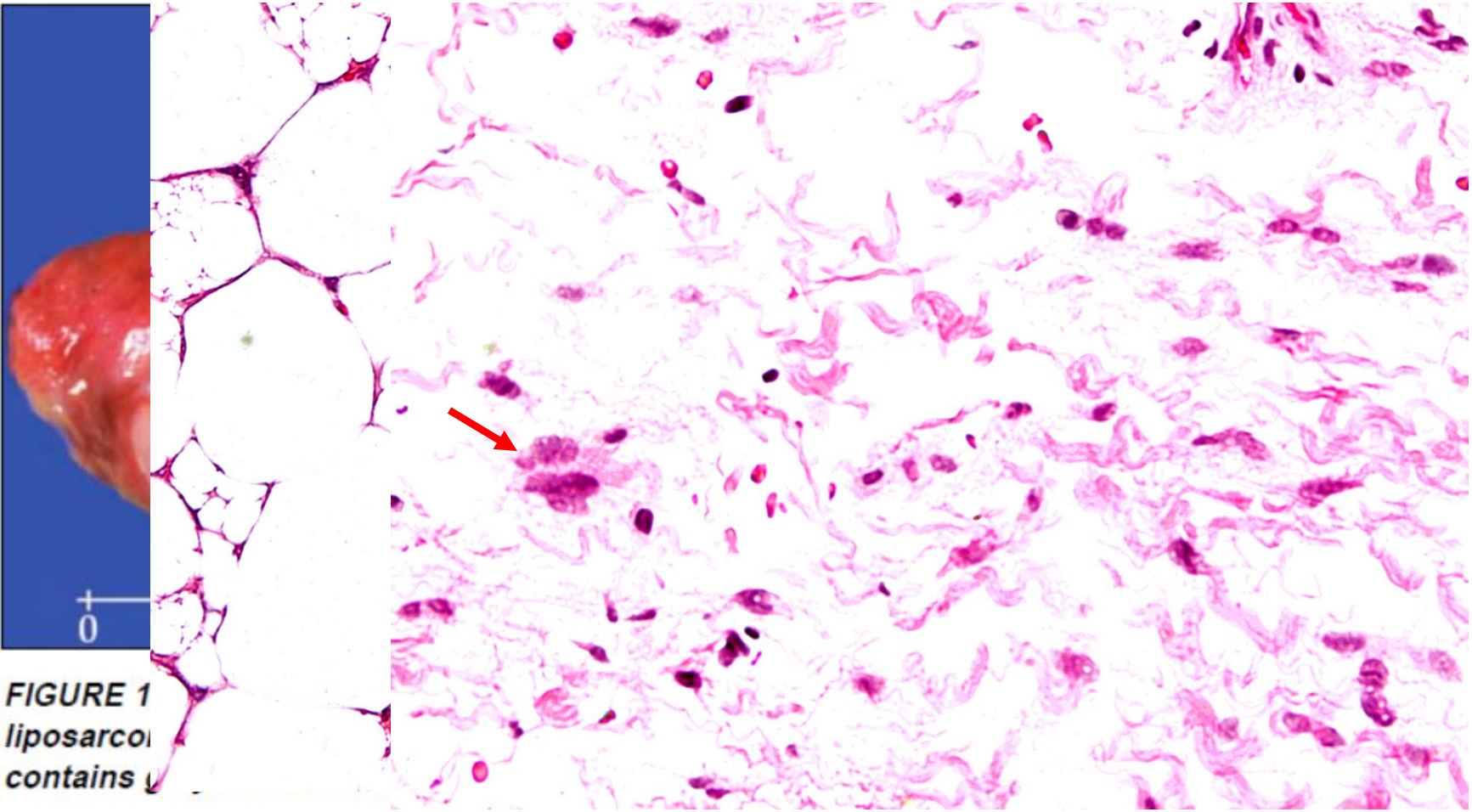
Mature adipocytes,

Modern Soft Tissue Pathology, 2010

Liposarcoma

- Locally aggressive mesenchymal neoplasm
- Variation cell size, nuclear atypia in both adipocyte and stromal cells
- Deep soft tissue of limb (thigh), retroperitoneum, paratesticular area and mediastinum

Liposarcoma



Lipoblast – Stromal atypia - bizzarre

Modern Soft Tissue Pathology, 2010