

# Musculoskeletal Pathology

18

Pathology MED & FINAL info. from PATHOMA book

\*Final material is in green squares\*

## SKELETAL SYSTEM

### I. ACHONDROPLASIA

- A. Impaired cartilage proliferation in the growth plate; common cause of dwarfism
- B. Due to an activating mutation in fibroblast growth factor receptor 3 (FGFR3); autosomal dominant
  - 1. Overexpression of FGFR3 inhibits growth.
  - 2. Most mutations are sporadic and related to increased paternal age.
- C. Clinical features
  - 1. Short extremities with normal-sized head and chest—due to poor endochondral bone formation; intramembranous bone formation is not affected.
    - i. Endochondral bone formation is characterized by formation of a cartilage matrix, which is then replaced by bone; it is the mechanism by which long bones grow.
    - ii. Intramembranous bone formation is characterized by formation of bone without a preexisting cartilage matrix; it is the mechanism by which flat bones (e.g., skull and rib cage) develop.
- D. Mental function, life span, and fertility are not affected.

### II. OSTEOPENIA

- A. Congenital defect of bone formation resulting in structurally weak bone
- B. Most commonly due to an autosomal dominant defect in collagen type I synthesis
- C. Clinical features
  - 1. Multiple fractures of bone (can mimic child abuse, but bruising is absent)
  - 2. Blue sclera—Thinning of scleral collagen reveals underlying choroidal veins.
  - 3. Hearing loss—Bones of the middle ear easily fracture.

### III. OSTEOPETROSIS

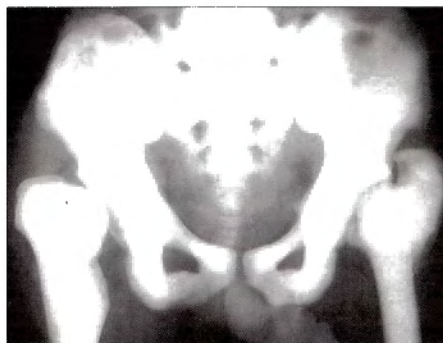
- A. Inherited defect of bone resorption resulting in abnormally thick, heavy bone that fractures easily
- B. Due to poor osteoclast function
- C. Multiple genetic variants exist; carbonic anhydrase II mutation leads to loss of the acidic microenvironment required for bone resorption.
- D. Clinical features include
  - 1. Bone fractures
  - 2. Anemia, thrombocytopenia, and leukopenia with extramedullary hematopoiesis—due to bony replacement of the marrow (myelophthitic process, Fig. 18.1)
  - 3. Vision and hearing impairment—due to impingement on cranial nerves
  - 4. Hydrocephalus—due to narrowing of the foramen magnum
  - 5. Renal tubular acidosis—seen with carbonic anhydrase II mutation
    - i. Lack of carbonic anhydrase results in decreased tubular reabsorption of  $\text{HCO}_3^-$ , leading to metabolic acidosis.
- E. Treatment is bone marrow transplant; osteoclasts are derived from monocytes.

#### IV. RICKETS/OSTEOMALACIA

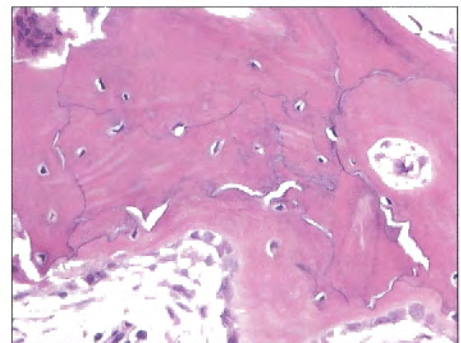
- A. Defective mineralization of osteoid
  1. Osteoblasts normally produce osteoid, which is then mineralized with calcium and phosphate to form bone.
- B. Due to low levels of vitamin D, which results in low serum calcium and phosphate
  1. Vitamin D is normally derived from the skin upon exposure to sunlight (85%) and from the diet (15%).
  2. Activation requires 25-hydroxylation by the liver followed by 1-alpha-hydroxylation by the proximal tubule cells of the kidney.
  3. Active vitamin D raises serum calcium and phosphate by acting on
    - i. Intestine—increases absorption of calcium and phosphate
    - ii. Kidney—increases reabsorption of calcium and phosphate
    - iii. Bone—increases resorption of calcium and phosphate
  4. Vitamin D deficiency is seen with decreased sun exposure (e.g., northern latitudes), poor diet, malabsorption, liver failure, and renal failure.
- C. Rickets is due to low vitamin D in children, resulting in abnormal bone mineralization.
  1. Most commonly arises in children < 1 year of age; presents with
    - i. Pigeon-breast deformity—inward bending of the ribs with anterior protrusion of the sternum
    - ii. Frontal bossing (enlarged forehead)—due to osteoid deposition on the skull
    - iii. Rachitic rosary—due to osteoid deposition at the costochondral junction
    - iv. Bowing of the legs may be seen in ambulating children.
- D. Osteomalacia is due to low vitamin D in adults.
  1. Inadequate mineralization results in weak bone with an increased risk for fracture.
  2. Laboratory findings include ↓ serum calcium, ↓ serum phosphate, ↑ PTH, and ↑ alkaline phosphatase.

#### V. OSTEOPOROSIS DEXA Scan

- A. Reduction in trabeculae bone mass
- B. Results in porous bone with an increased risk for fracture
- C. Risk of osteoporosis is based on peak bone mass (attained in early adulthood) and rate of bone loss that follows thereafter.
  1. Peak bone mass is achieved by 30 years of age and is based on (1) genetics (e.g., vitamin D receptor variants), (2) diet, and (3) exercise.
  2. Thereafter, slightly less than 1% of bone mass is lost each year; bone mass is lost more quickly with lack of weight-bearing exercise (e.g., space travel), poor diet, or decreased estrogen (e.g., menopause).
- D. Most common forms of osteoporosis are senile and postmenopausal.



**Fig. 18.1** Osteopetrosis. (Published with permission from LearningRadiology.com)



**Fig. 18.2** Paget disease of bone.

## E. Clinical features

1. Bone pain and fractures in weight-bearing areas such as the vertebrae (leads to loss of height and kyphosis), hip, and distal radius
2. Bone density is measured using a DEXA scan.
3. Serum calcium, phosphate, PTH, and alkaline phosphatase are normal; labs help to exclude osteomalacia (which has a similar clinical presentation).

## F. Treatment includes

1. Exercise, vitamin D, and calcium—limit bone loss
2. Bisphosphonates—induce apoptosis of osteoclasts
3. Estrogen replacement therapy is debated (currently not recommended).
4. Glucocorticoids are contraindicated (worsen osteoporosis).

## VI. PAGET DISEASE OF BONE

- A. Imbalance between osteoclast and osteoblast function
  1. Usually seen in late adulthood (average age > 60 years)
- B. Etiology is unknown; possibly viral
- C. Localized process involving one or more bones; does not involve the entire skeleton
- D. Three distinct stages are (1) osteoclastic, (2) mixed osteoblastic-osteoclastic, and (3) osteoblastic.
  1. End result is thick, sclerotic bone that fractures easily.
  2. Biopsy reveals a mosaic pattern of lamellar bone (Fig. 18.2).
- E. Clinical features
  1. Bone pain—due to microfractures
  2. Increasing hat size—Skull is commonly affected.
  3. Hearing loss—impingement on cranial nerve
  4. Lion-like facies—involvement of craniofacial bones
  5. Isolated elevated alkaline phosphatase—most common cause of isolated elevated alkaline phosphatase in patients > 40 years old
- F. Treatment includes
  1. Calcitonin—inhibits osteoclast function
  2. Bisphosphonates—induces apoptosis of osteoclasts
- G. Complications include
  1. High-output cardiac failure—due to formation of AV shunts in bone
  2. Osteosarcoma

## VII. OSTEOMYELITIS

- A. Infection of marrow and bone
  1. Usually occurs in children
- B. Most commonly bacterial; arises via hematogenous spread
  1. Transient bacteremia (children) seeds metaphysis. CM
  2. Open-wound bacteremia (adults) seeds epiphysis. AE
- C. Causes include
  1. *Staphylococcus aureus*—most common cause (90% of cases)
  2. *N gonorrhoeae*—sexually active young adults
  3. *Salmonella*—sickle cell disease
  4. *Pseudomonas*—diabetics or IV drug abusers
  5. *Pasteurella*—associated with cat or dog bite/scratches
  6. *Mycobacterium tuberculosis*—usually involves vertebrae (Pott disease)
- D. Clinical features
  1. Bone pain with systemic signs of infection (e.g., fever and leukocytosis)
  2. Lytic focus (abscess) surrounded by sclerosis of bone on x-ray; lytic focus is called sequestrum, and sclerosis is called involucrum.
- E. Diagnosis is made by blood culture.

staph.  
gonorrhoeae  
Salmonella

Pseudo  
Pas.  
TB

### VIII. AVASCULAR (ASEPTIC) NECROSIS

- A. Ischemic necrosis of bone and bone marrow
- B. Causes include trauma or fracture (most common), steroids, sickle cell anemia, and caisson disease.
- C. Osteoarthritis and fracture are major complications.

## BONE TUMORS

### I. OSTEOMA

- A. Benign tumor of bone
- B. Most commonly arises on the surface of facial bones
- C. Associated with Gardner syndrome

### II. OSTEIOD OSTEOMA

- A. Benign tumor of osteoblasts (that produce osteoid) surrounded by a rim of reactive bone
- B. Occurs in young adults < 25 years of age (more common in males)
- C. Arises in cortex of long bones (e.g., femur)
- D. Presents as bone pain that resolves with aspirin
- E. Imaging reveals a bony mass (< 2 cm) with a radiolucent core (osteoid).
- F. Osteoblastoma is similar to osteoid osteoma but is larger (> 2 cm), arises in vertebrae, and presents as bone pain that does not respond to aspirin.

### III. OSTEochondroma

- A. Tumor of bone with an overlying cartilage cap (Fig. 18.3); most common benign tumor of bone
- B. Arises from a lateral projection of the growth plate (metaphysis); bone is continuous with the marrow space.
- C. Overlying cartilage can transform (rarely) to chondrosarcoma.

### IV. OSTEOSARCOMA

- A. Malignant proliferation of osteoblasts
- B. Peak incidence is seen in teenagers; less commonly seen in the elderly
  1. Risk factors include familial retinoblastoma, Paget disease, and radiation exposure.
  2. Arises in the metaphysis of long bones, usually the distal femur or proximal tibia (region of the knee)
- C. Presents as a pathologic fracture or bone pain with swelling
- D. Imaging reveals a destructive mass with a 'sunburst' appearance and lifting of the periosteum (Codman triangle, Fig. 18.4A).

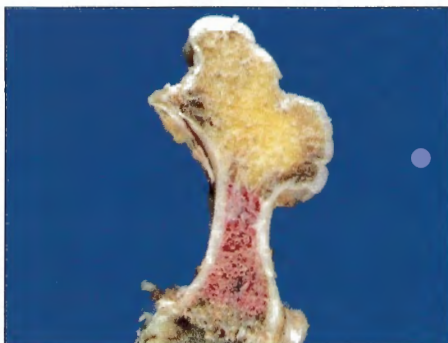


Fig. 18.3 Osteochondroma. (Courtesy of humpath.com)

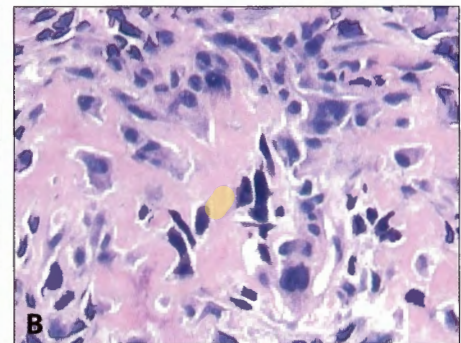


Fig. 18.4 Osteosarcoma. A, X-ray. B, Microscopic appearance. (A, Courtesy of Bulent Celasun, MD)

E. Biopsy reveals pleomorphic cells that produce osteoid (Fig. 18.4B).

#### V. GIANT CELL TUMOR

- Tumor comprised of multinucleated giant cells and stromal cells
- Occurs in young adults
- Arises in the epiphysis of long bones, usually the distal femur or proximal tibia (region of the knee)
- 'Soap-bubble' appearance on x-ray
- Locally aggressive tumor; may recur

#### VI. EWING SARCOMA

- Malignant proliferation of poorly-differentiated cells derived from neuroectoderm
- Arises in the diaphysis of long bones; usually in male children (< 15 years of age)
- 'Onion-skin' appearance on x-ray
- Biopsy reveals small, round blue cells that resemble lymphocytes (Fig. 18.5).
  - Can be confused with lymphoma or chronic osteomyelitis
  - (11;22) translocation is characteristic.
- Often presents with metastasis; responsive to chemotherapy

#### VII. CHONDROMA

- Benign tumor of cartilage
- Usually arises in the medulla of small bones of the hands and feet (Fig. 18.6)

#### VIII. CHONDROSARCOMA

- Malignant cartilage-forming tumor
- Arises in medulla of the pelvis or central skeleton

#### IX. METASTATIC TUMORS

- More common than primary tumors
- Usually result in osteolytic (punched-out) lesions
  - Prostatic carcinoma classically produces osteoblastic lesions.

## JOINT

### I. BASIC PRINCIPLES

- Connection between two bones
- Solid joints are tightly connected to provide structural strength (e.g., cranial sutures).
- Synovial joints have a joint space to allow for motion.
  - Articular surface of adjoining bones is made of hyaline cartilage (type II collagen) that is surrounded by a joint capsule.

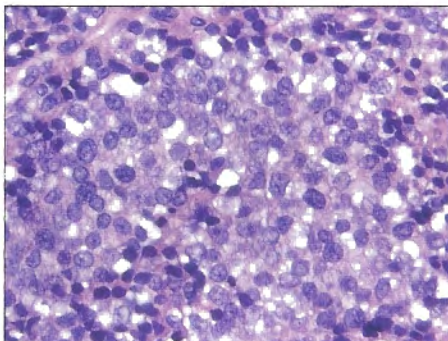


Fig. 18.5 Ewing sarcoma.



Fig. 18.6 Chondroma. (Published with permission from LearningRadiology.com)

2. Synovium lining the joint capsule secretes fluid rich in hyaluronic acid to lubricate the joint and facilitate smooth motion.

## II. DEGENERATIVE JOINT DISEASE (OSTEOARTHRITIS)

- A. Progressive degeneration of articular cartilage; most common type of arthritis
- B. Most often due to 'wear and tear'
- C. Major risk factor is age (common after 60 years); additional risk factors include obesity and trauma.
- D. Affects a limited number of joints (oligoarticular); hips, lower lumbar spine, knees, and the distal interphalangeal joints (DIP) and proximal interphalangeal joints (PIP) of fingers are common sites.
- E. Classic presentation is joint stiffness in the morning that worsens during the day.
- F. Pathologic features include
  1. Disruption of the cartilage that lines the articular surface (Fig. 18.7); fragments of cartilage floating in the joint space are called 'joint mice.'
  2. Eburnation of the subchondral bone
  3. Osteophyte formation (reactive bony outgrowths); classically arises in the DIP (Heberden nodes) and PIP (Bouchard nodes) joints of the fingers

## III. RHEUMATOID ARTHRITIS

- A. Chronic, systemic autoimmune disease
  1. Classically arises in women of late childbearing age
  2. Associated with HLA-DR4
- B. Characterized by involvement of joints
  1. Hallmark is synovitis leading to formation of a pannus (inflamed granulation tissue).
  2. Leads to destruction of cartilage and ankylosis (fusion) of the joint
- C. Clinical features
  1. Arthritis with morning stiffness that improves with activity.
    - i. Symmetric involvement of PIP joints of the fingers (swan-neck deformity), wrists (radial deviation), elbows, ankles, and knees is characteristic (Fig. 18.8); DIP is usually spared (unlike osteoarthritis).
    - ii. Joint-space narrowing, loss of cartilage, and osteopenia are seen on x-ray.
  2. Fever, malaise, weight loss, and myalgias
  3. Rheumatoid nodules—central zone of necrosis surrounded by epithelioid histiocytes; arise in skin and visceral organs
  4. Vasculitis—Multiple organs may be involved.
  5. Baker cyst—swelling of bursa behind the knee
  6. Pleural effusions, lymphadenopathy, and interstitial lung fibrosis

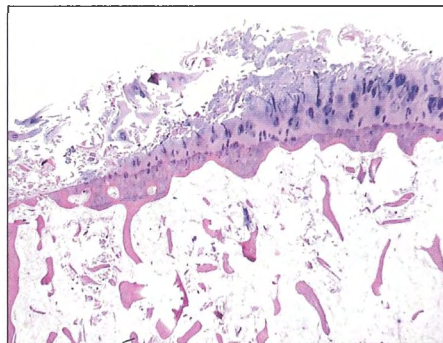


Fig. 18.7 Degenerative joint disease.



Fig. 18.8 Rheumatoid arthritis. (Courtesy of James Heilman, MD, Wikipedia)

- D. Laboratory findings
1. IgM autoantibody against Fc portion of IgG (rheumatoid factor); marker of tissue damage and disease activity
  2. Neutrophils and high protein in synovial fluid
- E. Complications include anemia of chronic disease and secondary amyloidosis.

#### IV. SERONEGATIVE SPONDYLOARTHROPATHIES

- A. Group of joint disorders characterized by
1. Lack of rheumatoid factor
  2. Axial skeleton involvement
  3. HLA-B27 association
- B. Ankylosing spondyloarthritis involves the sacroiliac joints and spine.
1. Arises in young adults, most often male
  2. Presents with low back pain; involvement of vertebral bodies eventually arises, leading to fusion of the vertebrae ('bamboo spine').
  3. Extra-articular manifestations include uveitis and aortitis (leading to aortic regurgitation).
- C. Reactive arthritis is characterized by the triad of arthritis, urethritis, and conjunctivitis. ↳ = Reiter's syndrome
1. Arises in young adults (usually males) weeks after a GI or *Chlamydia trachomatis* infection
- D. Psoriatic arthritis is seen in 10% of cases of psoriasis.
1. Involves axial and peripheral joints; DIP joints of the hands and feet are most commonly affected, leading to "sausage" fingers or toes.

#### V. INFECTIOUS ARTHRITIS = suppurative arthritis

- A. Arthritis due to an infectious agent, usually bacterial
- B. Causes include
1. *N gonorrhoeae*—young adults; most common cause
  2. *S aureus*—older children and adults; 2nd most common cause
- C. Classically involves a single joint, usually the knee
- D. Presents as a warm joint with limited range of motion; fever, increased white count, and elevated ESR are often present.
- ↳ erythrocyte sedimentation rate

#### VI. GOUT

- A. Deposition of monosodium urate (MSU) crystals in tissues, especially the joints
- B. Due to hyperuricemia; related to overproduction or decreased excretion of uric acid
1. Uric acid is derived from purine metabolism and is excreted by the kidney.
- C. Primary gout is the most common form; etiology of hyperuricemia is unknown.
- D. Secondary gout is seen with
1. Leukemia and myeloproliferative disorders—Increased cell turnover leads to hyperuricemia.
  2. Lesch-Nyhan syndrome—X-linked deficiency of hypoxanthine-guanine phosphoribosyltransferase (HGPRT); presents with mental retardation and self-mutilation
  3. Renal insufficiency—decreased renal excretion of uric acid
- E. Acute gout presents as exquisitely painful arthritis of the great toe (podagra)
1. MSU crystals deposit in the joint, triggering an acute inflammatory reaction.
  2. Alcohol or consumption of meat may precipitate arthritis.
- F. Chronic gout leads to
1. Development of tophi—white, chalky aggregates of uric acid crystals with fibrosis and giant cell reaction in the soft tissue and joints (Fig. 18.9A)
  2. Renal failure—Urate crystals may deposit in kidney tubules (urate nephropathy).

- G. Laboratory findings include **hyperuricemia**; synovial fluid shows **needle-shaped crystals with negative birefringence** under polarized light (Fig. 18.9B).
- H. Pseudogout resembles gout clinically, but is due to **deposition of calcium pyrophosphate dihydrate (CPPD)**; synovial fluid shows **rhomboid-shaped crystals with weakly positive birefringence** under polarized light.

## SKELETAL MUSCLE

### I. DERMATOMYOSITIS

- A. Inflammatory disorder of the skin and skeletal muscle
- B. Unknown etiology; some cases are associated with carcinoma (e.g., gastric carcinoma).
- C. Clinical features
1. Bilateral proximal muscle weakness; distal involvement can develop late in disease.
  2. Rash of the upper eyelids (heliotrope rash); malar rash may also be seen.
  3. Red papules on the elbows, knuckles, and knees (Gottron papules)
- D. Laboratory findings
1. Increased creatine kinase
  2. Positive ANA and anti-Jo-1 antibody
  3. Perimysial inflammation (CD4<sup>+</sup> T cells) with perifascicular atrophy on biopsy (Fig. 18.10)
- E. Treatment is corticosteroids.

### II. POLYMYOSITIS

- A. Inflammatory disorder of skeletal muscle
- B. Resembles dermatomyositis clinically, but skin is not involved; endomysial inflammation (CD8<sup>+</sup> T cells) with necrotic muscle fibers is seen on biopsy.

### III. X-LINKED MUSCULAR DYSTROPHY

- A. Degenerative disorder characterized by muscle wasting and replacement of skeletal muscle by adipose tissue
- B. Due to defects of dystrophin gene
1. Dystrophin is important for anchoring the muscle cytoskeleton to the extracellular matrix.
  2. Mutations are often spontaneous; large gene size predisposes to high rate of mutation.
- C. Duchenne muscular dystrophy is due to deletion of dystrophin.
1. Presents as proximal muscle weakness at 1 year of age; progresses to involve distal muscles
    - i. Calf pseudohypertrophy is a characteristic finding.
    - ii. Serum creatine kinase is elevated.
  2. Death results from cardiac or respiratory failure; myocardium is commonly involved.
- D. Becker muscular dystrophy is due to mutated dystrophin; clinically results in milder disease

## NEUROMUSCULAR JUNCTION

### I. MYASTHENIA GRAVIS

- A. Autoantibodies against the postsynaptic acetylcholine receptor at the neuromuscular junction
- B. More commonly seen in women



- C. Clinical features
  1. Muscle weakness that worsens with use and improves with rest; classically involves the eyes, leading to ptosis and diplopia
  2. Symptoms improve with anticholinesterase agents.
  3. Associated with thymic hyperplasia or thymoma; thymectomy improves symptoms.

## II. LAMBERT-EATON SYNDROME

- A. Antibodies against presynaptic calcium channels of the neuromuscular junction
- B. Arises as a paraneoplastic syndrome, most commonly due to small cell carcinoma of the lung
- C. Leads to impaired acetylcholine release
  1. Firing of presynaptic calcium channels is required for acetylcholine release.
- D. Clinical features
  1. Proximal muscle weakness that improves with use; eyes are usually spared.
  2. Anticholinesterase agents do not improve symptoms.
  3. Resolves with resection of the cancer

## SOFT TISSUE TUMORS

### I. LIPOMA

- A. Benign tumor of adipose tissue
- B. Most common benign soft tissue tumor in adults

### II. LIPOSARCOMA

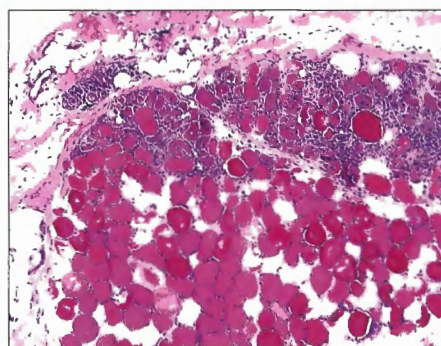
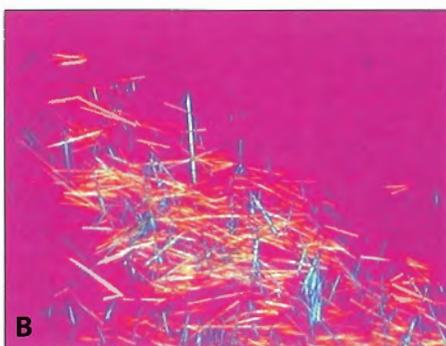
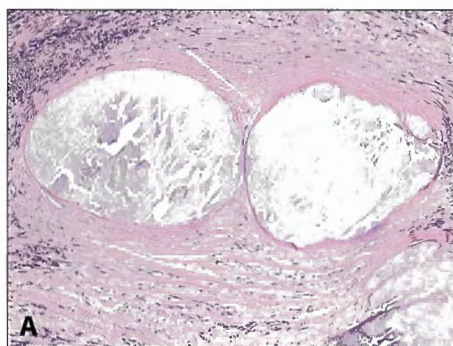
- A. Malignant tumor of adipose tissue
- B. Most common malignant soft tissue tumor in adults
- C. Lipoblast is the characteristic cell.

### III. RHABDOMYOMA

- A. Benign tumor of skeletal muscle
- B. Cardiac rhabdomyoma is associated with tuberous sclerosis.

### IV. RHABDOMYOSARCOMA

- A. Malignant tumor of skeletal muscle
- B. Most common malignant soft tissue tumor in children
- C. Rhabdomyoblast is the characteristic cell; desmin positive
- D. Most common site is the head and neck; vagina is the classic site in young girls.



**Fig. 18.9** Gout. **A**, Tophi. **B**, Negative birefringence. (B, Courtesy of Ed Uthman, MD)

**Fig. 18.10** Dermatomyositis. (Courtesy of Peter Pytel, MD)



## INTRODUCTION

### I. SKIN

- A. Functions as a barrier against environmental insults and fluid loss
- B. Composed of an epidermis and dermis
- C. Epidermis is comprised of keratinocytes and has four layers (Fig. 19.1).
  - 1. Stratum basalis—regenerative (stem cell) layer
  - 2. Stratum spinosum—characterized by desmosomes between keratinocytes
  - 3. Stratum granulosum—characterized by granules in keratinocytes
  - 4. Stratum corneum—characterized by keratin in anucleate cells
- D. Dermis consists of connective tissue, nerve endings, blood and lymphatic vessels, and adnexal structures (e.g., hair shafts, sweat glands, and sebaceous glands).

## INFLAMMATORY DERMATOSES

### I. ATOPIC (ECZEMATOUS) DERMATITIS

- A. Pruritic, erythematous, oozing rash with vesicles and edema; often involves the face and flexor surfaces
- B. Type I hypersensitivity reaction; associated with asthma and allergic rhinitis

### II. CONTACT DERMATITIS

- A. Pruritic, erythematous, oozing rash with vesicles and edema
- B. Arises upon exposure to allergens such as
  - 1. Poison ivy and nickel jewelry (type IV hypersensitivity)
  - 2. Irritant chemicals (e.g., detergents)
  - 3. Drugs (e.g., penicillin)
- C. Treatment involves removal of the offending agent and topical glucocorticoids, if needed.

### III. ACNE VULGARIS

- A. Comedones (whiteheads and blackheads), pustules (pimples), and nodules; extremely common, especially in adolescents
- B. Due to chronic inflammation of hair follicles and associated sebaceous glands
  - 1. Hormone-associated increase in sebum production (sebaceous glands have androgen receptors) and excess keratin production block follicles, forming comedones.
  - 2. *Propionibacterium acnes* infection produces lipases that break down sebum, releasing proinflammatory fatty acids; results in pustule or nodule formation
- C. Treatment includes benzoyl peroxide (antimicrobial) and vitamin A derivatives (e.g., isotretinoin), which reduce keratin production.

### IV. PSORIASIS

- A. Well-circumscribed, salmon-colored plaques with silvery scale, usually on extensor surfaces and the scalp (Fig. 19.2A); pitting of nails may also be present.
- B. Due to excessive keratinocyte proliferation

- C. Possible autoimmune etiology
  1. Associated with HLA-C
  2. Lesions often arise in areas of trauma (environmental trigger).
- D. Histology (Fig. 19.2B) shows
  1. Acanthosis (epidermal hyperplasia)
  2. Parakeratosis (hyperkeratosis with retention of keratinocyte nuclei in the stratum corneum)
  3. Collections of neutrophils in the stratum corneum (Munro microabscesses)
  4. Thinning of the epidermis above elongated dermal papillae; results in bleeding when scale is picked off (Auspitz sign)
- E. Treatment involves corticosteroids, UV light with psoralen, or immune-modulating therapy.

#### V. LICHEN PLANUS

- A. Pruritic, planar, polygonal, purple papules (Fig. 19.3A), often with reticular white lines on their surface (Wickham striae); commonly involves wrists, elbows, and oral mucosa
  1. Oral involvement manifests as Wickham striae.
- B. Histology shows inflammation of the dermal-epidermal junction with a 'saw-tooth' appearance (Fig. 19.3B).
- C. Etiology is unknown; associated with chronic hepatitis C virus infection

### BLISTERING DERMATOSES

#### I. PEMPHIGUS VULGARIS

- A. Autoimmune destruction of desmosomes between keratinocytes

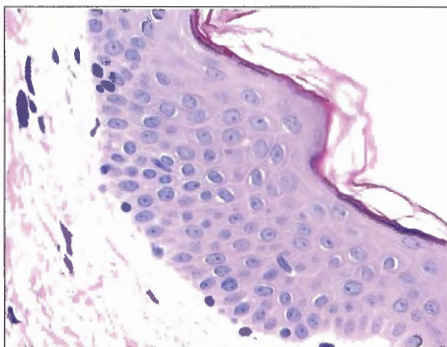


Fig. 19.1 Skin histology, normal.

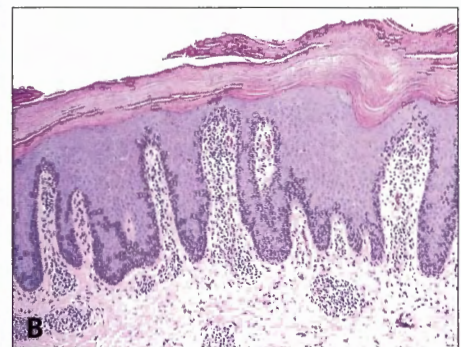


Fig. 19.2 Psoriasis. **A**, Clinical appearance. **B**, Microscopic appearance. (A, Courtesy of Vesna Petronic-Rosic, MD)

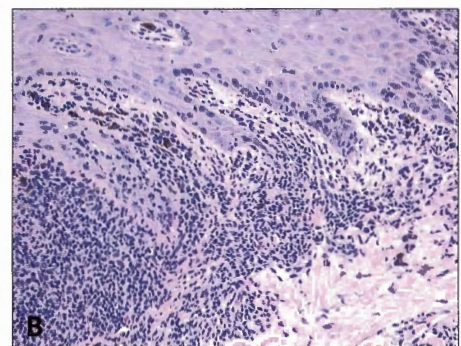


Fig. 19.3 Lichen planus. **A**, Clinical appearance. **B**, Microscopic appearance. (A, Courtesy of Vesna Petronic-Rosic, MD)

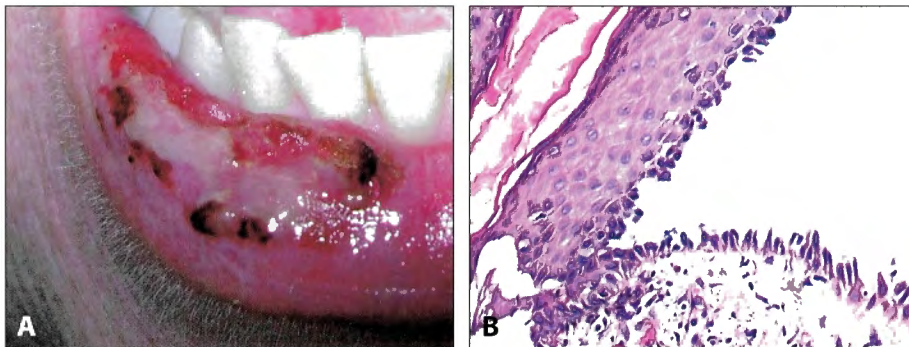
- B. Due to IgG antibody against desmoglein (type II hypersensitivity)
- C. Presents as skin and oral mucosa bullae (Fig. 19.4A).
  1. Acantholysis (separation) of stratum spinosum keratinocytes (normally connected by desmosomes) results in suprabasal blisters.
  2. Basal layer cells remain attached to basement membrane via hemidesmosomes ('tombstone' appearance, Fig. 19.4B).
  3. Thin-walled bullae rupture easily (Nikolsky sign), leading to shallow erosions with dried crust.
  4. Immunofluorescence highlights IgG surrounding keratinocytes in a 'fish net' pattern.

## II. BULLOUS PEMPHIGOID

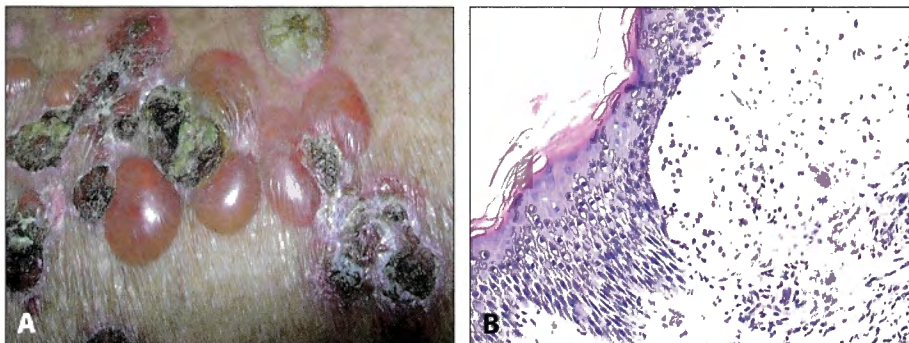
- A. Autoimmune destruction of hemidesmosomes between basal cells and the underlying basement membrane
- B. Due to IgG antibody against hemidesmosome components (BP180) of the basement membrane
- C. Presents as blisters of the skin (Fig. 19.5A), usually in the elderly; oral mucosa is spared.
  1. Basal cell layer is detached from the basement membrane (Fig. 19.5B).
  2. Tense bullae do not rupture easily; clinically milder than pemphigus vulgaris
- D. Immunofluorescence highlights IgG along basement membrane (linear pattern).

## III. DERMATITIS HERPETIFORMIS

- A. Autoimmune deposition of IgA at the tips of dermal papillae
- B. Presents as pruritic vesicles and bullae that are grouped (herpetiform, Fig. 19.6)
- C. Strong association with celiac disease; resolves with gluten-free diet



**Fig. 19.4** Pemphigus vulgaris. **A**, Clinical appearance. **B**, Microscopic appearance. (A, Courtesy of Vesna Petronic-Rosic, MD)



**Fig. 19.5** Bullous pemphigoid. **A**, Clinical appearance. **B**, Microscopic appearance. (A, Courtesy of Vesna Petronic-Rosic, MD)

#### IV. ERYTHEMA MULTIFORME (EM)

- A. Hypersensitivity reaction characterized by targetoid rash and bullae (Fig. 19.7)
  1. Targetoid appearance is due to central epidermal necrosis surrounded by erythema.
- B. Most commonly associated with HSV infection; other associations include *Mycoplasma* infection, drugs (penicillin and sulfonamides), autoimmune disease (e.g., SLE), and malignancy.
- C. EM with oral mucosa/lip involvement and fever is termed Stevens-Johnson syndrome (SJS).
  1. Toxic epidermal necrolysis is a severe form of SJS characterized by diffuse sloughing of skin, resembling a large burn; most often due to an adverse drug reaction

### EPITHELIAL TUMORS

#### I. SEBORRHEIC KERATOSIS

- A. Benign squamous proliferation; common tumor in the elderly
- B. Presents as raised, discolored plaques on the extremities or face; often has a coin-like, waxy, 'stuck-on' appearance (Fig. 19.8A)
  1. Characterized by keratin pseudocysts on histology (Fig. 19.8B)
- C. Leser-Trélat sign is the sudden onset of multiple seborrheic keratoses and suggests underlying carcinoma of the GI tract (Fig. 19.8C).

#### II. ACANTHOSIS NIGRICANS

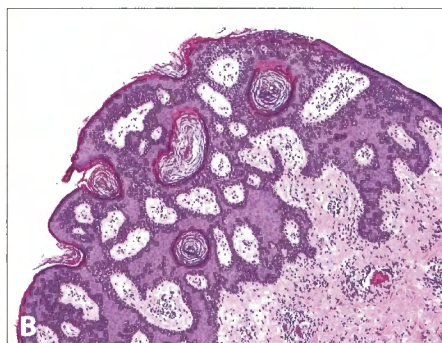
- A. Epidermal hyperplasia with darkening of the skin ('velvet-like' skin, Fig. 19.9); often involves the axilla or groin



**Fig. 19.6** Dermatitis herpetiformis. (Courtesy of Vesna Petronic-Rosic, MD)



**Fig. 19.7** Erythema multiforme. (Courtesy of James Heilman, MD, Wikipedia)



**Fig. 19.8** Seborrheic keratosis. **A**, Clinical appearance. **B**, Microscopic appearance. **C**, Sign of Leser-Trélat. (A and C, Courtesy of Vesna Petronic-Rosic, MD)