MSS practical 1
This is the normal fetal growth plate demonstrating the process of endochondral bone formation in a long bone.
Figure 26-3 Active growth plate with ongoing enchondral ossification. 1, Reserve zone. 2, Zone of proliferation. 3, Zone of hypertrophy. 4, Zone of mineralization. 5, Primary spongiosa.
This is irregular new bone, or woven bone, which is forming in the region of a fracture. **Osteoblasts** are seen lining the irregular trabeculae, and there is an **osteoclast** involved in bone remodelling.
Here is a region of fracture with remaining disrupted trabeculae at the left and bottom. The paler pink new bone is forming at the right and top.
Figure 26-1 Woven bone (A) is more cellular and disorganized than lamellar bone (B).
In this region of a recent fracture, callus is seen forming at the broken ends of bony trabeculae that extend to the center from the left and top.
An infection that becomes established in bone is difficult to treat, since bone is relatively avascular. The result is an osteomyelitis. If this process occurs over years, the bone becomes markedly remodelled. At the site of involvement, there is a central area of pale necrotic "sequestrum" that is surrounded by irregular remodelled "involutum" that produces marked distortion. The weakened bone is prone to fracture. In this case, the irregular involucrum is seen above in the upper femur. In the view below, the sequestrum is seen around the metallic prosthesis used to stabilize a femur at the hip.
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At high magnification can be seen acute inflammation as well as chronic inflammation with fibrosis and an irregular fragment of necrotic bone in this case of acute and chronic osteomyelitis. In this case, a diabetic foot ulcer extended into the underlying calcaneus.
At high magnification can be seen **acute inflammation** as well as chronic inflammation with fibrosis and an irregular fragment of **necrotic bone** in this case of acute and chronic osteomyelitis. In this case, a diabetic foot ulcer extended into the underlying calcaneus.
This is chronic osteomyelitis. Note the fibrosis of the marrow space accompanied by chronic inflammatory cells. There can be bone destruction with remodelling. Osteomyelitis is very difficult to treat.
This femur has a large eccentric tumor mass arising in the metaphyseal region. This is an osteosarcoma (a variant known as parosteal osteogenic sarcoma) of bone. These tumors most often occur in young persons (note that the epiphysis seen at the right is still present).
The neoplastic spindle cells of an osteosarcoma are seen to be making pink osteoid here. Osteoid production by a sarcoma is diagnostic of osteosarcoma.
Figure 26-25 Fine, lacelike pattern of neoplastic bone produced by anaplastic malignant tumor cells in an osteosarcoma. Note the abnormal mitotic figures (arrow).
Here is another example of a chondrosarcoma arising in the pelvis. Note the extensive nodules of white to bluish-white cartilagenous tumor tissue eroding and extending outward from the bone at the lower right. Chondrosarcomas can occur over a wide age range, and there is a slight male predominance. Many of them are slow growing, with symptoms present for a decade or more.
This is a femur that is hemisectioned to reveal an irregular tumor mass composed of islands of bluish-white cartilagenous tissue. This is a chondrosarcoma, which has a predilection for involvement of metaphysis or diaphysis. As seen here, the cortex is thickened and eroded, but there is little periosteal reaction.
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.
This is the low power microscopic appearance of a chondrosarcoma. The tissue is recognizable as cartilage, and there are chondrocytes in clear spaces, but there is no orderly pattern. At the bottom, this neoplasm can be seen invading and destroying bone.
This is a Ewing sarcoma. This type of primary bone tumor mainly occurs in the diaphysis of long bones of children and young adults. There is a slight male predominance. As seen here, the irregular tan to red to brown tumor mass is breaking through the bone cortex. More normal fatty marrow is seen at the far right.
Ewing sarcoma is one of the "small round blue cell" tumors of childhood.
This section of vertebral bone from autopsy shows multiple foci pale irregular metastases. The most common neoplasm involving bone is a metastasis. The most common primary bone tumors are benign. The most common malignant primary bone tumors are osteosarcomas.
At high magnification, metastatic infiltrating ductal carcinoma of breast is seen within bone and filling the marrow cavity. There is reactive new bone with pale pink osteoid being laid down next to a bony spicule at the upper left.
This is an example of an excised osteochondroma that has a broader base, but still consists of cancellous bone capped by cartilage.
The microscopic appearance of an osteochondroma displays the benign cartilaginous cap at the left and the bony cortex at the right. This bone growth, though benign, can sometimes cause problems of pain and irritation that leads to removal surgically.
Here is a giant cell tumor of bone. The proximal femur has been amputated and cut in half to reveal an irregular dark red-black hemorrhagic mass in the epiphyseal region. Giant cell tumors appear lytic on plain film radiography.
Figure 26-33  Benign giant cell tumor illustrating an abundance of multinucleated giant cells with background mononuclear stromal cells.
The gross appearance of an aneurysmal bone cyst (ABC) is shown here. The radiographic appearance of an ABC is typically that of ballooning, or aneurysmal dilation, of the affected bone—usually the metaphysis of a long bone or dorsal vertebral body. Grossly, there are fleshy aggregates of tumor surrounding cystic spaces filled with blood. The breakdown of the blood into hemosiderin has led to brownish staining of some of the cysts seen here.
Figure 26-35  Aneurysmal bone cyst with blood-filled cystic space surrounded by a fibrous wall containing proliferating fibroblasts, reactive woven bone, and osteoclast-type giant cells.
The center of the "brown tumor" contains osteoclasts and mononuclear cells and fibroblasts with focal hemorrhages. The hemosiderin from the hemorrhage produces the grossly brown color. Such lesions are nowadays uncommon because hyperparathyroidism is treated before such lesions develop.
This is Paget disease of bone in which the mixed osteoclastic and osteoblastic stage is present. A line of osteoblasts is present forming new bone, but lacunae containing multinucleate osteoclasts are at the same time destroying bone. The result is a patchwork mosaic of bone without an evenly formed lamellar structure. This stage of Paget disease is preceded by a mainly lytic phase and is followed by a "burnt out" sclerotic phase.
Figure 26-13 Mosaic pattern of lamellar bone pathognomonic of Paget disease.
Scoliosis

More severe curvature of the vertebral column is seen here. This patient had severe deformity and back pain. The
The bone in these vertebral bodies demonstrates marked osteoporosis with thinning and loss of bony trabeculae. The second body from the right shows a greater degree of compression than the others. Osteoporosis is accelerated bone loss with age and is particularly common amongst postmenopausal women, putting them at risk for fractures (hip, wrist, vertebrae).
Note the wedge-shaped area of avascular necrosis (osteonecrosis) at the upper right of this femoral head. Avascular necrosis results from bone ischemia, which can be due to many causes, including trauma and corticosteroid administration, though idiopathic cases are common. There is pain with activity, progressing to pain at rest. Eventually, the necrotic bone collapses, distorting the overlying articular cartilage and producing secondary osteoarthritis. [Image]
The changes of osteoarthritis are more felt than seen. There is minimal outward deformity to this left hand.
More advanced osteoarthritis leads to osteophyte formation, seen here as a small **protuberance** on the proximal interphalangeal joint (Bouchard node). A similar lesion of the distal interphalangeal joint is known as a Heberden node.
The knobby excrescences at the left side of this vertebral column are due to degenerative osteoarthritis. This is the pronounced "lipping" of the vertebral bodies representing prominent osteophyte formation.
The femoral head at the left (removed because of fracture) shows smooth, glistening articular cartilage, while the femoral head at the right shows a rough, eburnated, irregular appearance typical for 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).
The prominent ulnar deviation of the hands and "swan neck" deformity of the fingers seen here is due to rheumatoid arthritis (RA). This autoimmune disease leads to synovial proliferation with inflammation and joint destruction, typically in a symmetrical pattern involving small joints of hands and feet, followed by wrists, ankles, elbows, and knees. Rheumatoid factor can be identified serologically in most, but not all, RA patients.
This is the synovium in rheumatoid arthritis. There is chronic inflammation with lymphocytes and plasma cells that produce the blue areas beneath the nodular proliferations. This "pannus" is destructive and produces erosion of the articular cartilage, eventually destroying the joint.
Sometimes persons with rheumatoid arthritis (RA) have rheumatoid nodules form in subcutaneous locations at pressure points, such as the elbow shown here. Rheumatoid nodules may also appear viscerally, such as on the pleura of the lung.
Here is a rheumatoid nodule. Such nodules are seen in patients with severe rheumatoid arthritis and appear beneath the skin over bony prominences such as the elbow. They can occasionally appear in visceral organs. There is a central area of fibrinoid necrosis surrounded by pallisading epithelioid macrophages, and other mononuclear cells.
This is gout. Gouty arthritis results from deposition of sodium urate crystals in joints. The joint most often affected is the first MP joint (big toe) as seen here. Acute attacks are characterized by severe pain, swelling, and erythema of the joint.
The pale areas seen here are tophi, or aggregates of urate crystals surrounded by infiltrates of lymphocytes, macrophages, and foreign body giant cells. A tophus is the characteristic finding of gout. Tophi are most likely to be found in soft tissues, including tendons and ligaments, around joints. Less commonly tophi appear elsewhere. Tophaceous gout results from continued precipitation of sodium urate crystals during attacks of acute gout.
If synovial fluid is aspirated from a patient with gout, the fluid can be examined for the presence of sodium urate crystals, which are seen here to be needle shaped. If they are observed under polarized light with a red compensator, they appear yellow (negatively birefringent) in the main ("slow") axis of the compensator and blue in the opposite perpendicular direction.
A rhomboid shaped crystal of calcium pyrophosphate dihydrate (CPPD) appears bluish-white (weak positive birefringence) by polarized light microscopy with a red plate. Calcium pyrophosphate crystal deposition disease (sometimes called "pseudogout") is most often seen in persons over the age of 50, and can lead to acute, subacute, or chronic arthritis of knees, wrists, elbows, shoulders, and ankles. The articular damage is progressive, though in most persons the disease is not severe.
This baby's extremities are positioned oddly because there have been multiple fractures due to osteogenesis imperfecta (OI). This disease leads to multiple fractures. The basic problem is a defect in the formation of type 1 collagen that forms bone matrix. There are several types of OI with different inheritance patterns.
There is a bluish-gray appearance to the sclerae, which reflects the abnormal collagen structure with abnormal type 1 collagen synthesis. This is osteogenesis imperfecta type I, which is compatible with survival. Persons with this disorder have normal survival, have normal stature, but have increased risk for fractures and have dental and hearing problems.
This is a liposarcoma arising in the region of the lower thigh posterior to the knee. Note that it is a large, bulky mass. There is enough differentiation to provide a yellowish hue (suggesting adipose tissue differentiation) to this fleshy tumor mass. [Image courtesy of John Nicholls MD, Hong Kong University]
This is a lipoma. It is benign and tends to enlarge very slowly over time. Note how it is indistinguishable microscopically from normal adipose tissue. It is a neoplasm because grossly it formed a mass lesion.
At high magnification, the lipoblasts in this liposarcoma are visible.
This is another low grade lesion of soft tissue known as a desmoid tumor. These are aggressive fibroblastic proliferations that can occur in shoulder, chest wall, neck, and thigh in both men and women. In women during or just following pregnancy, they may appear in abdominal wall.
At high magnification, the very atypical spindle cells of this sarcoma (a malignant fibrous histiocytoma, or MFH) are seen along with a bizarre quadripolar mitotic figure at the right. In general, soft tissue sarcomas have a poor prognosis because they are large when diagnosed and histologically high grade, aggressive lesions.
The normal histologic appearance of the skin is shown here. At the top is the **epidermis**. A thin layer of **keratin** overlies the epidermis. This layer of keratinization is thicker on the palms and soles and in areas where skin is rubbed or irritates. Beneath the epidermis is the **dermis** containing connective tissue with collagen and elastic fibers. At the center can be seen a **hair follicle** with surrounding **sebaceous glands**.
This is a larger flat 4 cm long pigmented nevus on the upper back. Such larger nevi are often congenital. They are sometimes called "cafe-au-lait" spots.
Here is the low power microscopic appearance of a benign pigmented nevus. Small amounts of dark pigment are seen near the skin surface. The small blue nevus cells can extend into the dermis and around adnexal structures, but this is not invasion.
At high power, the benign nature of the nevus cells are seen below the epidermis. The cells form small aggregates in nests. The nevus cells (melanocytes) have a clear cytoplasm and small round blue nuclei without prominent nucleoli or mitoses.
In this junctional nevus, there are nevus cells in nests in the lower epidermis as well as nests appearing to "drop off" into the upper dermis. Unlike a melanoma, there is no significant atypia and no inflammation.
Seen on the hand are age or "liver" spots, termed senile lentigines, which are common on sun-exposed skin of older adults. Perhaps 90% of Caucasians over age 70 have them. They can be pinpoint to 1 cm in size and are often multiple.
This is the microscopic appearance of lentigo senilis, commonly known as an age or "liver" spot. The rete ridges are elongated and appear club-shaped or tortuous. Melanocytes are increased in the basal layer and melanophages appear in the upper dermis.
Vitiligo appears as irregular areas of hypopigmentation of the skin, as shown here on the hand. This is a localized form of hypopigmentation (as contrasted with the diffuse form known as oculocutaneous albinism). Many cases are idiopathic, though sometimes a systemic disease may be present.
A malignant melanoma of the skin is shown here. The lesion is larger than a centimeter, has irregular borders, and irregular pigmentation, with one very dark area on the left. The prognosis of a melanoma correlates best with the depth of invasion. Larger lesions are more likely to have invaded further. Sun exposure in light-skinned persons leads to melanoma formation.
This is the microscopic appearance of a malignant melanoma. Large polygonal cells (or spindle cells in some cases) have very pleomorphic nuclei which contain prominent nucleoli. The neoplasm is making brown melanin pigment. A Fontana-Masson stain for melanin may help to detect small amounts of cytoplasmic melanin.
This is a *squamous cell carcinoma* arising on the dorsum of the hand. Besides sun exposure, risk factors for squamous cell carcinoma arising in skin include carcinogens such as tars, chronic ulcers, burn scars, arsenic poisoning, and radiation exposure. In this case there was a history of both sun exposure as well as exposure to carcinogens.
A squamous cell carcinoma is shown at high magnification. Many of the cells demonstrate keratinization with abundant pink cytoplasm. Note the prominent cell borders between which can be seen intercellular bridges (desmosomes). A mitosis is seen near the center.
Nests of basaloid cells are dropping off into the upper dermis in this example of a basal cell carcinoma of the skin. These neoplasms can be multifocal. They are slow growing but relentless. The problems they cause are related to local invasion. Metastases are quite rare.
For comparison, a large scar is seen here below the medial aspect of the right knee. The original large laceration was not closed with sutures and "granulated in" by "second intention" to form this large, irregular, dense white scar. However, it is not nodular.
Bundles of dense collagen form the keloid as seen here microscopically.
This little yellow plaque is called a xanthelasma. It is just a focal collection of lipid in macrophages in the dermis of the skin. Such lesions may appear in persons with hyperlipidemia.
This is a simple friction blister of the skin from irritation (using a garden spade for a prolonged time). The superficial epidemis has separated and fluid has collected.
A common wart, or verruca vulgaris, is shown here. There is epithelial hyperplasia marked by hyperkeratosis along with papillomatosis to produce the rough, warty gross appearance. The granular layer is prominent. These lesions are usually a few millimeters to 1 cm in size and are most often located on the hands. However, such lesions can also
This is psoriasis. The thick, silvery, scaling lesions are most often found over bony prominences, scalp, genitalia, and hands. It occurs when there is abnormal proliferation and turnover of epidermis (reduced from a month to only 4 days for a cell to transit from basal layer to surface).
Microscopically, psoriasis is characterized by downward elongation of the rete ridges with thinning of overlying stratum granulosum, with parakeratosis above this. Small aggregates of neutrophils with surrounding spongiform change are seen in the superficial epidermis. Capillaries within dermal papillae are brought close to the surface.
There is a **large, tense bulla** at the center and a small bulla at the left. Bullous lesions may occur with infections and drugs. The lesions seen here developed with a condition known as bullous pemphigoid.
This is normal skeletal muscle in cross section at low power power. A connective tissue band, called the epimysium, surrounds several fascicles. A perimysium surrounds an individual fascicle. An individual muscle fiber in a fascicle is invested in an endomysium.
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At high power in cross section, normal skeletal muscle is seen to be composed of muscle fibers. Each fiber contains the contractile proteins: thick myosin filament interdigitating with thin actin filaments. The multiple nuclei of the fiber are at the periphery of the muscle fiber.
At medium power in cross section with ATPase stain at pH 9.4, the pattern of type 1 and type 2 fibers is seen. These fibers are normally intermixed to form a checkerboard pattern. The type 1 fibers (slow twitch, oxidative) are light tan and the type 2 fibers (mainly glycolytic) stain dark brown.
Denervation and atrophy

B

Reinnervation and regeneration

C

E

F
This is Duchenne muscular dystrophy. There is degeneration of muscle fibers along with some regeneration and scattered chronic inflammatory cells, fibrosis, and hypertrophy of remaining muscle fibers. Duchenne's is due to a defective gene on the X chromosome that leads to an inability to produce the membrane skeletal protein dystrophin. Thus, this is an X-linked recessive disorder. About 30% of cases represent new mutations.
This immunoperoxidase stain utilizes antibody to the muscle protein called dystrophin, which is seen to be localized at the periphery of the normal muscle fibers shown here. Dystrophin, which is coded by a gene on the X chromosome, appears to stabilize the membrane.
This immunoperoxidase stain utilizes antibody to the muscle protein called dystrophin, which is absent in this patient with Duchenne muscular dystrophy, because the normal gene on the X chromosome is not present.
This immunoperoxidase stain utilizes antibody to the muscle protein called dystrophin, which is present in only small amounts in this patient with Becker type muscular dystrophy. In this case, some dystrophin is made, but not normal amounts. Persons with Becker muscular dystrophy have an onset of disease in adolescence to young adulthood, and have a less severe course than persons with the Duchenne type of muscular dystrophy.
Figure 27-11 Duchenne muscular dystrophy. Histologic images of muscle biopsy specimens from two brothers. A and B, Specimens from a 3-year-old boy. C, Specimen from his 9-year old brother. As seen in A, at a younger age fascicular muscle architecture is maintained, but myofibers show variation in size. Additionally, there is a cluster of basophilic regenerating myofibers (left side) and slight endomysial fibrosis, seen as focal pink-staining connective tissue between myofibers. In B, immunohistochemical staining shows complete absence of membrane-associated dystrophin, seen as a brown stain in normal muscle (inset). In C, the biopsy from the older brother illustrates disease progression, which is marked by extensive variation in myofiber size, fatty replacement, and endomysial fibrosis.
This is polymyositis. Note the marked inflammatory cell infiltrate. This is an autoimmune disease that can be associated with polymyositis or dermatomyositis. Polymyositis results from the cytotoxic effects of CD8+ lymphocytes recognizing HLA class 1 MHC molecules on sarcolemmal membranes. Dermatomyositis is mainly mediated via a vasculitis affecting small capillaries, and has a skin rash (typically the violaceous "heliotrope" rash of eyelids).
Inclusion body myositis is a rare myopathy that, like polymyositis, is thought to be mediated by an immune reaction to muscle fibers via cytotoxic T-lymphocytes. The typical presentation is insidious onset of slowly progressive, non-painful, muscular weakness over years in a person over age 50. Males are affected twice as often as females. Unlike polymyositis, no response to corticosteroid therapy occurs. There is chronic inflammation, and within some muscle fibers can be seen vacuoles.
By electron microscopy, filamentous cytoplasmic or intranuclear inclusions can be present with inclusion body myositis. Seen here is a nucleus with filamentous inclusions.
A, Dermatomyositis. Note the heliotrope rash affecting the eyelids. B, Dermatomyositis. The histologic appearance of muscle show muscle fibers and inflammation. (Courtesy Dr. Dennis Burns. Department of Pathology, University of Texas Southwestern)