Chapter 2
Structure and Function of Joints

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Abstract This chapter covers many aspects of joint anatomy, histology, and cell biology. First, joint types and movements allowed are covered, followed by a brief review of joint embryology. Next, a review of joint anatomy and histology is given covering innervations, synovial membrane histology, as well as synoviocytes and synovial fluid characteristics. Various aspects of articular cartilage histology and cell biology are discussed in this chapter as well as aspects adaptive remodeling of cartilage after joint loading. A discussion of joint pathology completes the chapter.

Keywords Joint anatomy • Joint histology • Joint pathology • Rheumatoid arthritis • Osteoarthritis • Cytokines • Growth factors

Introduction

Segmentation of the skeleton allows for movement and segmental growth. A joint is the articulation or union between two or more bones or parts of bones. Joints are most commonly classified according to the material by which the articulating bones are united. Thus, there are synarthroses (that include syndesmoses that have intervening fibrous tissue, synchondroses, that have intervening cartilage synostoses, that have intervening bone and symphyses that have intervening fibrocartilage) and synovial joints (also called diarthrodial joints) (Table 1). Syndesmoses, eventually convert to synostosis after the fibrous tissues joining the bones ossify. The *diarthroses* are designed for movement and include all synovial joints. As is the case with all aspects of the musculoskeletal system, the structure of a joint, in this case concerning the manner in which the joints are held together, determines its function. As described further below, some of these joint types allow no movement; others allow only slight movement, while others are free movable.

Joint Classification

(1) *Syndesmoses* (fibrous joints) are defined as joints in which the adjoining bones are bound together by a thin sheet of fibrous tissue, either a ligament or a fibrous membrane. Since the fibrous tissue is flexible, these joints allow partial movement. The amount of movement allowed depends on the length of the fibers uniting the bones. Examples of syndesmoses are the suture joints of the skull and the union of the radius and ulna in the forearm by the interosseous membrane. A gomphosis or dentoalveolar syndesmosis (the bonds between the roots of teeth and the jaw bones) is also included in this category. (2) *Synchrondroses* are joints joined together by cartilage and permit slight bending in early life. A key example of this type of cartilaginous joint is the joining of the epiphysis of a long bone with the metaphysis by a cartilaginous epiphyseal plate, a region also known as the growth plate (Fig. 1a and 1b). This is a temporary synchondrosis since the epiphyseal plate eventually ossifies in the mature adult. (3) *Symphyses* are joints joined by fibrocartilage and in which the two opposing surfaces are covered by hyaline articular cartilage. Symphyses are also considered cartilaginous joints. The strength of the fibrocartilage allows for only a little movement but much stability, while the hyaline cartilage on the articulating surfaces allows for shock absorption. The pubic symphyses and intervertebral joints are examples of symphyses. The intervertebral disc is the binding fibrocartilage joining two vertebrae. (4) *Synostoses* are temporary joints that eventually close by bony union. With aging, many syndesmoses and all synchondroses ossify. Once ossified, these joints allow no movement. (5) *Synovial joints* are the most common types of joints and are defined as two or more bones whose ends are covered by hyaline cartilage, united by a fibrous tissue capsule that encloses the joint, and separated by a joint cavity (Fig. 1c). The cavity is filled with synovial fluid produced by a synovial membrane lining the interior of the fibrous capsule. The synovial fluid is a lubricant providing a smooth, nearly frictionless, gliding motion of the opposing joint surfaces.

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Table 1 Classification of joints by type of union.

Syndesmosis – fibrous material joins the bones; fibrous joint
Synchondrosis – cartilage joins the bones; cartilaginous joint
Synostosis – fibers/cartilage ossify, totally closing joint; bony union
Symphysis – fibrocartilage joins the bones; cartilaginous joint
Synovial – a loose fibrous capsule joins the bones separated by a joint cavity

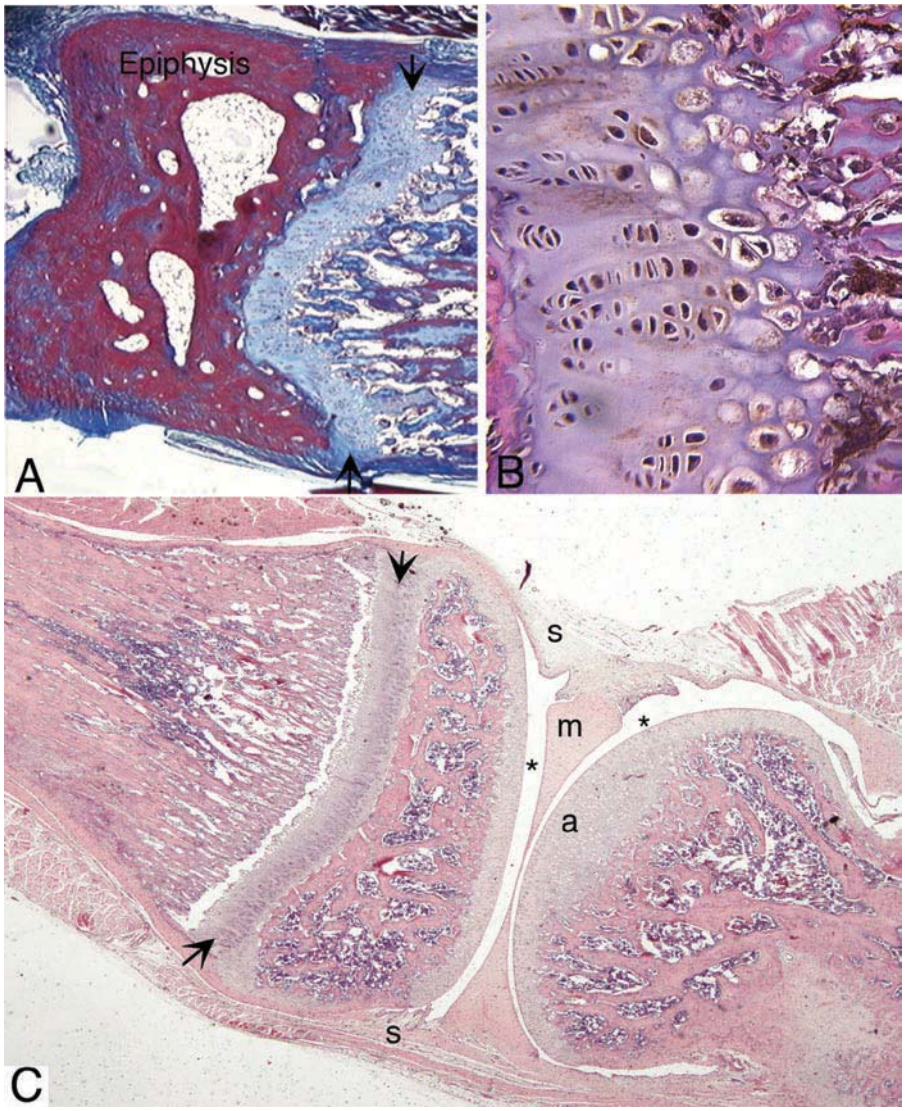

Fig. 1 Photomicrographs showing examples of joints classified by type of union. **A** A synchondrosis in a rat radial bone. The epiphyseal plate (indicated by black arrows) located below the epiphysis of a long bone of a young mammal is an example of a cartilaginous type of bony union. This type of union eventually ossifies. Masson trichrome stain. **B** Higher power of the syndesmosis showing rows of chondrocytes stained positive for the cytokine, interleukin 6. **C** A synovial joint, the knee joint, in a rat. Synovial joints are defined as two or more bones whose ends are covered by hyaline articular cartilage (a), and possessing a joint cavity (*) lined with a synovial membrane (s). The knee joint also contains medial and lateral menisci (m) for additional cushioning and congruence between the bones. The arrows indicate the epiphyseal plate in the femur of this young rat. Figure (**C**) is stained with hematoxylin and eosin (H&E)

This type of joint allows more movement at the cost of reduced stability. As a consequence, synovial joints are usually reinforced by extrinsic ligaments or strategic thickenings of the joint capsule (intrinsic ligaments). Some synovial joints also have other distinguishing features such as menisci (Fig. 1c), labrums, or fibrocartilage articular discs that allow for shock absorption and/or additional stability. Nearly all of the joints of the limbs are synovial.

Movements Allowed by Different Types of Joints

Osteokinematics describes the relative movement between two bones on either side of a joint. Although all bony segments on either side of a joint are theoretically capable of three rotations about three axes of motion and three translations in three planes of motion, otherwise known as the six degrees of freedom of movement in three-dimensional space, soft tissue constraints along with bony shape frequently constrain osteokinematics to fewer axes and planes of motion. Arthrokinematics describes the movements occurring between the joint surfaces, such as rolling, spinning, and gliding of joint surfaces. *Plane joints* are characterized by opposing bony surfaces that are flat, or nearly so (Fig. 2a). The arthrokinematics of a plane joint include gliding and spinning, or a combination thereof. Gliding refers to a translation of one surface with respect to another, whereas spinning refers to a clockwise or counterclockwise rotation of one surface with respect to another. Depending on the precise curvature of the surfaces of a plane joint, their orientation and their constraints by soft tissue structures, the osteokinematics of plane joint movement ranges from uniaxial to triaxial. Examples of plane joints include the acromioclavicular joint, which is triaxial, and the vertebral zygopophyseal (facet) joints, which are uniaxial. The osteokinematics of *hinge joints* are constrained to movement in one plane, usually sagittal, about one axis of rotation, usually mediolateral. The elbow joint is one example of a hinge joint. *Saddle (sellar) joints* are characterized by opposing surfaces that are concave and convex, but along opposite planes so that they are contoured to fit together (Fig. 3). The osteokinematics of saddle joints are inconsistently described as either biaxial (motion about two primary axes in two planes) or triaxial. This inconsistency can be explained by the fact that the majority of motion typically occurs in two planes (usually flexion–extension and abduction–adduction), while there is a small amount of internal–external rotation. The carpometacarpal joint of the thumb is an example of a saddle joint in which flexion–adduction–internal rotation combine to produce the action of opposition. *Condyloid joints* are composed of a nearly spherical convex surface opposing a shallow, nearly flat concave surface. The osteokinematics of these joints are considered biaxial owing to the predominance of movement about two axes and in two planes. The arthrokinematics during movement of condyloid joints are described by the "concave–convex rule," which specifies that to maintain congruence of joint surfaces during bone movement, the convex condyloid component must roll in the direction of bony movement and glide in the opposite direction with respect to the concave component (Fig. 4). Examples of condyloid joints include the metacarpophalangeal joints of the fingers, in which the condyloid distal portion of the metacarpal joint forms the knuckle of the finger ray; the knee joint, in which the distal femoral condyles articulate with the shallow, concave tibial plateaus; and the atlanto-occipital joint between the occipital condyles and the atlas (C1). *Ball and socket joints* are distinguished by one bone with an ovoid or spherical convex surface that moves within a relatively deep concave surface (Fig. 2b). Ball and socket joints allow movement about all three axes and in all three planes of motion, flexion–extension, abduction–adduction, and internal–external rotation. The coxofemoral (hip) and glenohumeral (shoulder) joints are examples of ball and socket joints. *Pivot joints* are characterized by one

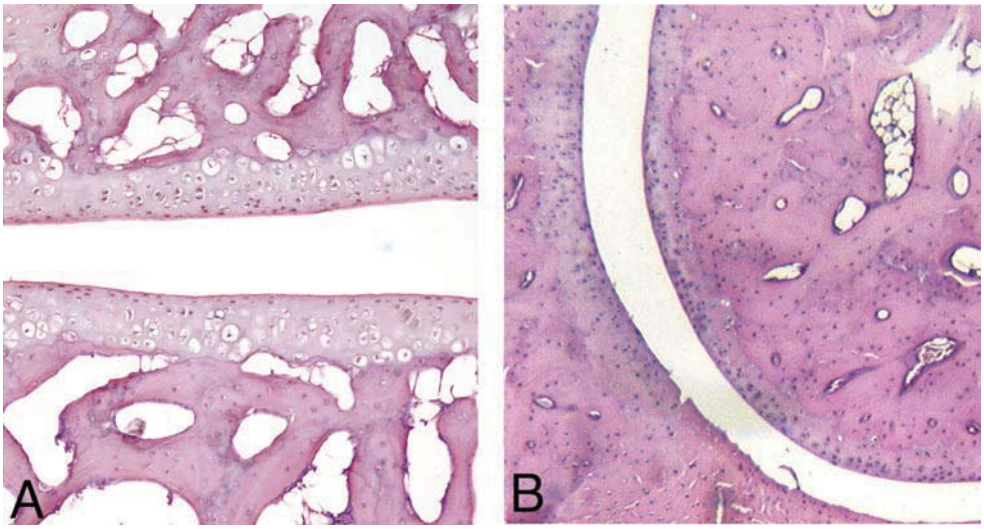

Fig. 2 Photomicrographs showing **A** a plane joint and **B** a ball-and-socket joint. H&E staining

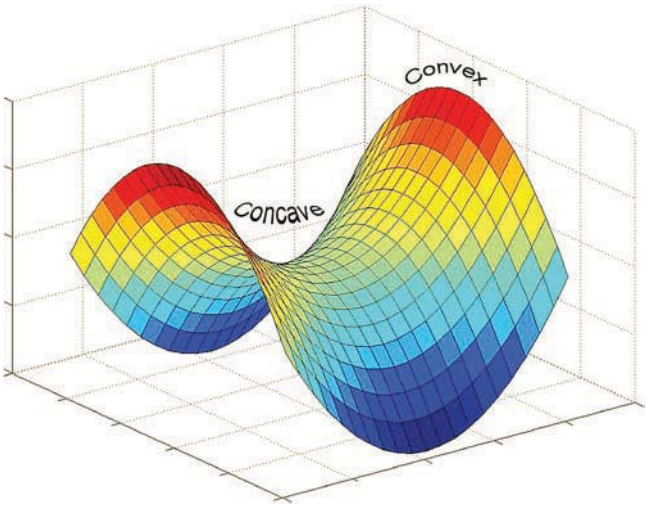

Fig. 3 Mesh grid representation of a saddle-shaped (sellar) joint showing that the joint surface is concave along one axis and convex along the axis perpendicular to the first. In a saddle joint, the opposing joint surface would have concavity and convexity rotated 90° so that the two surfaces would be maximally congruent. While the majority of motion occurs along the axis defined by the concavity and convexity, depending on the leverage of muscles acting on the joint, a small amount of rotation (spinning) is also permitted, as with the carpometacarpal joint of the thumb during opposition

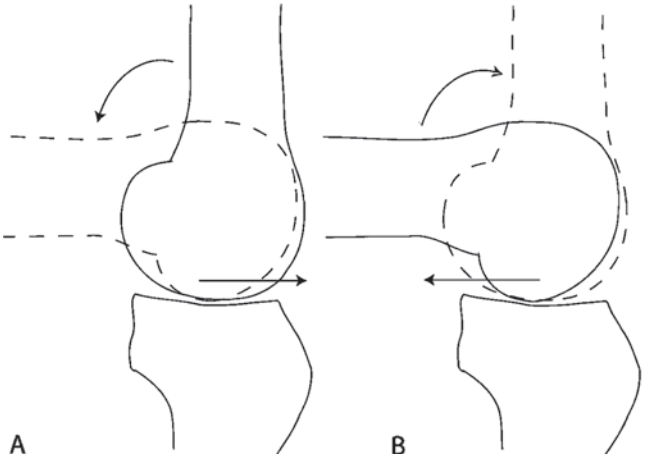

Fig. 4 The arthrokinematics of the condyloid knee joint during the motions of flexion and extension and an example of the concave–convex rule. **A** During flexion of the femur on a fixed tibia, the convex femoral condyles roll posteriorly and glide anteriorly. **B** During extension of the femur on a fixed tibia, the convex femoral condyles roll anteriorly and glide posteriorly. These complimentary arthrokinematics maintain joint congruence. Modified from Oatis (1, Figure 7.4, p. 101). Cartoon Compliments of Susan Fecho

bone with a rounded process that moves within a sleeve or ring formed by the opposing bone. They permit rotation about a single axis, and are therefore uniaxial joints. Examples include the proximal radioulnar and atlantoaxial joints.

Joint Embryology and Ossification

Embryology of Synovial Joints

The development of joint tissue begins shortly after the emergence of the primitive limb buds (days 26–28 of gestation). The limb bud initially contains a central continuous condensation of mesenchymal cells, which will develop into a cartilage model of the bones and their joints (see Chap. 1). Constrictions appear in the limbs, dividing them into recognizable segments by week 6 of embryological development. While the external shape of the limb is being defined, a hyaline cartilage model is formed during the same week (week 6). An articular disc of mesenchyme, the primitive joint plate, appears within the condensing mesenchymal cells at the site of future synovial joints. These cells of the primitive joint plate organize into a trilayer structure composed of two chondrogenic regions and a central layer of mesenchymal material. The outer chondrogenic region surrounds the primitive joint plate and is the forerunner of the joint capsule. By the seventh or eighth week of embryonic life, the central layer undergoes cavitation along planes destined to become the articular surfaces of the joints. Spaces filled with tissue fluid appear in the primitive joint plate. These spaces gradually coalesce to form a single joint cavity. The outer chondrogenic region of the joint capsule condenses and differentiates into fibrous tissue, while the inner chondrogenic region differentiates into the synovial membrane. Hartmann and Tabin (2) have shown that Wnt-14 is expressed in primitive joint plate regions prior to segmentation of the cartilage model, and plays a central role in initiating synovial joint formation in the chick limb. It is known that intrauterine movements of the limbs begin in the third month of fetal life and are essential for normal embryonic development of synovial joints.

Embryology of Intervertebral Discs

The vertebra and intervertebral discs are axial skeletal elements that arise from the sclerotome portion of segmental somites arranged on each side of the notochord. During week 4 of embryonic life, cells of the sclerotome shift in position to surround the spinal cord and notochord. The caudal portion of each sclerotomal segment proliferates extensively, condenses, and then moves into the subjacent intersegmental tissue. This proliferation is so strong that the caudal half of one sclerotome segment binds to the cephalic half of the subjacent sclerotome. Some of the densely packed sclerotomal cells move cranially and form the intervertebral disc, while the remainder forms the centrum of the vertebral body.

In this manner, vertebral bodies become intersegmental and come to lie beside intersegmental arteries located on each side of the vertebral bodies. The notochord later degenerates and forms the gelatinous nucleus pulposus of the intervertebral disc, which is later surrounded by the harder, circular fibers of the annulus fibrosis. Chondrification of the vertebral body begins in embryonic week 6. Extensions form dorsally and laterally from the chondrification centers in the vertebral arch and begin the formation of the neural arch and costal processes. Chondrification spreads until a cartilage model of the vertebrae is formed. The conversion of the cartilage model into bone (*ossification*) begins in embryonic week 9 and continues until year 25 of life.

Joint Ossification

Ossification of the limb bones via the mechanisms of endochondral ossification begins by the end of the embryonic period of development (week 12). Primary ossification centers are present in the diaphysis of long bones by the 12th week of embryonic life, while the epiphyses remain cartilaginous until birth. After birth, ossification centers (secondary ossification centers) appear on each end of long bones, a region known as the epiphyses. At that point of joint development, the synchondrosis type joint (described earlier) appears, joining the epiphyseal ossifying ends with the rest of the ossified long bone. The cartilage plate of this joint, the epiphyseal plate, allows for growth of the long bone on both sides of that plate. When the bone has reached full length, these epiphyseal plates ossify as well, merging the ossified end of the long bones with their ossified shafts (diaphysis).

Dynamic axial loading can suppress longitudinal bone growth by acting directly on the growth plate (3). High axial compressive loads (17N) on the ulna for 10 min/day for 8 days, followed by a 7-day waiting period prior to tissue collection and examination, results in complete suppression of longitudinal mineralization rate at the distal growth plate. Longitudinal growth recovers within 1 week after lower compressive loads (4N and 8.5N). Several morphological changes are observed in the growth plate after 17N loading including trauma-induced cracks in the growth plate, increased vascular endothelial growth factor (VEGF; a coordinator of chondrogenesis and angiogenesis), suppression of cartilage mineralization, and capillary invasion beneath the growth plate. The authors of this study postulate that there is a correlation between loading force magnitude and the period for recovery of growth suppression, and that if they had allowed the rats to recover for a longer period (e.g., 1 month) that endochondral ossification growth rates might have returned (3).

Synovial Joint Anatomy and Histology

The basic overall structure of a synovial joint consists of a fibrous capsule joining and surrounding the adjoining bony surfaces. The capsule is often reinforced by localized thickenings of collagen fibers (intrinsic ligaments) as well as additional ligaments outside the capsule (extrinsic ligaments). The joint capsule is lined by a synovial membrane, which is divided into inner and outer parts (see below for more details). The two bones are separated by a joint cavity filled with synovial fluid, and the articulating bony ends are covered by articular cartilage (see below for more details).

Joint Capsule Anatomy, Vasculature, and Innervation

The joint capsule is composed of two layers of connective tissue. The outer layer is the fibrous membrane and consists of collagenous fibers. This layer surrounds the entire joint and attaches firmly to the periosteum of the adjoining bones. Although it is poorly vascularized, the joint capsule is highly innervated by a variety of somatic sensory fibers mediating sensations of pain, proprioception, pressure, and vibration. Most joint blood vessels, normally from periarticular anastomotic plexes, penetrate the capsule to pass to the synovial membrane and the epiphyses.

The inner layer of the joint capsule is the synovial membrane (Fig. 1). It is highly vascularized, but poorly innervated. The articular cartilage also lacks innervation. Thus, the synovial membrane and the articular cartilage are insensitive to pain. However, joint ligaments and the periosteum associated with the adjoining bones are highly innervated, as are adjacent attaching tendons and the outer layer of the joint capsule. Any swelling within a joint from disease or trauma stimulates nociceptors (pain endings) in joint structures, giving rise to the sensation of pain in or near a joint.

Joint pain, such as that associated with osteoarthritis, is the result of underlying acute or chronic joint inflammation or injury. Increased response to painful stimuli at the site of injury or inflammation is termed *hyperalgesia*. Animal models have been developed to study joint hyperalgesia and the control of this type of pain. In one such well-characterized model, kaolin and carrageenan is injected into the knee joint to produce an initial inflammatory response that coverts in about 1 week to chronic inflammation (4). The inflammation is associated with decreased latency to paw withdrawal in response to heat (hyperalgesia), increased withdrawal after compression of the inflamed knee, and increased response to mechanical stimuli of the paw (mechanical allodynia). The hyperalgesia and mechanical allodynia are a result of

increased sensitization of joint nociceptors, increased nociceptor spontaneous activity, and increased response of previously silent neurons (5). The kaolin and carrageenan model of joint inflammation has been used to assess the effectiveness of various treatments of arthritic pain. For example, high and low frequency transcutaneous electrical nerve stimulation (TENS) has been used successfully to reverse the hyperalgesia induced by carrageenan injections (6).

In addition to nociceptors, there are other types of nerves innervating joint structures. The joint capsule contains Ruffini-type endings and paciniform corpuscles (small, elongated pacinian corpuscles). These receptors respond to the bending of joints (proprioception), as do some of the free nerve endings in the joint capsule. These two types of joint capsule receptors play a protective function against the extremes of hyperextension and hyperflexion (7–9). However, the receptors just named are not the only nerves involved in joint proprioception. Apparently, pressure receptors and free nerve endings localized in skin surrounding the joint also serve this same function, since patients with anesthetized or removed joint capsules experience no loss of joint position sense (7–9). The Ruffini endings (also referred to as Ruffini corpuscles, flower spray organs, and SAII axons) also function as slow adapting mechanoreceptors that fire with changes in joint angle and motion (10). Finally, Golgi tendon organs can be found in the fibrous ends of tendons that attach on or immediately adjacent to a joint capsule. These afferents detect both muscle and capsule tension. They terminate in and among collagen fibers, so that when the collagen fibers are stretched by muscle contractions or joint capsule movements, the terminals of the Golgi tendon organs are compressed and discharge (9). In summary, joint structures are innervated by a variety of sensory nerve endings that detect motion, compression, tension, proprioception, and pain.

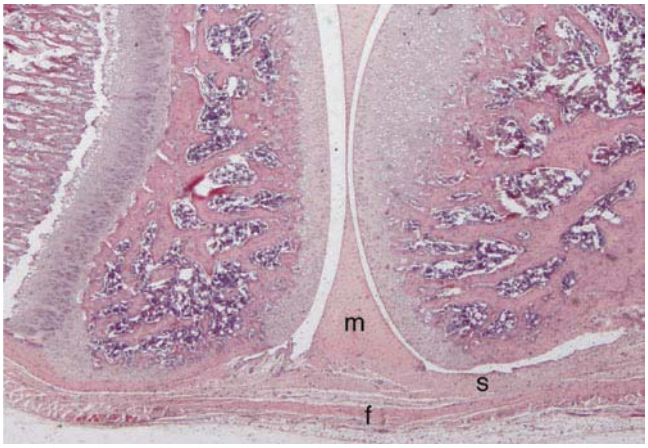

Fig. 5 Photomicrograph showing the inner synovial membrane (s) and the outer fibrous capsule (f) surrounding a synovial joint. Note the articular cartilage (a) on the articulating bone surfaces. H&E staining

Synovial Membranes

Synovial membranes and the fluid that they produce are components of synovial joints only. These membranes have the ability to absorb as well as secrete. They consist of cuboidal cells or *synoviocytes* that are arranged one to four cell layers deep along the inner surface of the fibrous capsule surrounding the joint (Fig. 5). The synovial membrane lines the entire joint cavity except for on the articular cartilage surface. The outer fibrous capsule is composed of irregularly arranged connective tissue. There are three key types of variations of synovial membranes: fibrous, areolar, and adipose. The fibrous type, which is located over tendons, consists of a thin cellular layer resting on connective tissue fibers that merge with the outer fibrous capsule. The areolar type allows movement of the membrane over the fibrous capsule, while the adipose type is found over intraarticular fat pads, such as those found in the knee joint. The inner layer of the areolar type of synovial membrane is thicker than the other two types and consists of fibroblasts and synovial cells. The outer layer of this type of synovial membrane consists of fibroblasts, mast cells, macrophages, as well as collagen and elastic fibers. The synovial cells and macrophages of synovial membranes are key producers of inflammatory cytokines associated with arthritic degenerative joint diseases to be discussed in another chapter.

During joint movement, synovial tissues and cells contribute to bearing mechanical loads (11). The synovial membrane is the initial target of rheumatoid arthritis, and becomes a primary source of matrix metalloproteinases (MMPs) and cytokines in the synovium and synovial fluid (11, 12). Affected chondrocytes also contribute MMPs to synovial fluid.

Synoviocytes

Traditionally, the synoviocytes are separated into type A cells (macrophage-like), which are phagocytic and synthesize hyaluronic acid, and type B cells (fibroblast-like) which produce various proteins. It is possible that these cells belong to one cell population, but have altered phenotypes. Synoviocytes secrete collagen and proteoglycan and have a highly characteristic phenotype that includes the strong expression of vascular cell adhesion molecule-1 (VCAM-1). Synoviocytes are also immunoreactive for vimentin, an interfilament molecule, but not for epithelial markers.

Synovial cells are flexible in order to line fibrous capsules and cover exposed osseous surfaces and intracapsular ligaments during joint movements (11). In rheumatoid arthritis, a chronic autoimmune disease, the fibroblast-like synoviocytes

proliferate aggressively and invade adjacent cartilage and bone (*pannus*) (12, 13). The hyperplastic synovial cell activity eventually destroys both the cartilage and the underlying bone (14).

Synovial Fluid

Synovial fluid from a normal joint is clear or pale-yellow in color, viscous, and consists of hyaluronic acid and lubricin, a glycoprotein that reduces friction (15). The hyaluronic acid provides viscosity, reduces friction between joint surfaces, and provides nutrients to chondrocytes in the articular cartilage. The hyaluronic acid is also known as hyaluronate and is a large, highly polymerized mucopolysaccharide (glycosaminoglycan). The synovial fluid is a plasma dialysate with many electrolytes present at levels comparable to that of blood. However, it lacks most proteins, particularly those with high molecular weights, under normal conditions. Also, synovial fluid is acellular under normal conditions. However, under arthritic and other inflammatory conditions, synovial fluid contains infiltrating immune cells (monocytes/macrophages and T cells) and inflammatory mediators such as cytokines.

It has long been known that the long-term integrity of a joint and its articular cartilage is dependent upon synovial fluid nourishment and protection from friction-induced wear. Lubricin, a key component of synovial fluid, as mentioned above, is a secreted glycoprotein encoded by the gene PRG4 (16). An autosomal recessive disorder in humans called camptodactyly-arthropathy-coxa vara-pericarditis syndrome (CACP), associated with a loss of lubrican function leading to precocious joint failure (16), has been studied for the expression of PRG4 mRNA during mouse joint development, and created a lubricin-mutant mice strain. It was found that as the mice aged, abnormal protein deposits appeared on the articular cartilage surface and the chondrocytes of the underlying superficial zone disappeared. Also, synovial cells became hyperplastic, further contributing to joint destruction. Addition of purified or recombinant lubricin inhibited the synoviocytes proliferation in vitro, suggesting that lubrican functions to protect articulating surfaces and control of synovial cell growth (16).

Effects of Mechanical Stress of Synovial Cavities and Membranes

Under both normal and pathological conditions, the synovial cavity is exposed to a high degree of mechanical stress (13). Mechanical stress from the load of body weight is present, as are shearing forces during movement. The motion of synovial fluid during exercise is one of the primary sources of shear forces on the synovial cavity (17, 18). Shear forces by fluids have been shown to activate the mitogen-activated protein kinase (MAPK) pathways, which then results in c-jun and c-fos transcription factor activation leading to cell growth and proliferation (19, 20). Such changes allow the tissues to adapt to many stressful conditions. Besides MAPKs, mechanical shear forces can influence other signaling pathways, such as those inducing the production of heat shock proteins (hsps) 60 and 70. Hsps when induced protect the stressed and/or injured cells against apoptotic death (21, 22). Given that the rate of cell death from apoptosis is low in synovial membrane, cells are obviously able to adapt to a variety of mechanical stresses successfully, unless additional joint pathologies are present such as rheumatoid arthritis or osteoarthritis.

> A study of normal tidemark histology is pertinent to pathologists since early osteoarthritic changes occur in the deep layer of cartilage near the tidemark. The tidemark is an important clue to the surgical pathologist, as a marker of articular cartilage. This is because cartilage injury at the histological level of the tidemark (stained with hematoxylin and eosin) precedes any visible denudation of articular cartilage. Surgical specimens are often fragmented, and architectural clues are lost – the presence of a tidemark may help establish the origin of submitted fragments from the articular region, implying that accidental breach may have occurred.

Articular Cartilage

Articular cartilage covers the end of long bones and is usually hyaline cartilage in composition. It varies in thickness from 2 to 4 mm and is thickest at the periphery of concave surfaces and in the central portions of convex surfaces. This type of cartilage is usually the remains of the original hyaline cartilage model from which the bones and joints derived. No perichondrium covers the bone at this point. Instead, the bony ends within a joint are covered with a sparse number of cartilage cells embedded in a hyaline cartilage matrix. The cartilage cells are arranged in rows parallel to the surface in distinct zones. There is a superficial tangential zone (STZ) of elongated chondrocytes with their long axes arranged tangentially to the articular surface. The STZ contributes to the maintenance of joint lubrication through fluid film and boundary

lubrication mechanisms (23). Chondrocytes in the STZ have higher elastic moduli (i.e., are stiffer) and have higher apparent viscosities compared to those in deeper zones (24, 25). In addition, the STZ contributes to both lateral and deep load transmission under compressive loading conditions (26). The STZ is adjacent to a transitional or intermediate zone where the chondrocytes are oriented more randomly in small groups. Subjacent to this, and comprising the majority of the cartilage, there is a deep radial zone where chondrocytes are oriented perpendicular to the surface. This deep radial zone undergoes substantial loss in height and increase in stiffness under compressive loads (26). A thin zone of calcified cartilage lies between the deep radial zone and the subchondral bone. The deepest layer of articular cartilage, a thin zone, is firmly apposed to bone and is calcified. This calcified zone contains a sinuous hematoxyphilic line called the "tidemark," which separates the uncalcified articular cartilage from the underlying subchondral bone (Fig. 6).

The articular cartilage matrix is highly hydrophilic, but fluid moves freely between the matrix of the cartilage and the intracapsular joint space under conditions of intermittent loading. The thickness of cartilage varies from one joint to another, from one area of a joint to another, and across the course of a day (due to cumulative pressure on the cartilage throughout the day). Articular cartilage is also thinner in aged joints, partially due to the reduced ability of aged cartilage to hold water. The volume of articular cartilage in patients can be quantified using a volummetric, fat-suppressed spoiled gradient-recalled signal acquisition in the steady-state (SPGR) magnetic resonance (MR) sequence (for further information, see Dupuy et al. (27)).

Articular cartilage chondrocytes, although sparse in number, are metabolically active and capable of cell division under pathologic stimuli and these chondrocytes show all the ultrastructural features of a dividing cell. Chondrocyte division (also termed chondrocyte cloning) can be seen in a number of situations such as osteoarthritis, and is not necessarily an indication of malignancy. The articular cartilage is avascular and the cells receive sustenance by absorption of nutrients from the synovial fluid. The basal chondrocytes may also get some nutrition from the vasculature at the cartilage bone interface.

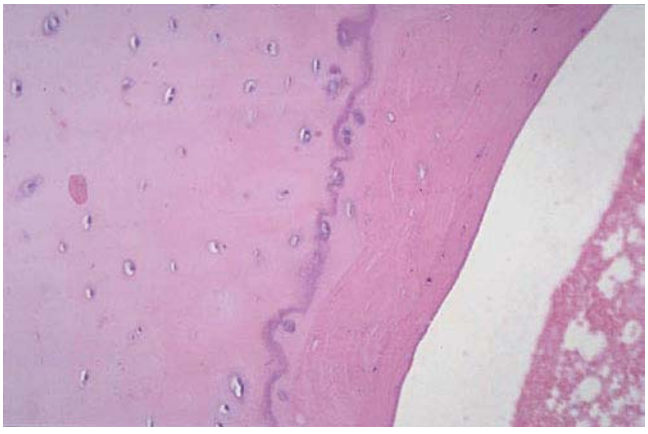

Fig. 6 Photomicrograph showing hyaline articular cartilage. The cartilage cells in the superficial zone are flattened, while those in the middle zone are rounded. The deep layer is separated from the subchondral bone by a tidemark (*arrow*). H&E staining

Hyaline Articular Cartilage

Hyaline articular cartilage is a specialized type of joint cartilage that has the consistency of firm, resilient rubber. It was termed hyaline cartilage originally due to its pearly, translucent, glass-like quality. This type of cartilage is composed of chondrocytes (less than 2% of its weight) embedded in an extensive extracellular matrix (ground substance) consisting of water (70–80% of the weight of the cartilage), a dense network of collagen (10–15%) and elastin fibers, and proteoglycan molecules (10–15%) cross-linked into an integrated network with hyaluronic acid (also known as hyaluronate) (28, 29). Most of the collagen in hyaline cartilage is type II. Cartilage also contains a number of noncollagenous proteins, such as cartilage oligomeric matrix protein (COMP), which is structurally related to the thrombospondins (30). Studies have shown that the proteoglycan aggregate of hyaline cartilage is composed of a central core of hyaluronic acid, link proteins, and bristle-like rods of three glycosaminoglycans: chondrotin-4-sulfate, chondroitin-6-sulfate, and keratan sulfate (31–33).

Hyaline articular cartilage is arranged into three zones. The superficial zone (horizontal zone) is characterized by collagen fibers and small oval cells that are arranged parallel to the surface. This zone is also called the limiting membrane or lamina splendans. The middle zone (vertical zone) contains younger, more active chondrocytes. As a consequence, mitotic figures may be present in this zone. In the deep zone, bundles of collagen fibers can be seen that ascend vertically from their deep attachment to the subchondral bone in the surface of the cartilage. These collagen bundles become more apparent after articular cartilage fracture and other injuries. Such bundles have been called *Benninghoff's arcades*. These collagen bundles are visible as darker pink streaks in hyaline articular cartilage after staining with hematoxylin and eosin (Fig. 6).

Fibrous Articular Cartilage

At some articulations, such as the acromioclavicular and sternoclavicular joints, the bony ends are covered with *fibrous-type articular cartilage* rather than hyaline articular cartilage. Fibrous cartilage is a combination of collagen fibers and chondrocytes, the latter in lacunae lying within hyaline cartilage surrounds. In contrast to hyaline cartilage, most of the collagen in fibrous articular cartilage is type I.

Intervertebral discs are thick fibrocartilaginous discs located between two opposing vertebral bodies. An outer region, termed the annulus fibrosis, consists of many layers of fibrous tissue in a matrix of cartilage that are strongly attached to the ends of the vertebral bodies and thus serves to bind them together. An interior soft center, called the nucleus pulposus, is a semigelatinous material containing 70–80% water molecules. Together, the annulus fibrosis and the nucleus pulposus serve as shock absorbers for the vertebral bodies. Because of the high water content of the intervertebral discs, they are prone to dehydration. Also, compressive forces on the discs during standing and moving cause water to be squeezed out of the discs into the bloodstream. Adaptive remodeling of this type of cartilage to loading is discussed further below.

Articular Cartilage Vascularization and Innervation

Articular cartilage lacks blood supply, lymph channels, and innervation (as mentioned earlier). Metabolic exchange is made by diffusion through the cartilage matrix to and from synovial fluid, capillaries in nearby periosteum, and vessels in the underlying bone. Exchange of nutrients chiefly comes via diffusion from synovial fluid. This lack of blood supply hinders repair and regeneration of the injured or torn cartilage. However, the mixture of elastic solid and viscous liquid (the hyaluronate) in cartilage gives it strong biomechanical resilience, allowing the cartilage to distribute joint loads over a wide joint surface and decrease the stress of compression on the subchondral bone. The hyaluronate, also called mucin, in cartilage and synovial fluid is a "weeping" type of lubrication that allows easy movement of opposing joint surfaces with limited wear.

Menisci-Cartilaginous Joint Modifications

The menisci of the knee (medial and lateral) are cartilaginous modifications that serve to reduce loading damage to subchondral bone and improve joint stability by providing a more congruous articular surface between the femur and the tibia (Figs. 1 and 5). Collagen type I is the key component of meniscal cartilage matrix (28). Surgical removal of menisci typically leads eventually to secondary degenerative arthritis and joint destruction.

Adaptive Remodeling of Joint Cartilage to Loading

Water, proteoglycans, and collagen are the main components of the extracellular matrices of articular cartilage, the fibrocartilage of intervertebral discs, and ligaments. Type I collagen is the key component present in connective tissues subjected to loading forces and tension and adds tensile strength to these tissues. A dynamic balance of synthesis and degradation of collagen is needed for adequate health and maintenance of connective tissues (34, 35). Adaptive remodeling such as increasing the synthesis of collagen occurs with increasing mechanical loading, strengthening the tissue and its ability to withstand higher forces in the future (36). Unfortunately, a greater amount of collagen in the matrix reduces the water binding properties of connective tissue and may impair other aspects of tissue integrity such as viscoelastic deformation. In humans, greater levels of physical loading leads to spinal shrinkage (height loss of spinal segments and cross-sectional areas of intervertebral discs) and to increasing levels of serum biomarkers of collagen type I synthesis (35). These biomarkers, the carboxyterminal propeptide of type I collagen, and the carboxyterminal telopeptide region of type I collagen, may be predictive for degenerative changes in the spine and are under further exploration.

The Importance of Knowing Typical Joint Anatomy and Development During Radiological Diagnoses of Joint Pathologies

Many joint pathologies, as well as a few others, can be evaluated radiographically. In fact, the radiograph is the primary tool for evaluating osteoarthritis as well as other types of arthritis (37). Joint narrowing in arthritic conditions is due to articular cartilage destruction (Table 2). One should also be aware that the epiphyses of a growing synchondrosis-type joint can be displaced and separated from the surrounding bone, and may be interpreted as a fracture. Thus, knowing the patient's age and the location of epiphyses is necessary for appropriate interpretation of radiological images. The key differences between fractures and epiphyseal displacements are that bone fractures leave a sharp and usually uneven edge of bone, while the edges of the epiphysis and diaphysis are smooth and curved in the region of the growth plate.

Table 2 Typical radiographic findings in arthritis that alter joint structure

Osteoarthritis	Rheumatoid arthritis	Gout arthritis
Irregular joint narrowing	Symmetric joint narrowing	Osteoporosis is absent
Cysts or pseudocysts	Periarticular soft tissue thickening (earliest finding)	Sharply marginated articular and juxtaarticular erosions
Osteophytes form on joint margins	Bony ankylosis of joint (a late finding)	Tissue nodules

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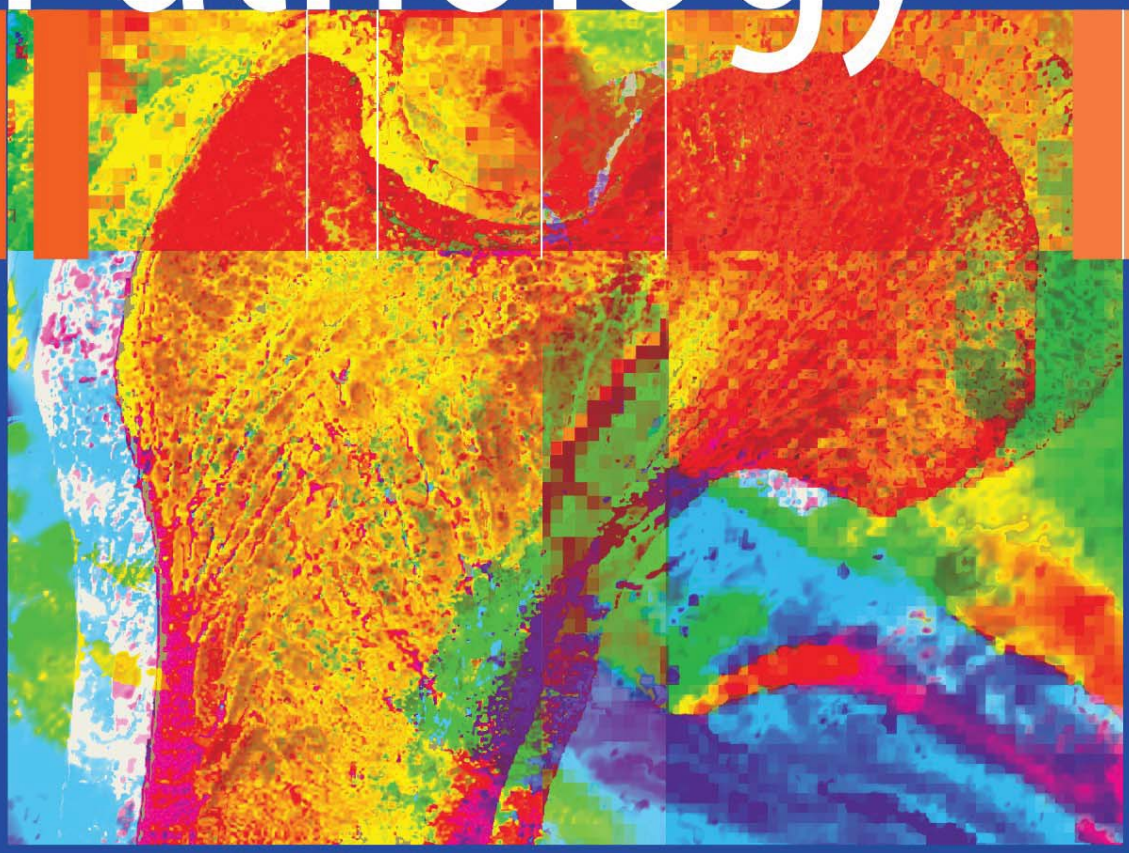

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