CHAPTER 1

Musculoskeletal System and Organs Affected in Rheumatic and Musculoskeletal Diseases (RMDs)

The diseases that are included under the umbrella of 'rheumatic and musculoskeletal diseases' (RMDs) affecting the musculoskeletal (MSK) system, involve the following body parts/organs:

1. **Joints:** Although there are several types of joints in the body, for rheumatologists, '*diarthrodial (freely movable) cartilaginous joints*' are of main interest. An example of the same is provided in **Fig. 1.1**.

   Such joints are surrounded by a fibrous capsule, lined by a delicate bicellular membrane without basement membrane. This lining membrane of the joint capsule is called '*synovial membrane*'. The cavity created by the fibrous capsule is called 'the joint space'. It is filled by a clear transparent smooth sticky (honey-like) fluid called '*synovial fluid*'. It provides lubrication to the joints for facilitating their smooth range of movements over smooth glistening hyaline/articular cartilage that cap the end of the bones that makeup the joint. Any disease of the joints is called '*arthritis*'.

   a. **Articular cartilage:** Of the 3 types of cartilage in the body (fibrocartilage, hyaline cartilage, and elastic cartilage), the type that lines the joints and caps the ends of

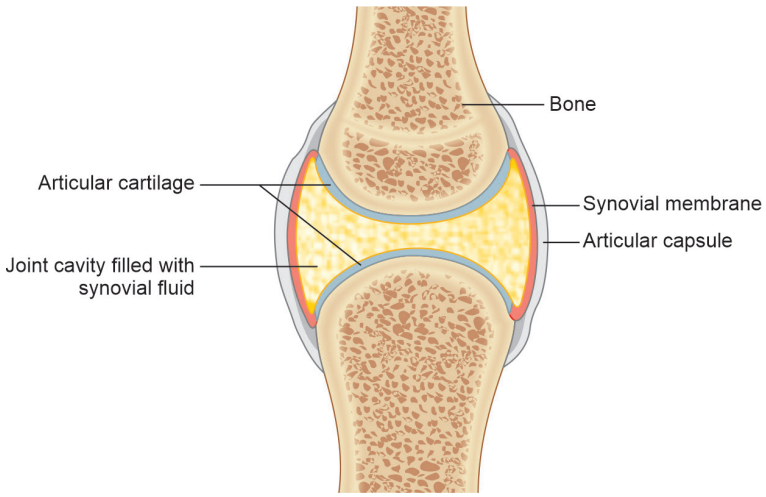


Fig. 1.1: A typical diarthrodial joint. (*Courtesy:* Miss Aashita Aggarwal)

the bones (e.g. distal surface of femur and proximal surface of tibia that make up the knee joint) is hyaline cartilage, which when part of the joint anatomy, is often called 'articular cartilage'. It is an avascular structure that gets its nutrition from the synovial fluid to which it is exposed continuously. Therefore, if the synovial fluid becomes unhealthy/abnormal it has a direct effect on the cartilage health and structure thus affecting the normal function of the joint. *Synovial membrane—involvement of the synovial membrane with any diseases is called 'synovitis':* In normal health synovium is a *sparsely cellular membrane* with 2 layers of loosely packed 1–2 cell-thick intimal layer without any basement membrane. The superficial layer (facing the joint cavity) contains type A cells, which produce synovial fluid for joint lubrication (*see* below). The second layer (away from the joint cavity) is relatively acellular containing scattered blood vessels, fat cells, and fibroblasts present in varying depth of the synovial sublining layer. These fibroblasts are called 'fibroblast-like synoviocytes' (FLS), the key cells involved in a major serious joint disease called '*rheumatoid arthritis*'. This synovial layer also contains a few lymphocytes and macrophages that are called 'macrophage-like synoviocytes' (MLS) that are part of the 'resident stromal cell network' similar to Kupffer cells in the liver. Understanding the histology of the synovium helps in recognizing the histopathological abnormalities in joint diseases, where *inflammation of the synovial membrane is referred to as 'synovitis'*.

b. **Synovial fluid:** This complex lubricating fluid is produced by the ultrafiltration of plasma (of the blood). It consists of substances that make it smooth and viscous, primarily composed of hyaluronan and lubricin that provide its lubricating property. There are several additional components in the synovial fluid that are in small/trace amounts needed to maintain normal healthy synovial fluid. In any type of joint disease, synovial fluid becomes abnormal, losing its transparency (becomes turbid due to the presence of inflammatory cells) and loses its lubricating property. This as well as the property of synovial fluid to provide nutrition to the hyaline cartilage on the surface of which the joints move, leads to cartilage damage (that can be seen on plain radiographs as 'erosions') and loss of joint function. A simple procedure of joint aspiration for obtaining synovial fluid and its analysis goes a long way in confirming diagnosis in specific clinical situations (discussed in Part I, Chapter 8).

2. **Enthesis (plural is 'entheses') and enthesitis (a disease in enthesis/entheses):** Enthesis is an organ in the musculoskeletal system that does not get that much importance in the undergraduate curriculum of anatomy when compared to bones, muscles, or joints. Yet, in the field of RMD, the importance of enthesis is next only to the joints. Understanding anatomy, physiology and its pathology is pivotal for understanding the 2nd most common form of arthritis called 'spondyloarthritis'. Therefore, understanding entheses are possibly more important for understanding RMDs than bones or muscles. In the MSK system, tendons are the tissues that attach muscles to bones. Similarly, ligaments attach bones to one another. The anatomical site where a tendon or ligament attaches to the bone, is called an enthesis (plural is entheses). Any disease of enthesis is called '*enthesitis*'. **Figure 1.2** shows an example of enthesitis.
   There are clinical conditions where the disease/damage/pathology is entirely localised to enthesis. On the other hand, there are several diseases under the

The area where the fibres of the Achilles tendon attach to the periosteum on the posterior surface of the calcaneus is a common site for inflammation, known as 'enthesitis'. This condition frequently occurs in spondyloarthritis, particularly psoriatic arthritis.
In this photograph, the site circled in red on the left side highlights swelling. In contrast, the site circled in green on the right side appears normal.

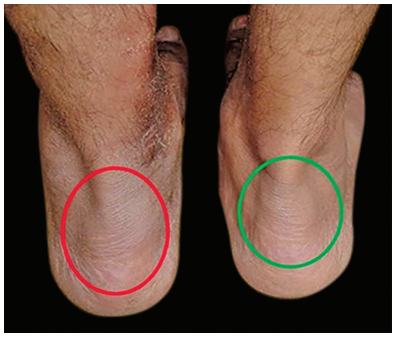


Fig. 1.2: Enthesitis at the insertion of Achilles tendon on the posterior surface of calcaneus

category of RMD where the pathology may not be localised to one enthesis but be more widespread affecting entheses in several parts in the musculoskeletal system. Moreover, in certain diseases the pathology may start at entheses but spread to involve other parts of the joints, including synovium (classic example is synovitis in psoriatic arthritis). Despite obvious synovitis in such patients, they still remain classified as 'enthesitis-related' because that was the site of the initiation of its pathology e.g. 'enthesitis-related arthritis' (ERA) in paediatric patients who are labelled 'spondyloarthritis' on reaching adulthood.

3. **'Back' and 'spine':** The spine is the largest structure in the musculoskeletal system and the most important one. It is said that the phenotype of vertebrates mainly depends on the anatomy of their spine. Thus, humans have a particular phenotype because our spine supports standing on 2 legs (bipeds) as against quadrupeds who cannot stand on 2 legs mainly because of the differences in the structure of their spine. It is also a fact that *Homo sapiens* have a particular body shape, which is largely due to the specific anatomical structure of our spine. Moreover, the spine shows a certain glaring paradox. It is very strong to be able to bear the body weight while standing upright yet, it is flexible to allow bending/twisting and move about freely with flexibility. Despite such flexibility, it is designed to protect a delicate vital structure, namely the spinal cord and its major nerves that connect the brain with the rest of your body making it possible to control the body movements. Therefore, it becomes important to understand its anatomy that provides such strength in the face of remarkable flexibility. The strong muscles, bones, and cartilage with flexible ligaments and muscles in the spine make the spine such an ingenious structure. This complexity of its anatomy and physiology makes it susceptible to sprain, strain, injury, and certain diseases that are characterised with back pain, the most common symptoms in the field of RMDs. It is not the aim of this chapter to describe the detailed anatomy, mechanics, and the physiology of the spine except to name some of the important structures that should be kept in mind with reference to spinal complaints/diseases.
   a. **The vertebrae:** The spine consists of 33 vertebrae stacked over each other with 'cushion-like' spongy vertebral disks (*see* below). The spine has 5 distinct areas:

i. The cervical spine with 7 vertebrae in the neck that support the head.
ii. The thoracic (or dorsal) spine with 12 vertebrae.
iii. The lumbar spine consists of 5 vertebrae, a main component of 'lower back'.
iv. The sacrum consists of 5 fused (in adults) sacral vertebrae; and
v. Coccyx that (usually) consists of 4 fused (in adults) coccygeal vertebrae (the number of coccygeal vertebrae can vary from 3 to 5). The different segments of spine are depicted in **Fig. 1.3**.

b. **Intervertebral disks:** The intervertebral disks are made of an external ring-like structure that consists of fibrous cartilage, a highly resilient structure that can withstand high physical forces and act as shock absorbers. It is lined by the annulus fibrosus that encases a gelatinous core called the nucleus pulposus.
c. **Spinal ligaments:** These are robust fibrous bands that hold the vertebrae in proper alignment, stabilize the spine, and shield the disks. There are 4 major ligaments of the spine. These are:
   i. Anterior and the posterior longitudinal ligaments (ALL and PLL) that join and hold the vertebral bodies. These are the 2 primary spine stabilizer ligaments.
   ii. The supraspinous ligament connects the tips of the vertebral spine.
   iii. Interspinous ligament is a thin and short structure that attaches to another ligament called the ligamentum flavum.
   iv. Ligamentum flavum connects the laminae (thin plate of bone that makes the roof of the vertebral canal) of adjacent vertebrae. It is the strongest ligament in the spine traversing the length of the spine from the base of the skull to the pelvis. Its main role is the protection of the spinal cord and nerves. Posteriorly, it touches the facet joint capsules.

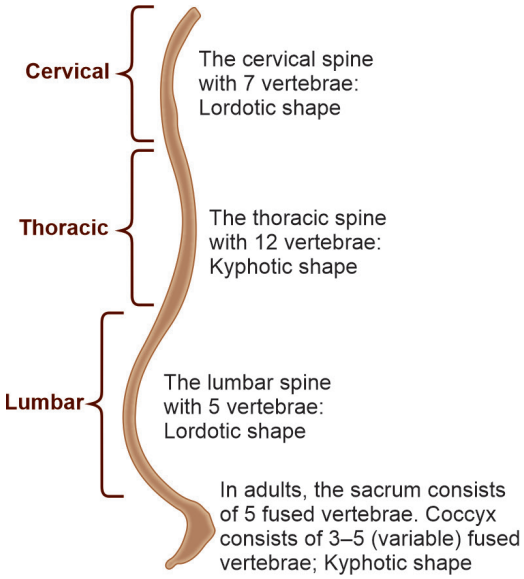
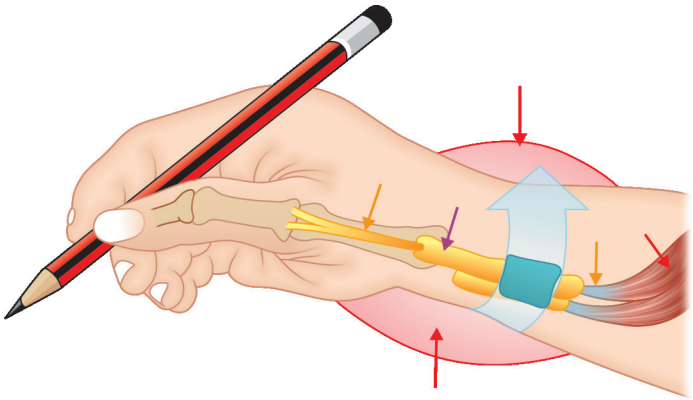


Fig. 1.3: A diagrammatic representation of the spine (wavy dark brown line): The spinal curvatures, segments and the number of vertebrae in each segment

d. **Muscles:** There are several muscles that help the spinal movements. The muscles are covered with fascia that taper off making tendons that attach to the bone. In the thoracic region the spinal muscles are:
   i. *Longissimus thoracis* that helps thoracic spinal extension and lateral flexion as well as rib rotation.
   ii. *Iliocostalis thoracis* that aids to the function of longissimus thoracis.
   iii. *Spinalis thoracis* is the main muscle for extending the thoracic spine, in the lumbar region.
   iv. *Psoas major* flexes the spine at lumbar and lower levels and at the hip joint.
   v. *Quadratus lumborum* causes lateral flexion of the spine.
   vi. *Multifidus* is the strongest muscle in the spine consisting of short triangular muscles that make the deep back muscle in the transversospinalis group on either side of the vertebral column from the cervical to the lumbar spine.

e. **Lumbar zygapophyseal joints:** These are the only synovial joints in the spine that form part of the posterior element of the spinal deeply involved in load transmission at the vertebrae. These are small joints present at the postero-lateral articulation between vertebrae with capacity of ~1–2 ml of fluid they comprise. Being involved in load transmission, they are prone to degenerative (osteoarthritic) joint disease. Involvement in inflammatory joint diseases or other types of inflammatory arthritis including crystal arthropathies is not well described.

4. **Soft tissue:** Tissues between bone and dermis are called 'soft tissue'. Soft tissue makes up the bulk of MSK. Its components include:
   a. **Striated muscles:** The organ that moves the joints.
   b. **Tendons**
      i. *The fibro-collagenous components:* The thread/ropes that transmit the muscle force to the bones for the movement of the joints.
      ii. *The tendon sheaths:* Delicate covers of the tendons on which they glide smoothly when muscles contract helping normal joint movements.
   c. **Ligaments:** Fibro-collagenous tissues with extremely high tensile strength that keep the bones joined together yet permitting their movements at the joints. **Figure 1.4** depicts some of the soft tissues mentioned above.
   d. **Panniculus:** This term is used differently by the rheumatologists and the rest of the medical community. Generally, it refers to obesity and its grading, often used by bariatric surgeons. In contrast, rheumatologists identify panniculus as the subcutaneous tissue that covers most of the body excluding certain areas of the head-face and parts distal to wrist and ankle. It consists of fat lobules separated by septae. Septae support arterioles, venules and superficial nerves reaching the skin (dermis, epidermis). As an organ, there could be involvement of the panniculus that can then be classified as 'lobular panniculitis', 'septal panniculitis'; either of them with or without vasculitis. Thus, there are several varieties of RMDs involving/affecting panniculus. Understanding panniculitis, especially with their histopathological



Arrows of different colours represent different soft tissues as follows: *Red:* Muscles; *Dark yellow:* Tendons; *Purple:* Tendon sheath; *Light yellow:* Retinaculum (ligaments are similar soft tissues, not shown in the diagram)

Fig. 1.4: Soft tissues in the musculoskeletal system (*Courtesy:* Miss Aashita Aggarwal)

examination, helps the diagnosis of both 'primary' panniculitides as well as panniculitides seen in other RMS, thus aiding the diagnosis of the primary RMD (e.g. *lupus profundus*, a specific type of panniculitis seen in patients with systemic lupus erythematosus (SLE)). **Figure 1.5** gives a diagrammatic representation of the anatomy of panniculus.

Inflammation which primarily involves septa without affecting the vessels is called 'septal panniculitis'; erythema nodosum being its prototype. In contrast, inflammation in lobules is called 'lobular panniculitis' the prototype of that being 'erythema induratum of Bazin' (supposed to be due to sensitivity to tubercle bacilli). If the septal blood vessels also show inflammation, then the term is *panniculitis with vasculitis* (e.g. leukocytoclastic vasculitis, cutaneous polyarteritis nodosa).

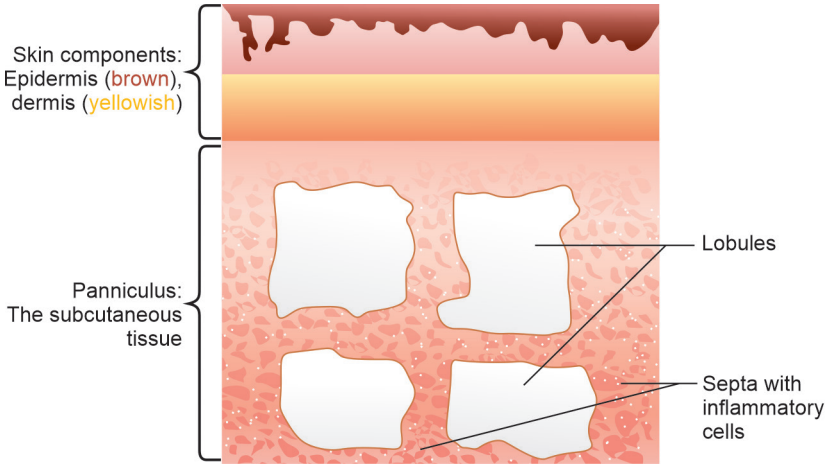


Fig. 1.5: Line diagram showing cross-section of panniculus. Lobules (containing lobular adipose cells) are encased in septa (consisting of fibrous tissue that partitions the lobules and supports the arterioles, venules and the nerves that traverse from deeper tissues to the dermis)

e. **Bursae:** Bursa (plural is bursae) is a sack-like structure in the MSK system that cushions the bones, tendons and muscles in the vicinity of joints. It absorbs sudden pressures that may be fall any region of the MSK system. Several, relatively big bursae are seen around the 4 main large joints of the body, namely shoulders, elbows, hips, and the knees. Bursae in and around ankles are also important. Disease of bursae are called '*bursitis*'. A common clinical feature that brings the patients to rheumatologists. **Figure 1.6** gives examples of bursae present around the knee.

f. **Fascia:** A connective tissue sheath that surrounds every organ of the body is called fascia. The fascia covering the MSK organs may get involved in certain diseases, called '*fasciitis*'. There could be some RMDs where fasciitis is a prominent feature, e.g. '*eosinophilic fasciitis*'.

5. **Diseases without borders' but immunoinflammatory in nature, often with autoantibodies:** This group has diseases that are not limited to a particular organ, e.g. blood vessels. Thus, *systemic vasculitides*, although not part of the musculoskeletal system, make one of the most serious groups of diseases that are managed by rheumatologists. The main reason that rheumatologists are the treating specialists for systemic vasculitides is that their treatment involves immunomodulatory/immunosuppressive drugs, an area of expertise in which rheumatologists are at the forefront. Similarly, there is one disease with a group of autoantibodies called 'antiphospholipid antibodies' in which thromboembolism can affect any size and any type of blood vessels (veins/arteries) in any organ of the body. This disease is called 'antiphospholipid syndrome (APS)'. Interestingly, one of the antibodies seen in this disease (called anti-β_2-glycoprotein 1) directly 'attacks' the decidual tissue causing pregnancy loss, pregnancy complications, foetal growth retardation and foetal death. In recent years a large number of similar multisystem inflammatory diseases are being discovered under an umbrella term 'autoinflammatory syndromes' that

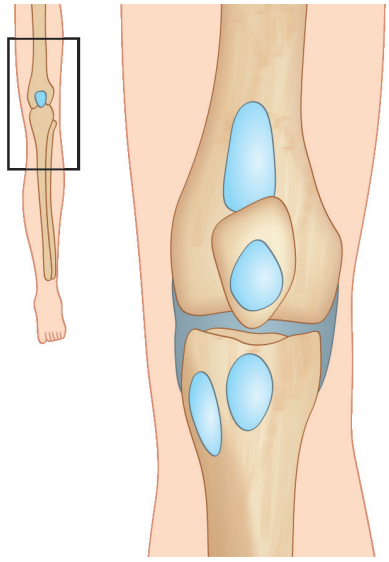


Fig. 1.6: Common bursae around the knee *shown in light blue colour* (*Courtesy:* Miss Ashita Aggarwal)

are due to uncommon/rare genetic mutations. Quite often, rheumatologists are consulted for such diseases.

6. **Organs that may get affected in RMDs:** Theoretically, any organ in the body can get involved in some of the systemic RMDs, However, a few of them get involved so often that rheumatologists should have good grounding in the anatomy and physiology of those organs. The most important and often involved organ is skin, kidney, gastrointestinal tract, lung, and nervous system. Of course, haematological changes are common in most systemic diseases and that also includes RMDs. An area that is also important for rheumatologists concerns conception, pregnancy, puerperium and foetal health. Although direct involvement of heart is not a common feature of the most of the common RMDs, indirect effect of decreased mobility (lack of physical activity and regular exercise causing metabolic syndrome) and generalised inflammation increase the risk of atherosclerotic cardiovascular disease (ASCVD) that may be ~1.5 times more than the general population and may rise almost equal to that of diabetes mellitus. Among endocrine diseases, hypothyroidism is one of the commonest multimorbidity seen with RMDs.

   The above description provides the commonly affected musculoskeletal organs and regions that are involved in diseases with the main symptoms being pain and inability to perform movement-related body functions. In contrast, some diseases have multisystem manifestations that test the clinical acumen of the physicians. It is not uncommon that rheumatologists are consulted in such cases who, with their experience of dealing with most such diseases, can make a diagnosis without difficulty.