

Arthritis of the Spine

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Abstract Arthritis is the common term used to describe pathological changes of joints and adjoining parts of the bone. Several types of arthritis commonly affect the spine. Osteoarthritis, a non-inflammatory type of arthritis, most often affects the cervical spine and the lumbar spine. Neck pain, limited neck and head motion, low back pain, and limited flexibility of the low back can result from progressive joint damage. Degeneration of the intervertebral disk may accompany cervical and lumbar osteoarthritis, and can cause either nerve root or spinal cord compression. Ankylosing spondylitis is the most common inflammatory arthritis that principally affects the spine rather than other joints, and is characterized by slow development of bony fusion among the adjacent vertebrae. Rheumatoid arthritis, the most common type of inflammatory arthritis, affects mostly the limb joints but can also affect the cervical spine, causing neck pain and headache. Cervical spine arthritis also often occurs in children with juvenile idiopathic arthritis. Radiography is an essential diagnostic tool in the evaluation of patients with spinal arthritis, but provides limited information on the posterior spinal structures. Magnetic resonance imaging can be useful for defining abnormalities in the posterior spinal joints, the nerve roots, and the spinal cord.

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1 Overview

1.1 Spine Anatomy and Classification of Arthritis

Vertebrae are the bony structure of the spine. The anterior parts of the vertebrae, the vertebral bodies, are interconnected by the intervertebral disks. The outer layer of the intervertebral disk is a dense fibrous tissue, called the annulus fibrosis. The annulus fibrosis and its adjacent vertebral body form the discovertebral joint. The posterior part of the vertebra consists of the neural arch. At each vertebral level, the inferior processes of one vertebra articulate with the superior processes of the vertebra immediately below it, forming a facet joint (also known as the zygoapophyseal joint) on both the right and left sides. The neural arch forms the spinal canal, containing the spinal cord, spinal nerves, spinal membranes, and spinal fluid. There are openings on the side at each vertebra level, called the intervertebral foramen. The spinal nerves, originating from the spinal cord, exit the spinal canal through the foramen. The vertebral bodies are lined with ligaments on the front and back that provide stability. At the neural arch, the ligamentum flavum connects vertebrae to each other.

Arthritis is the common term used to describe pathological changes to joints and their associated structures, including bones, cartilage, and ligaments. Depending on whether the immune system is involved or not, arthritis can be categorized into two main subtypes: inflammatory and non-inflammatory. Several types of arthritis can affect the spine. Osteoarthritis, a degenerative process often associated with aging, is the most common type of non-inflammatory arthritis. The cervical spine and the lumbar spine are often affected in osteoarthritis. When the spine is affected by osteoarthritis, it is termed spondylosis. Degenerative changes occur in the intervertebral disks as well, causing degenerative disk disease. Structural changes of the vertebrae and the disks may lead to compression on the spinal cord or the spinal nerve roots, causing a condition known as spinal stenosis. Rheumatoid arthritis is the most common type of inflammatory arthritis. Although it primarily targets joints of the extremities, rheumatoid arthritis may affect the cervical spine. In children, juvenile idiopathic arthritis may damage the cervical spine in a similar fashion. Ankylosing spondylitis is the prototypic inflammatory arthritis that primarily involves the spine and the sacroiliac joints, with a prominent feature of slow development of bony fusion among the adjacent vertebrae.

1.2 Uses of Imaging in Diagnosis, Prognosis, Treatment, and Assessment of Treatment Response

Plain radiography is the essential diagnostic tool for spinal arthritis, not only because it can demonstrate much of the relevant pathological changes in the spinal structures, but also because it is widely available and inexpensive. However, plain

radiography provides limited information about the posterior spinal structures and the intervertebral disk pathology. Magnetic resonance imaging (MRI) and computer tomography (CT), as three-dimensional imaging tests, provide superior structural information and a better resolution. MRI is ideal for visualizing pathology of the intervertebral disk, neural structures such as the spinal cord, and is often the spinal imaging test of choice for patients with neurological symptoms. MRI is also useful to depict inflammatory changes in bones and soft tissues. Therefore it has gained interest as a method to assess the treatment response in inflammatory spine diseases. CT is most often used in patients who have contraindications to MRI. CT is also an ideal imaging modality for bony structures. CT myelography remains the gold standard for diagnosing the cause of nerve root compression, differentiating osteophytes from disk pathology. Spinal CT is also used in research settings to assess the progression of bony pathology in ankylosing spondylitis.

2 Osteoarthritis

2.1 Cervical and Lumbar Spondylosis

2.1.1 Definition and Occurrence

Spondylosis refers to degenerative arthritis of the spine, including osteoarthritis of the discovertebral and facet joints, and degenerative changes of related soft tissues, including surrounding ligaments and muscles.

The cause of spondylosis remains unclear. A widely cited hypothesis states that degenerative changes begin with the loss of water content in the annulus fibrosis [1]. The annulus gradually becomes drier and weaker, and eventually the disk content leaks out, resulting in intervertebral disk protrusion and narrowing of the disk space. This subsequently leads to increased mechanical stress at the discovertebral joints, the facet joints and the spinal ligaments, causing both bony overgrowth and ligament thickening. Bony growths at the front and side of the vertebral bodies are commonly seen. These so-called marginal osteophytes originate from the end plate of the vertebral body. At the microscopic level, the cartilage endplate degenerates and is replaced by bony proliferation; over time, it becomes hard and protrudes into the intervertebral disk and the edge of the vertebral body [2]. Similar changes occur at the facet joints, with overgrowth of bone (osteophytes) and narrowing of the joint spaces. The spinal ligaments, especially the ligamentum flavum, become thickened and may eventually calcify. These degenerative changes are most commonly found at the fifth cervical, eighth thoracic and third lumbar spinal levels, possibly due to greater spinal flexibility in these areas [3]. Progression of degenerative changes may lead to compression of the adjacent structures, particularly on the spinal cord and/or the spinal nerve roots, causing spinal stenosis. This condition is discussed in detail below.

Degenerative changes of the spine are found to be present as early as age of 15, but symptoms only develop in much older individuals [4]. In a community-based study in the United States, facet joint osteoarthritis was found on CT scan in 36 % of people younger than 45 years old, in 67 % who were 45–64 years old, and in 89 % who were older than 65 years [5]. A large epidemiologic study in Japan reported the prevalence of radiographic lumbar spondylosis as 75.8 % in people older than 60; however, only 28.8 % of these people had symptoms of low back pain [6]. Aging and trauma are the main risk factors for developing spondylosis. No associations have been established with other conditions, such as lifestyle, height, obesity, physical activity, smoking and alcohol use.

2.1.2 Clinical Manifestations

Patients may present with a wide spectrum of symptoms. The majority of patients with spondylosis do not have any symptoms, even with advanced changes on radiographs.

In symptomatic patients, pain is the most common complaint. It may present as acute episodes, or may be chronic. In some patients, pain is caused by osteoarthritis of the facet joints, called facet joint syndrome. In lumbar facet joint syndrome, pain travels down to the buttock and the back of the thighs, and typically improves with bending forward and worsens with bending to the affected side. In cervical facet joint syndrome, patients often complain of neck pain traveling along the spine, the shoulder blades and the back of the head.

Limited motion of the neck or the back may occur, especially when trying to extend the back or raise the head to look up. Osteophytes at the cervical facet joints sometimes compress the arteries and decrease the blood supply to the brain, causing dizziness.

Patients with spondylosis may have concurrent degenerative disk disease, or may progress to develop spinal stenosis. These conditions often present with neurologic symptoms, such weakness of the legs or the arms, numbness, or urinary and/or bowel dysfunction. These conditions will be discussed in detail in the following sections.

2.1.3 Treatment

Conservative management is the mainstay treatment for patients who do not have neurologic symptoms. Patient education on the natural history of spondylosis, self-care options and coping techniques is the first step. A long-term follow-up of patients with neck pain found that in 79 % patients, the pain resolved after 15 years without surgical intervention [7]. Immobilization of the cervical spine with a soft collar is often used, however its effectiveness is not proven. In patients with back pain, maintaining daily activity, instead of rest, is beneficial. Physical therapy, including mechanical traction and manipulation, are sometimes used. Exercise,

stretching, and muscle strengthening are also recommended. Heating pads or blankets may provide local relief. In general, evidence for these measures is not based on controlled trials.

Pain management often includes the use of medications. Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen or naproxen are the first line treatments. In patients with severe pain who do not improve sufficiently with these treatments, opioids can be considered. Muscle relaxants may provide relief in acute pain episodes. However, they are often associated with side effects such as dizziness, so long term use is not recommended. Local injections with corticosteroids or anesthetics are sometimes used, with variable results.

Surgery is indicated for patients with progressive nerve symptoms and compression of the spinal cord or the spinal nerve roots. For neck pain or back pain without nerve compression, surgery is not recommended due to lack of effectiveness.

2.1.4 Imaging

Plain radiographs of the cervical spine and lumbar spine are typically adequate to reveal spondylosis. Because the correlation between symptoms and radiographic changes is poor, radiographs have limited usefulness in the evaluation of neck pain or back pain. In the absence of systemic symptoms such as fever or weight loss, history of trauma, or progressive nerve symptoms, radiographs are typically not obtained until after 6–8 weeks of conservative management.

However, radiographs may still provide valuable information. Osteophytes, narrowing of the intervertebral disk spaces, narrowing of the facet joints, sclerosis (increased radiographic density) of the facet joints and the endplates of the vertebral bodies, and narrowing of the neural foramen are common findings in spondylosis (Figs. 1 and 2). Radiographs are also useful to assess the alignment of the spine and to exclude other diagnoses. The Kellgren/Lawrence system was developed to classify the degree of osteoarthritic change in the spine, including the facet joints. Lateral views of cervical spine and lumbar spine are obtained for grading. Five features are considered in the Kellgren/Lawrence system: osteophytes, ossicles near the joints, narrowing of joint spaces with subchondral sclerosis, pseudocysts, and altered bone shape (Table 1). Radiographic changes are classified into five grades (0–4), with a grade of 2 or higher as the conventional standard of diagnosis [9].

In patients with progressive neurologic symptoms, or in patients with persistent pain and severe radiographic spondylosis, MRI is the imaging test of choice. It provides a better resolution for structural changes, and is ideal for visualization of the spinal cord, the intervertebral disk, and the soft tissues.

CT is superior for detection of bony changes, especially small osteophytes or erosions arising from the lateral edge of the vertebral body and the facet joints (Fig. 3). However, because of the exposure to radiation, it is only used in patients

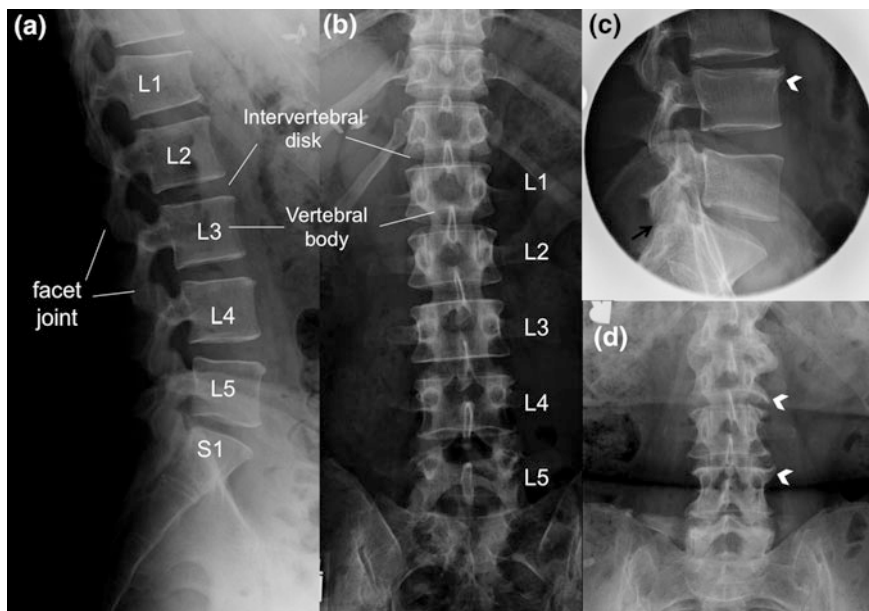


Fig. 1 Plain radiograph of a normal lumbar spine and of lumbar spondylosis. **a** Lateral view of a normal lumbar spine. **b** Anteroposterior view of a normal lumbar spine. **c** Lateral view of a patient with lumbar spondylosis. Marginal osteophyte (*arrowhead*) and narrowing of a facet joint (*arrow*) are present. **d** Anteroposterior view of a patient with lumbar spondylosis. Notice the marginal osteophytes (*arrowhead*) at multiple levels

with contraindications to MRI, and when establishing a firm diagnosis is needed to guide treatment.

As degenerative changes are common in older people and are not always symptomatic, the interpretation of MRI results (or CT with myelogram) should be cautious and correlated with the clinical findings for diagnosis and further management.

2.2 Degenerative Disk Disease

2.2.1 Definition and Occurrence

Degenerative disk disease is a group of conditions caused by wear and tear changes of the intervertebral disks. It is usually a part of the aging process; however, in rare conditions, accelerated degeneration occurs, causing juvenile degenerative disk disease.

The intervertebral disk is composed of the gelatinous nucleus pulposus in the center, surrounded by the annulus fibrosis, which is composed of layers of dense,

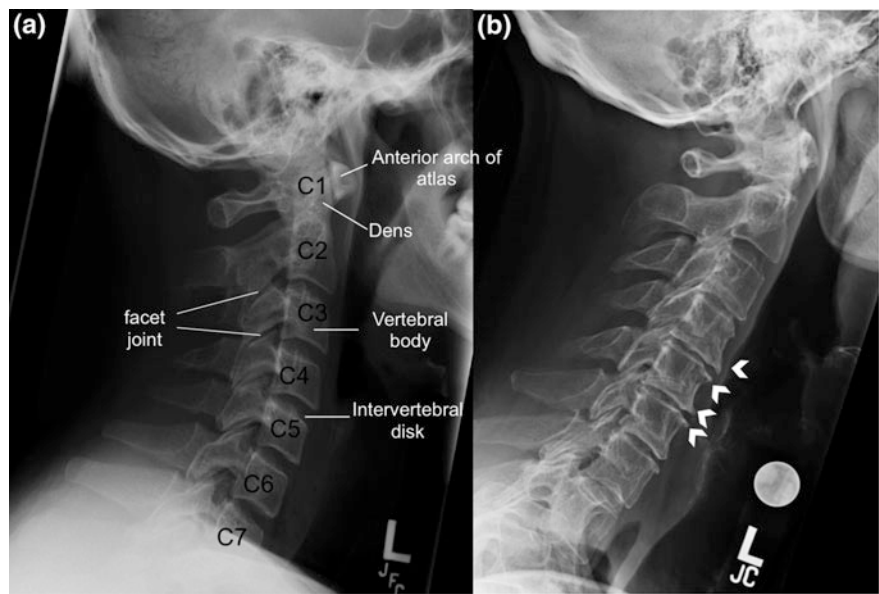


Fig. 2 Plain lateral radiographs of a normal cervical spine (a) and of a patient with cervical spondylosis (b). Marginal osteophytes are denoted by *arrowheads*

Table 1 Kellgren Lawrence grading system: osteoarthritis is divided into five grades as follows [8]

Grade 0	None
Grade 1	Doubtful
Grade 2	Minimal
Grade 3	Moderate
Grade 4	Severe

fibrotic tissue. With aging, the disk undergoes three phases of degenerative changes [10]. In phase I, or the dysfunctional phase, microtrauma from repetitive use causes small tears and fissures in the annulus fibrosis, associated with pain. Meanwhile, the nucleus pulposus loses water content. MRI study often reveals disk bulging without herniation and tears in the annulus. In phase II, or the unstable phase, more tears occur and lead to disk disruption, resorption, and loss of the disk space. Local inflammation may follow if the herniated disk compresses the spinal nerve root. Cartilage degeneration and malalignment can develop in the facet joints. Clinically, patients often present with spine instability and symptoms related to nerve irritation. Phase III is the stabilization phase. With disk resorption and disk space narrowing, mechanical stress leads to fibrosis of the disk and degenerative changes at the vertebral endplates.

The prevalence of degenerative disk disease is difficult to estimate. In a MRI study in 239 asymptomatic individuals with a mean age of 39 years, degenerative cervical disk disease progressed in 81 % of the study subjects over 10 years [11].

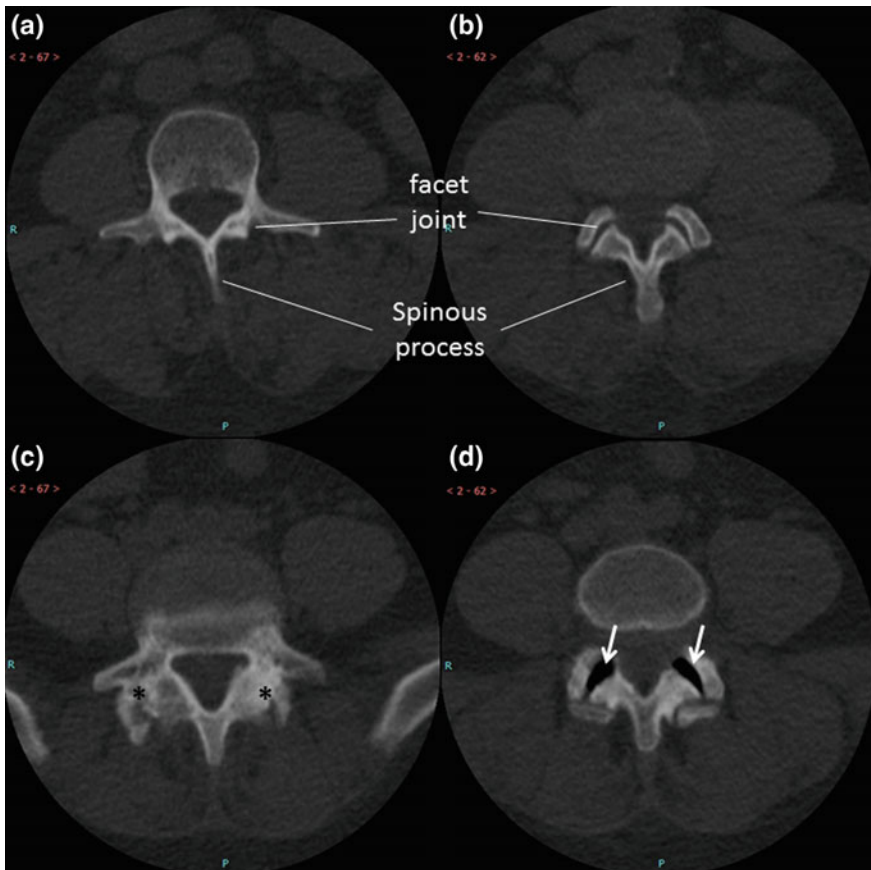


Fig. 3 Facet joint osteoarthritis on computed tomography. **a, b** Axial view of a normal lumbar spine. **c, d** Axial view of a lumbar spine with facet joint osteoarthritis. Hypertrophy (*asterisks*) and erosions (*arrows*) are common findings in facet joint osteoarthritis

In patients with cervical radiculopathy, disk protrusion was identified as the cause in 21.9 % of patients [12]. In a study of cervical MRI scans of patients undergoing throat surgery who had no neck pain, cervical disc protrusion or herniation was incidentally seen in 20 % of patients aged 45–54, and 57 % of those older than 64 [13]. Lumbar degenerative disk disease affects young to middle aged people as well, with a peak incidence at age 40 years. A recent study using MRI of the whole spine of 975 individuals found degenerative disk disease in 71 % of men and 77 % of women younger than age 50 years, and in more than 90 % of men and women older than age 50 years [14].

2.2.2 Clinical Manifestations

Degenerative disk disease may present a wide spectrum of symptoms, and MRI studies have shown that the degree of disk degeneration does not correlate with the symptoms [15, 16]. The majority of patients with degenerative changes on MRI remain asymptomatic for years [11].

Common symptoms include pain and nerve dysfunction such as radiculopathy. Radiculopathy is caused by the compression of a spinal nerve root from a laterally herniated disk. It is one of the most common causes of acute pain of the neck or the back. In cervical disk herniation, pain usually affects the arms, shoulders, the region between the shoulder blades, or the rib cage, and can mimic chest pain. Persistent compression will lead to numbness, tingling, and weakness of the arms or the hands, in the areas supplied by the compressed spinal nerve. In one series, 70 % of patients with cervical radiculopathy were found to have lesions at the disk between the sixth and seventh cervical vertebrae (C6–C7), and 20 % of patients had lesions at the C5–C6 intervertebral disk [17].

In lumbar disk herniation, pain is usually in the low back, travelling to the buttocks or down the leg to below the knee. Pain is usually worsened with bending forward, coughing, or sneezing. Numbness, tingling, and weakness of the leg may occur. The straight leg test is a physical exam test used to assess lumbar disk herniation, with specificity of 89 % and sensitivity of 52 % [18].

A large central disk herniation may cause compression of the spinal cord, with neurological symptoms compatible with myelopathy or cauda equina syndrome in the lower lumbar spine. Detailed clinical manifestation will be discussed in the section on spinal stenosis.

Disk pain is caused by irritation on the annulus fibrosis. It comprises neck pain or back pain, extending along the spine, without associated neurologic symptoms. A diagnosis of discogenic pain is based a fluoroscopic provocative test, and will be discussed in detail in the imaging section.

2.2.3 Treatment

No treatment is needed for asymptomatic patients. For patients with pain along the spine without nerve symptoms, conservative management is appropriate. Most patients have a benign course. In a study with 19 years of follow up, 75 % of patients had only one episode of pain or mild recurrent symptoms [7]. Pain management with NSAIDs, muscle relaxant during acute episodes, exercise, and cervical or lumbar traction, are commonly used.

In patients with progressive neurologic symptoms, MRI is indicated. If compression of the spinal nerves or nerve roots by a herniated disk is found to be the cause of symptoms, local injection of corticosteroids is often used, especially in cases of lumbar disk herniation. Without treatment, persistent compression may

lead to permanent damage of the nerve, and lead to irreversible nerve symptoms. If compression of the spinal cord is present with clinical symptoms of myelopathy, definitive surgery is indicated.

2.2.4 Imaging

Plain radiographs of the spine have limited use in diagnosing degenerative disk disease, although some radiographic findings indicate degenerative disk disease. These findings include narrowing or loss of the disk height (Fig. 4), sclerotic changes of the vertebral endplates, and, in later stages, the presence of osteophytes and sclerosis of the facet joints. “Vacuum phenomenon” is considered a specific radiographic indicator of disk degeneration. With degeneration of the disk, gases transpired from the circulation accumulate in the space that the nucleus pulposus once occupied, causing the intervertebral disk space to appear radiolucent (Fig. 4). In general, in the absence of trauma, radiographs are not always needed.

Fig. 4 Severe degenerative disk disease and lumbar spondylosis on plain radiograph. Lateral view of a lumbar spine. Narrowing of intervertebral disk space (*black arrow*), complete loss of disk space (*asterisk*), and vacuum phenomenon (*white arrow*) are characteristic features of degenerative disk disease. Osteophytes originating from vertebral bodies (*black arrowheads*) and facet joint narrowing (*white arrowheads*) are present, signifying associated spondylosis



Provocative discography may be used to confirm that a degenerative disk is the source of neck pain or back pain in difficult cases [19]. Under fluoroscopy, a diseased disk is injected at a certain pressure to see if this procedure reproduces the patient's pain. If the injection to an adjacent normal disk does not reproduce the pain, the test is confirmatory.

MRI is the standard imaging modality for detecting disk disease. It is indicated in patients who have progressive neurological symptoms despite conservative management, or in patients who plan to undergo surgery. On MRI, a degenerated disk has decreased intensity on T2 weighted images, due to loss of water content and glycosaminoglycans [20]. Bulging of the annulus (Fig. 5a), herniation of the disk contents (Fig. 5b), and loss of intervertebral disk height can be demonstrated on MRI. Early changes of disk degeneration, such as tears of the annulus fibrosis, can be seen as high intensity zone lesions [21, 22].

CT scan can depict degeneration, bulging and herniation of the disk, but with much less detail than MRI. CT can also show sclerotic changes of the vertebral endplate and loss of the disk height, which are commonly seen in degenerative disk disease, but these findings most often can be readily seen on plain radiographs. Clinically, CT is used in patients with contraindications to MRI.

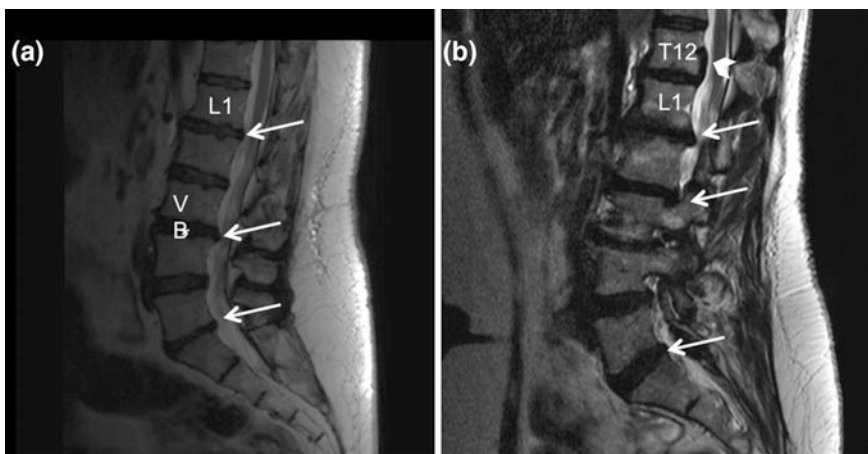


Fig. 5 Degenerative disk disease by magnetic resonance imaging. Sagittal view of a lumbar spine, T2 weighted images. **a** Disk bulging at multiple levels, most prominent at L1–L2, L3–L4 and L5–S1, and indenting the spinal canal (arrows). VB indicates vertebral body; Asterisk indicates intervertebral disk. **b** Disk herniation at the T12–L1 level, with migration of disk material posterior to the T12 vertebral body (arrowhead). Disk bulging (arrow) is present at L1–L2 and L2–L3 as well

2.3 Spinal Stenosis

2.3.1 Definition and Occurrence

Spinal stenosis is a condition of narrowing of the central spinal canal, causing compression on the structures within the canal, mainly the spinal cord and spinal nerve roots, with associated nerve dysfunction. The spinal cord extends from the base of the brain and ends at the level of the first and second lumbar vertebrae (L1–L2). Spinal nerves branch off the spinal cord and course alongside it before exiting the spinal canal. Below the L1–L2 level, the spinal nerves form a bundle called the cauda equina. Anatomically, when compression happens above the L1–L2 level, both the spinal cord and the nerve roots can be affected, while below the L1–L2 level, compression of the nerve roots alone is seen. Both direct mechanical compression and secondary changes due to lack of blood supply contribute to damage of the spinal cord and nerve roots. When the spinal cord is affected, it is called myelopathy, and when the spinal nerve roots are involved, it is termed radiculopathy.

Spondylosis is the most common cause of spinal stenosis in people older than 60 [23]. Osteophytes of the facet joints, disk bulging, and calcification and overgrowth of the posterior longitudinal ligament and ligamentum flavum can slowly encroach the spinal canal, and eventually lead to compression of the spinal cord or nerve roots. Spondylolisthesis, a condition in which the one vertebra slips relative its neighboring vertebra, can be a cause of lumbar spinal stenosis, especially at the L4–L5 level.

Conditions other than degenerative changes can cause spinal stenosis, including tumors and post-operative scar tissue. Inflammatory conditions, such as rheumatoid arthritis, may lead to overgrowth of the synovium at the facet joints, with compression of the spinal cord in severe cases. Some people are born with a narrow spinal canal and are susceptible to spinal stenosis with even minor changes in spine anatomy or mild degrees of degenerative disease. Spina bifida is another congenital cause of spinal stenosis.

Spinal stenosis usually has an insidious onset. It can be an incidental finding on radiologic study in asymptomatic individuals. It occurs in 20–30 % of people older than 60 years of age [24]. In a study of 187 individuals, the prevalence of lumbar spinal stenosis increased with age, affecting 2.1 % of people aged 40–49, 6.1 % of people aged 50–59, and 16.3 % of people older than 60 years [25].

2.3.2 Clinical Manifestations

In patients with cervical spinal stenosis, neck pain or pain in the area below the shoulder blades is frequently reported. When the narrowing and compression damage the cord, neurological symptoms develop. Clumsiness and weakness are common, and both the arms and legs may be affected. Many patients experience

loss of sensation, often associated with numbness and tingling. When the spinal cord is compressed, a sensory plane can be detected, separating the body into areas with normal sensation above the plane and areas without normal sensation below the plane. If a nerve root is affected, the sensory change is often distributed in the skin area supplied by the compressed spinal nerve, or in other words, in a dermatomal pattern. Patients may also experience difficulty with urination or having bowel movements. On physical exam, patients are found to have an abnormal gait early in the course of disease, indicating weakness of the legs. Neck motion is often limited. Lhermitte's sign is a characteristic finding, and can be induced by bending the neck. When this sign is present, patients experience a sensation of an electric shock in the neck, shooting down to the arms and along the spine.

Rarely, cervical spinal stenosis presents acutely. This can happen after minor injury or whiplash injury. These patients often have pre-existing degenerative changes, and a minor disturbance then leads to worsening and onset of nerve symptoms, with rapid progression of weakness, sensory changes, and bladder or bowel dysfunction.

The common clinical presentation of lumbar spinal stenosis was well characterized in a cohort of 68 patients [26]. Back pain, often travelling down the legs, numbness, and weakness of the legs are common. A prominent feature is neurogenic claudication, with worsening of symptoms on walking or standing, and relief when sitting or bending forward. On exam, patients are often found to have a wide-based gait. Weakness and sensory changes are distributed in one or more spinal nerve areas, indicating radiculopathy. Cauda equina syndrome is a rare complication of lumbar spinal stenosis, with weakness of both legs associated with urinary dysfunction. If spinal stenosis occurs higher in the spine than the L1–L2 level, damage of the spinal cord will cause myelopathy, with presentation similar to that of cervical spinal stenosis, but involving the legs.

2.3.3 Treatment

Conservative management is the mainstay treatment for spinal stenosis. In patients with cervical spinal stenosis, immobilization with a soft collar or a brace is often recommended. Activities such as action sports or intense neck movements should be avoided. Prevention of whiplash injury during motor vehicle accident is important. For patients with lumbar spinal stenosis, although evidence is lacking, exercise is recommended with a goal to strengthen muscles and to maintain correct posture. Pain control with acetaminophen and NSAIDs is commonly used, and can be escalated to opioids if needed. Epidural injection of corticosteroids is used in lumbar spinal stenosis, but with limited evidence supporting its effectiveness.

In some cases, compression can be relieved by surgery. However, the indications for surgery and its timing have not been well studied. Commonly, surgery is considered in patients with progressive nerve symptoms or moderate to severe symptoms with difficulty performing daily tasks [26]. In patients with spinal

stenosis but without neurologic symptoms, surgery can be deferred with close monitoring [26, 27].

Acute nerve symptoms may be the first presentation in some patients, and is a medical emergency. Immediate MRI is indicated for diagnosis and assessment of severity. Neurosurgery or orthopedic evaluation for potential surgical intervention is essential. Treatment with high dose intravenous corticosteroids to decrease acute inflammatory changes in the spinal cord may improve outcomes [28].

2.3.4 Imaging

The diagnosis of spinal stenosis is based on imaging and a compatible clinical presentation. Plain radiographs have limited utility for this condition. It is used in cases of neck pain or back pain without neurologic symptoms to exclude other conditions. In patients with nerve symptoms, MRI is the study of choice, while CT with myelography is used in patients with contraindications to MRI. Direct compression of the spinal cord can be visualized on MRI, and it may or may not be associated with a signal change in the spinal cord. Findings may be present in one or multiple vertebral levels.

Measurement of the anteroposterior diameter of the spinal canal or the intra-spinal canal area has been suggested as radiologic diagnostic criteria of spinal stenosis [24], and for assessment of myelopathy [29, 30], however it has not been routinely used in clinical practice. More importantly, radiologic spinal stenosis is an incidental finding in 6–7 % of asymptomatic individuals, and its prevalence increases to 20–30 % in people older than 60 years [24].

Abnormal MRI signal in the spinal cord can be a useful marker of myelopathy (Fig. 6). Hyperintense signal on T2-weighted imaging, hypointense signal on T1-weighted imaging, and hyperintense signal on diffusion-weighted imaging (DWI) have been evaluated for their correlation with clinical findings, and DWI has a better correlation [31, 32].

2.4 Diffuse Idiopathic Skeletal Hyperostosis

2.4.1 Definition and Occurrence

Diffuse idiopathic skeletal hyperostosis (DISH) is a non-inflammatory condition characterized by calcification and ossification of ligaments, with a predilection for the spine. It most commonly affects the anterior longitudinal spinal ligament, particularly in the thoracic spine. Large flowing osteophytes with an appearance of ‘candle wax dripping down the spine’ is the typical finding in this condition. Thickening, calcification, and ossification may also involve peripheral ligaments, especially at sites of the tendon insertions. Unlike spondylosis, in which the primary pathologic target is cartilage, the discovertebral joints and the facet joints are

Fig. 6 Cervical spinal stenosis with spinal cord compression by magnetic resonance imaging. Sagittal view of a cervical spine, T2 weighted images. At the C4–C5 level, intervertebral disk bulge compresses the spinal cord, associated with hyperintense signal at the corresponding level (*arrow*), indicating structural damage of the spinal cord. *Asterisks* mark intervertebral disks



usually intact in DISH. Lack of sacroiliac joint involvement and inflammation distinguishes DISH from ankylosing spondylitis [33, 34]. The cause of DISH remains unclear.

DISH is rare in people younger than 40 years old. It generally affects people older than 50, with a prevalence of 15 % in women and 25 % in men. This prevalence increases to 26–28 % in those over 80 years [35].

2.4.2 Clinical Manifestation

DISH is largely asymptomatic. Patients may report pain in the spine and legs, morning stiffness, and limited spine flexibility. Pain in the upper back is common, and is often associated with limited chest expansion. The cervical spine and lumbar spine may also be involved. Although rare, in severe cases, large calcifications may impinge on the airway to cause difficulty or pain with swallowing, hoarseness, or high-pitched sounds from the throat with breathing. In the peripheral joints, calcification of the ligaments and entheses (sites where tendon attach to the bone) cause local pain, and can limit movement of the affected joints. Some patients have tenderness and nodules of the entheses.

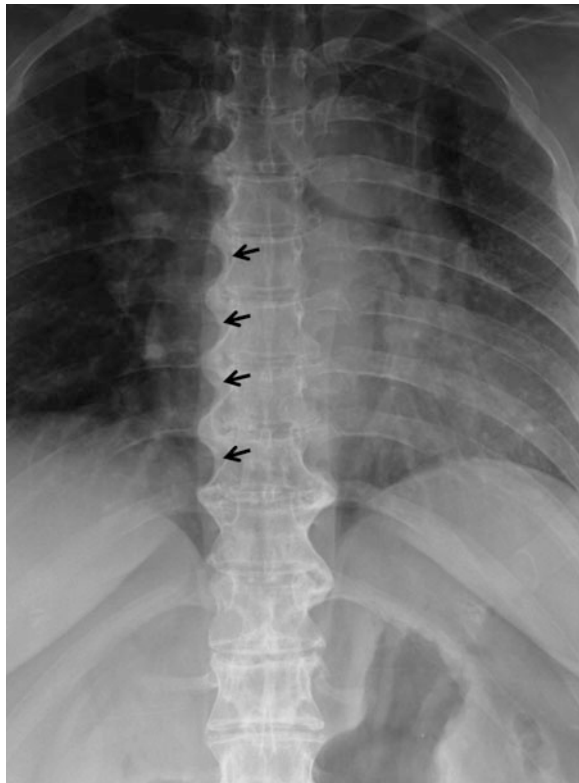
2.4.3 Treatment

Pain control with acetaminophen and NSAIDs is the mainstay of treatment. Physical therapy and exercise may relieve some symptoms and improve function. Surgery is needed if compression is present and causing symptoms.

2.4.4 Imaging

The current accepted diagnostic criteria for DISH is based on plain radiography of the thoracic spine [36]. Large, flowing right-sided ossification over the thoracic spine is typical, extending over at least four vertebral bodies (Fig. 7). Preservation of intervertebral disk heights and absence of facet joint and sacroiliac joint involvement are also required for diagnosis.

Fig. 7 Plain radiograph of the thoracic spine in a patient with diffuse idiopathic skeletal hyperostosis. Anteroposterior view of a thoracic spine. Radiolucent areas (*arrow*) indicate space between ossified longitudinal ligament and the vertebral bodies. The changes are predominantly located on the right side of the thoracic spine



3 Inflammatory Arthritis

3.1 Ankylosing Spondylitis

3.1.1 Definition and Occurrence

Ankylosing Spondylitis (AS, from the Greek *ankylos*, fused; *spondylos*, vertebrae; *-itis*, inflammation) is the prototypic disease of the seronegative spondyloarthritis family, a group of inflammatory spinal arthritis that includes AS, psoriatic arthritis, reactive arthritis, spondyloarthritis associated with inflammatory bowel disease, and undifferentiated spondyloarthritis. In contrast to rheumatoid arthritis, patients with seronegative spondyloarthritis usually do not produce autoantibodies, such as rheumatoid factor or anti-cyclic citrullinated protein (anti-CCP) antibody, and therefore are termed “seronegative.” AS primarily involves the axial skeleton, including the spine and sacroiliac joints, with features of chronic inflammation and new bone formation. The sacroiliac joints are the connections between the lower end of the spine (sacrum) and the pelvis.

Genetic factors are important in the susceptibility to AS. Early study of AS in 1970s discovered an association with a gene called human leukocyte antigen B27 (HLA-B27) [37]. It is estimated that 85–90 % of patients with AS have HLA-B27, compared to under 10 % of the general population [38]. Among those who have HLA-B27, AS is more common among those with a close relative who also has AS than in those without any close relative with AS [39]. This indicates other genetic factors are involved in the pathogenesis of AS. Recent genome-wide association studies have advanced our understanding of the genetic basis of AS. More than 20 genes, e.g. ERAP1, IL-23R, KIF21B, etc., and a few intergenic regions, e.g. 2p15 on chromosome 2, are now identified to be associated with AS [40–42]. Substantial evidence suggests environmental factors trigger the onset of AS in people with certain genetic background, a theory well supported by the study of HLA-B27 transgenic rats. These rats develop arthritis and gut inflammation, resembling human HLA-B27 associated diseases. Interestingly, they are protected from the disease if raised in germ-free conditions [43].

Chronic inflammation of the entheses and new bone formation are two cardinal features of AS. Entheses are the sites where tendons or ligaments insert into bones. Immunohistologic staining of entheses from the sacroiliac joints [44] and the foot ligaments [45] of patients with AS showed inflammatory cell infiltration at these sites. In addition to enthesitis, inflammation occurs in bone (osteitis) and synovium (synovitis), and can cause pain and swelling.

New bone formation is a slow and insidious process, with new skeletal tissues formed in connection with, but extending outside the original bone [46]. Bony growths originating from the ligament insertions of the spine are called syndesmophytes, while those originating from the entheses in the extremities are called enthesophytes. Growth of syndesmophytes starts at the thoracolumbar junction, gradually involves other spinal areas, and may eventually lead to bridging of

vertebral bodies and complete fusion (ankylosis) of the spine, causing significant loss of mobility. The same process happens at the sacroiliac joints, causing ankylosis. Several molecular pathways have been proposed to be involved in this process, including bone morphogenic proteins (BMPs), Wnt protein, hedgehog protein and fibroblast growth factors (FGFs) [46]. The relationship between chronic inflammation and new bone formation remains unclear.

The prevalence of AS ranges from 0.1 to 1 % of the population, depending on the ethnic groups studied. Caucasians and Native Americans have the highest prevalence, while AS is rare in Africans. Men are 3 times more likely to have AS than women, and often have more severe disease. AS tends to run in families, with an estimated heritability of more than 90 % [47]. It usually begins during adolescence or early adulthood, and is life-long.

3.1.2 Clinical Manifestations

Inflammatory back pain is the most common symptom in patients with AS. Patients often describe pain in their lower back or the buttock, worse after rest, especially during the second half of the night. They often report waking up in significant pain and stiffness in the morning. Exercise and NSAIDs improve the back pain. The symptoms usually fluctuate, and are often associated with fatigue.

With progression of the disease and the growth of syndesmophytes, ankylosis of the spine becomes a more prominent feature in the disease presentation. In advanced stages of AS, patients may develop a stooped posture, have decreased movement of their spine, and significant loss of function. Fusion of the cervical spine leads to a forward flexion of the head, and patients may have difficulty raising their head to look straight ahead. Involvement of the thoracic spine and the chest wall may make it difficult for patients to expand their chest and take deep breaths, affecting the function of the lungs. In severe cases, patients may develop roundback, which prohibits them from sleeping on their back. Lumbar spine involvement may make it difficult for patient to bend forward and reach the floor. Complete fusion of the spine makes patients more susceptible to trauma and spine fractures. The extent of spine fusion varies greatly among patients, and progression to complete fusion is not inevitable.

Complaints in the limbs are common, mainly due to enthesitis and arthritis. Inflammation of the entheses causes intermittent pain and swelling at various tendon insertion sites, for example, at the heel, where the Achilles tendon attaches, or at the bottom of the foot. Hips, shoulders and collarbone joints are frequently involved with pain, stiffness, and sometimes swelling, indicating ongoing inflammation. Over time, inflammation may causes damage, with erosion of the bone and loss of cartilage and the joint space. Joint movements may become limited, for example, with flexion contracture of the hips.

Paradoxically, despite the propensity to add extra abnormal bone to the spine, patients with AS often develop osteoporosis, a condition of decreased bone density, with increased risk of fracture. Organs other than musculoskeletal system are affected in AS. Common manifestations include uveitis (inflammation of eyes),

aortitis (inflammation of the aorta, the largest artery in the body, originating from heart), and colitis (inflammation of the large bowel). Inflammation can also lead to secondary amyloidosis (a process of protein deposition in internal organs), usually associated with kidney dysfunction.

Laboratory tests have limited use in diagnosing AS. Patients may not have elevated blood markers of inflammation, even if they are actively having inflammatory symptoms. HLA-B27 is not required for diagnosis, and absence of HLA-B27 does not rule out the diagnosis of AS. However, in the appropriate clinical setting, HLA-B27 may suggest the diagnosis.

The modified New York criteria have been used for 30 years for the classification of AS. By these criteria, patients need have a characteristic clinical presentation and characteristic radiographic changes in the sacroiliac joints. Inflammatory back pain, limited motion of lumbar spine and limited chest wall expansion comprise the clinical components; at least one of these features is required for classifying a person as having AS by these criteria. Radiographic changes of the sacroiliac joints will be discussed in the Imaging section.

3.1.3 Treatment

The goal of the treatment is to control inflammation and pain, reduce new bone formation, and improve or maintain function. This is achieved through a combination of medications and non-pharmacologic modalities.

NSAIDs are the first line therapy for pain control and to decrease inflammation. If one NSAID is not effective or causes side effects, usually another NSAID from a different class can be tried. After an adequate trial of NSAIDs, if patients still have symptoms suggesting active inflammation, anti-tumor necrosis factor (anti-TNF) agents are usually considered as the next step. TNF is a pro-inflammatory cytokine. Anti-TNF agents are effective in decreasing pain, stiffness, fatigue, and joint swelling in AS, and in improving patient's function. With a tolerable side effect profile, anti-TNF agents are a mainstay treatment for AS. Discovery of the association between AS and the interleukin-23 pathway brings new treatment options. While these medications have shown effectiveness in controlling active inflammation, whether they can reduce new bone formation in AS remains unclear.

Physical therapy and exercise are essential in the treatment of AS. Patients usually experience a significant reduction of symptoms after exercise, and it helps them to maintain function. Stretching exercises, such as yoga, may increase spinal mobility, and deep-breathing may increase chest wall expansion and prevent the loss of lung function. Postural training is important and patients should avoid a flexed position for a prolonged period of time.

Patients with advanced AS may need corrective surgeries for complications associated with AS. In patients with severe hip involvement, total hip replacement often provides pain relief and functional improvement. In patients with complete fusion of the spine, the risk of spinal fracture is increased; surgical stabilization is needed if spinal fracture occurs.

3.1.4 Imaging

Plain radiography is important in the diagnosis of AS and in the exclusion of other diagnoses, particularly in patients with advanced disease. Usually an anteroposterior (AP) view of the pelvis is obtained for evaluation of the structural changes of the sacroiliac joints. Erosions, sclerosis and ankylosis of the sacroiliac joints are the common findings in AS. These changes are graded as 0–4, from normal to the most advanced disease (Fig. 8 and Table 2). Presence of bilateral grade 2 changes or unilateral grade 3 or 4 changes is required for classifying AS by the modified New York criteria. Structures other than the sacroiliac joints can be assessed by pelvis X-ray. Erosions and loss of the joint space of the hips, and calcification along the tendon insertions are seen in patients with AS.

However, pelvis radiographs have limitations. They have low sensitivity and specificity for bony changes early in the course of AS, and cannot show inflammation in the bone or joints. In patients with a short duration of symptoms, MRI of the pelvis and the lumbar spine is often used to detect early disease. Active

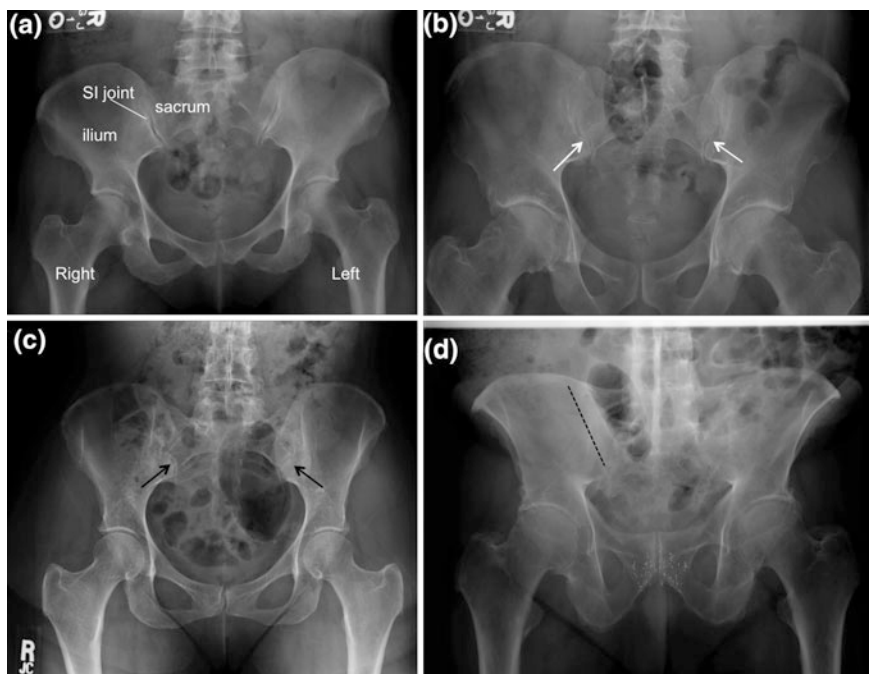


Fig. 8 Radiographic grading of sacroiliac joint involvement in ankylosing spondylitis. **a** Right sacroiliac (SI) joint grade 0 (normal); left sacroiliac joint grade 1 (suspicious for changes). **b** Right sacroiliac joint grade 2, left sacroiliac joint grade 2 (small localized narrowing, indicated by white arrows). **c** Right sacroiliac joint grade 3, left sacroiliac joint grade 3 [partially fused with residual joint space (black arrows)]. **d** Right sacroiliac joint grade 4, left sacroiliac joint grade 4 (complete fusion). Dotted line indicates the location of the fused right sacroiliac joint

Table 2 Radiographic grading of sacroiliac joint changes [48]

Grade 0	Normal
Grade 1	Suspicious changes
Grade 2	Minimum abnormality (small localized areas with erosion or sclerosis, without alteration in the joint width)
Grade 3	Unequivocal abnormality (moderate or advanced sacroiliitis with erosions, evidence of sclerosis, widening, narrowing, or partial ankylosis)
Grade 4	Severe abnormality (total ankylosis)

inflammatory lesions are best visualized in T2 weighted fat-saturated sequence or short tau inversion recovery (STIR) sequence as hyperintense signals. When the hyperintense signal appears in the sacrum or iliac bone, it represents bone marrow edema or osteitis, which is thought to represent inflammation of the bone. It may appear in other locations, such as tendon insertions or synovium, indicating enthesitis or synovitis. Active sacroiliitis is defined by the presence of bone marrow edema/osteitis, and is very suggestive of AS or a condition in the spondyloarthritis family. Erosions, sclerosis, and fatty change can also be detected by MRI. They are chronic sequelae of active inflammation, but their utility in diagnosing AS is not clear at this time.

Spine radiographs are useful to exclude other conditions, and are also useful to assess disease progression in patients with an established diagnosis of AS. Anteroposterior and lateral views of the cervical and lumbosacral spine are usually obtained for evaluation. The vertebral bodies are best visualized on the lateral views. Erosions, sclerosis, or squaring of the vertebral bodies are early findings; with disease progression, syndesmophytes may develop, bridging syndesmophytes form between the neighboring vertebrae, and may eventually lead to a completely fused spine, or a ‘bamboo spine’ (Fig. 9). The modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) is a scoring system used to assess the extent of this process by examining changes at the anterior corners of the cervical and lumbar vertebrae on lateral radiographs. Structural changes of the facet joints can be visualized on AP view, with sclerosis and loss of the joint space being the most common findings.

The treatment goal for AS is to reduce inflammation and to reduce new bone formation. To assess treatment response objectively, imaging modalities to visualize inflammation and that are sensitive to bone growth are ideal. Plain radiography has several disadvantages for these purposes. First, as two-dimensional imaging modality, it has poor visualization of syndesmophytes due to overlying shadows. Second, scoring systems based on plain radiograph are semi-quantitative, and therefore tend to be insensitive to change. Third, as mentioned earlier, it does not detect inflammatory changes. Three-dimensional imaging modalities may potentially address these issues.

MRI of the spine is considered the “gold standard” for visualizing inflammation. Similar to the changes seen in the sacroiliac joints, hyperintense signal on T2 fat saturated sequence or STIR sequence depicts inflammation in the spine (Fig. 10b). Structural changes, such as erosions, can be detected as well (Fig. 10a). Studies

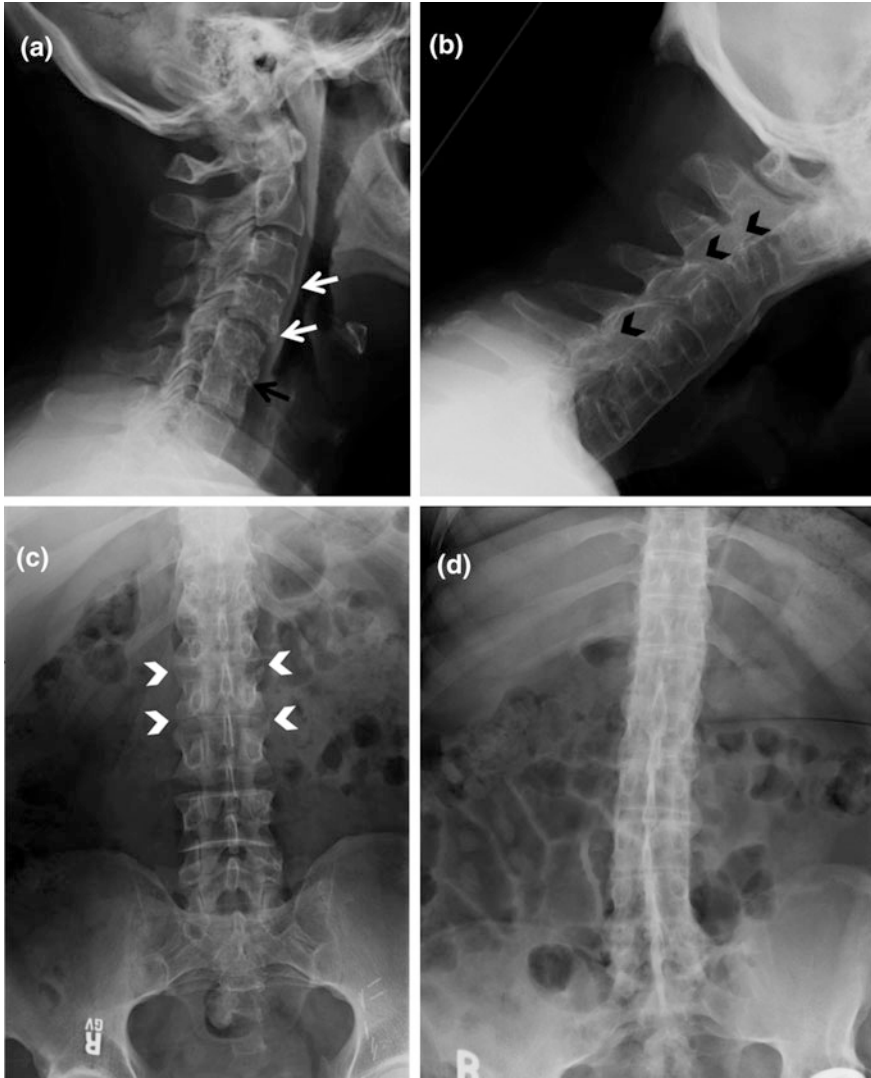


Fig. 9 Plain radiographs of the spine in patients with ankylosing spondylitis. **a** Lateral view of cervical spine. Syndesmophytes (*white arrows*) that projected vertically from the edge of the vertebral body. There is loss of intervertebral disk space (*black arrow*). **b** Lateral view of a completely fused cervical spine. Notice the 'bamboo' shape of vertebral column and complete loss of facet joints (*black arrowheads*). **c** Anteroposterior view of lumbar spine showing syndesmophytes (*white arrowheads*), some of which are almost bridging. **d** Anteroposterior view of a completely fused lumbar spine (*bamboo spine*). The linear vertical density in the center of the spine is formed by calcification of the ligaments between adjacent spinous processes

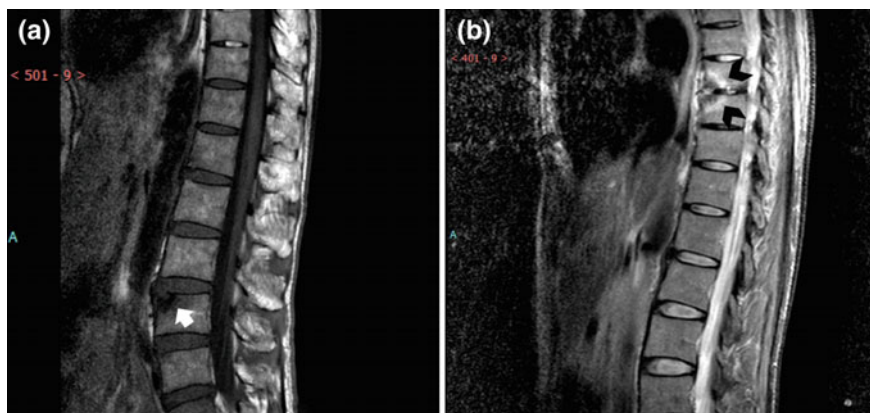


Fig. 10 Spine abnormalities on magnetic resonance imaging in a patient with ankylosing spondylitis. Sagittal view of lumbar spine. **a** Erosion of the anterior portion of a lumbar vertebral body (arrow) is shown as hypointense signal in T1 weighted image. **b** Erosions and osteitis (arrowheads) on adjacent vertebral bodies is shown as hyperintense signal on a STIR weighted image

have shown that anti-TNF therapy can decrease inflammation as detected by spinal MRI. Therefore, MRI scoring systems have been developed to assess the inflammatory signals and their changes with treatment [49]. It has also been reported that the combination of bone marrow edema and fatty deposits on MRI may predict the development of new syndesmophytes [50]. However, its utility for evaluating structural damage is still under investigation.

CT provides an accurate and sensitive assessment of changes of bony structures, so it is ideal to detect new bone formation. CT of the lower thoracic spine has been used to quantitate the volume of syndesmophytes and changes in their size over 2 years, and demonstrated good validity. Compared to MRI or plain radiograph, CT was more sensitive to change [51]. At this time, its application is limited to research due to its radiation exposure.

Spondyloarthritis associated with inflammatory bowel disease, also called enteropathic arthritis, develops in 20 % of patients who have Crohn's disease or ulcerative colitis, conditions that involve bowel inflammation. Many have spine involvement with the same Pathogenetic process of AS.

3.2 Psoriatic Arthritis

3.2.1 Definition and Occurrence

Psoriatic arthritis is a chronic inflammatory arthritis in patients with psoriasis that involves the spine and peripheral joints. In 60–80 % of cases, the skin rash of psoriasis precedes the development of arthritis; in 15 % patients, arthritis is the presenting symptom; occasionally, psoriasis and arthritis develop concurrently [52].

Prominent features in psoriatic arthritis are synovitis, enthesitis, erosions and new bone formation. Biopsies of the joint tissue revealed increased white blood cells and prominent blood vessels, and 47 % patients develop erosions in bones within 2 years of diagnosis [53]. Enthesitis and bone marrow edema on MRI demonstrate its similarity with other seronegative spondyloarthritis.

Psoriatic arthritis develops in 4–30 % patients with psoriasis [52, 54], with a prevalence of 0.1–0.2 % of the general population [54]. It affects men and women equally, most commonly developing in people aged 30–55 years.

3.2.2 Clinical Manifestations

Five clinical patterns have been described in psoriatic arthritis: asymmetric oligoarthritis, symmetric polyarthritis, distal interphalangeal (DIP) arthropathy, arthritis mutilans, and spondylitis with or without sacroiliitis [55]. Patients may have features of more than one pattern, and their presentations may change during the course of the disease.

Asymmetric oligoarthritis is the most common pattern, and involves inflammation in fewer than 5 joints. Large joints, such as knees or hips, are affected most often. The symmetric polyarticular pattern resembles rheumatoid arthritis, and mainly involves small joints such as fingers, hands and wrists. DIP arthropathy, affecting the finger joints closest to the nails, is a characteristic of psoriatic arthritis, being rarely seen in rheumatoid arthritis. Patients with peripheral joint involvement often complain pain and swelling of these joints, associated with morning stiffness. Synovitis, or inflammation of lining of the joint, is the underlying pathology. Arthritis mutilans is a rare destructive condition caused by absorption of the finger bones, and is also characteristic of psoriatic arthritis.

Spine involvement is less common than limb arthritis in psoriatic arthritis. Back pain, buttock pain, stiffness, and fatigue are the main complaints in these patients. Involvement of the sacroiliac joints is not always present in psoriatic arthritis, or may only affect the right or left side, as opposed to both sacroiliac joints in AS. Another commonly affected site is the cervical spine. As seen in rheumatoid arthritis, inflammation and erosions can cause atlantoaxial (C1–C2) subluxation, which can lead to cervical myelopathy.

Enthesitis is often present in patients with psoriatic arthritis. Patients may report pain and sometimes swelling at the heel or the bottom of the foot. A few features help to distinguish psoriatic arthritis from AS. Psoriatic skin and nail changes are seen in most patients, providing the major diagnostic clue. Sausage-shaped swelling of a finger or toe is a characteristic manifestation of psoriatic arthritis [56]. Ultrasound and MRI studies show that inflammation of the tendon sheath (tenosynovitis) is the cause of this type of finger or toe swelling.

Laboratory tests are non-diagnostic. Elevated blood markers of inflammation may be present [57]. As one of the seronegative spondyloarthritis, rheumatoid factor and anti-CCP antibody are often absent. HLA-B27 is present in some patients, particularly those with spine involvement.

3.2.3 Treatment

Treatment of psoriatic arthritis is varied because of the diversity of clinical presentations. For mild arthritis, NSAIDs are the first line treatment to control symptoms. For patients with peripheral arthritis affecting more than 3 joints, a disease modifying anti-rheumatic drug (DMARD) is often considered, such as leflunomide, sulfasalazine, cyclosporine, or methotrexate [58, 59]. Methotrexate is the first choice of many rheumatologists.

Anti-TNF agents have shown effectiveness in controlling acute inflammation and preventing bony erosions in psoriatic arthritis. Alefacept, a fusion protein targeting lymphocyte function antigen 3 (LFA3), and ustekinumab, an interleukin 12/23 inhibitor, are also effective.

Conventional DMARDs and newer biologics may have some effect on other manifestations, such as enthesitis and spondylitis. However, responses of these manifestations have not been well studied.

3.2.4 Imaging

Plain radiography remains the standard for diagnosing psoriatic arthritis and monitoring its progression. A characteristic finding of psoriatic arthritis is the co-existence of erosions and new bone formation, most prominent at the finger joints. Absorption and lysis of the finger bones may lead to typical ‘pencil-in-cup’ appearance on radiographs. Fusion of hand bones, fluffiness of the bony cortex, and calcification of entheses are evidence of new bone formation. The sacroiliac joints are occasionally involved in psoriatic arthritis, and erosion, sclerosis and ankylosis of these joints are common findings. Dynamic imaging of the cervical spine, with flexion and extension of the head, may reveal instability of the cervical spine. Spinal radiographs may depict syndesmophytes, which tend to originate from the mid-part of the vertebral body rather than the vertebral corner, and spine involvement is often discontinuous.

Radiographic progression of psoriatic arthritis is slow. Radiographic scoring systems have been adapted from rheumatoid arthritis but modified to include the distal interphalangeal joints, and are used to assess joint erosions and disease progression in clinical trials.

MRI has been used to assess enthesitis in psoriatic arthritis, and led to new understanding of its pathogenesis. Inflammation of the entheses and associated bone marrow edema are the most common MRI finding. It has been proposed to use MRI of the spine and sacroiliac joints as a more sensitive way to assess spinal involvement in psoriatic arthritis; however, at present, it is still limited to research settings.

Musculoskeletal ultrasound is a sensitive way to detect inflammation, and has been used to assess the response of tenosynovitis, synovitis, and enthesitis to treatment.

3.3 Reactive Arthritis

Reactive arthritis is a form of seronegative inflammatory arthritis that develops after an infection somewhere in the body outside of the joints. Some gastrointestinal and urinary infections are considered causal, including those due to the bacteria *Chlamydia trachomatis*, *Yersinia*, *Salmonella*, *Shigella*, *Campylobacter* [60], *Escherichia coli*, *Clostridium difficile* and *Chlamydia pneumonia* [61].

Reactive arthritis is uncommon, and affects men and women equally. Symptoms of arthritis develop several days or weeks after the initial infection [60]. A preceding infection is not always identified, even in patients with a typical presentation. Often, pain and swelling develops in a few joints, particularly in the knees or ankles. Enthesitis is not uncommon. Patients may have signs of eye inflammation, urinary symptoms, and skin rashes. In most patients, the arthritis subsides after 6 months, however, in a small proportion, it may become chronic.

Spine involvement usually manifests as inflammatory back pain. Twenty-five percent of patients develop radiographic changes of the sacroiliac joints, usually affecting only one side. Extensive spine fusion is very uncommon. Patients with spine involvement often have HLA-B27 [62].

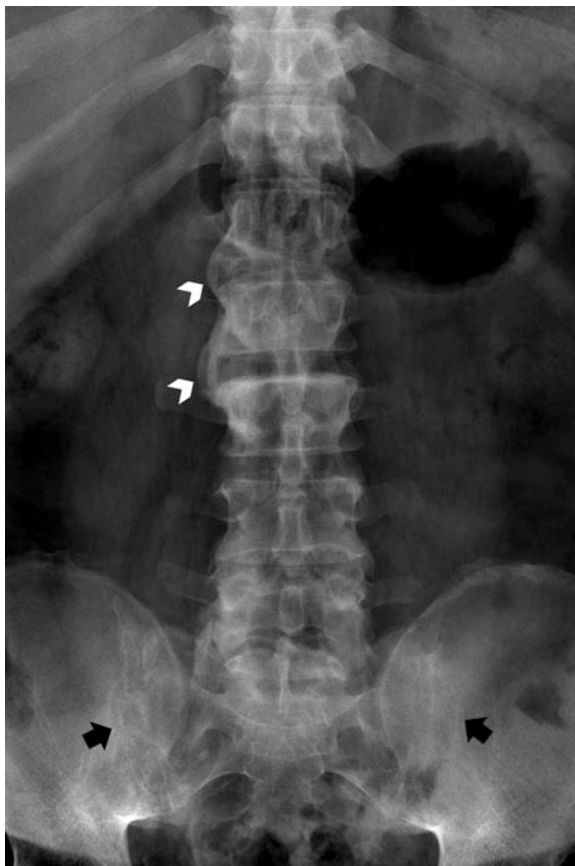
Treatment of reactive arthritis is mainly symptomatic. NSAIDs are used to control acute inflammation. Limited evidence supports the use of antibiotics when *Chlamydia* is the cause [63]. In chronic reactive arthritis, methotrexate, sulfasalazine, and biologics have been used with various responses.

In acute reactive arthritis, plain radiographs of the affected joints are mainly used to exclude other diagnoses. In patients with spinal involvement, radiographic changes of the sacroiliac joint can be seen after some duration of symptoms, with more severe changes on one side compared to the other. Syndesmophytes may develop that are often bulky, asymmetric and extend laterally [64] (Fig. 11). MRI of the spine and entheses is potentially useful for the assessment of inflammation and monitoring responses to treatment, but has not been evaluated extensively.

3.4 Undifferentiated Spondyloarthritis

Undifferentiated spondyloarthritis refers to spondyloarthritis that does not fulfill criteria for AS, psoriatic arthritis, reactive arthritis, or enteropathic spondyloarthritis [65]. Most patients are young men with inflammatory low back pain who may have HLA-B27. Some may have arthritis in peripheral joints or enthesitis. The major

Fig. 11 Plain radiograph of the lumbar spine in a patient with reactive arthritis. Notice the asymmetric distribution of the syndesmophytes (arrowheads), affected primarily the right side. This patient also has grade 3 changes in both sacroiliac joints (arrows)



difference between undifferentiated spondyloarthritis and AS is the presence or degree of the sacroiliac joint changes on plain radiography. In patients with undifferentiated spondyloarthritis, the sacroiliac joint changes are absent or very mild, and do not meet the radiographic requirement for AS. MRI of the sacroiliac joints in the undifferentiated patients may reveal active inflammatory lesions similar to those present in AS. Patients with undifferentiated spondyloarthritis may evolve into a more specific type of spondyloarthritis, with AS being the most common. Alternatively, these patients may persist without differentiating to a more defined disease, or it may resolve completely after several years [66].

3.5 Rheumatoid Arthritis

3.5.1 Definition and Occurrence

Rheumatoid arthritis (RA) is the most common type of inflammatory arthritis in adults, affecting 0.5–1 % of the population. RA typically begins in middle-age or old-age, and women are three times more likely to have RA than men. The cause of RA is unknown. There are a number of gene variations that are associated with an increased risk of RA, but RA is not strictly hereditary. Current theory holds that RA develops as a consequence of exposure to an environmental trigger in a genetically-susceptible person [67]. Whether the trigger is the same for all patients is unknown. Smoking has been identified as a risk factor for RA, and smokers who have particular variants of the HLA-DR gene are at greatly increased risk. For most patients, RA is a life-long disease. While there is currently no cure for RA, medications can improve and control symptoms, and remission is possible with treatment. A small proportion of patients may have their RA spontaneously go into remission.

RA is an autoimmune disease. Autoimmune diseases are a category of diseases characterized by immune reactions against the body's own tissues. While the primary roles of the immune system are to provide protection from infections and to seek and destroy cells that may progress to tumors, these immune responses become subverted in autoimmune diseases. In autoimmune diseases, the immune system senses certain normal proteins or cells as foreign or abnormal. In RA, the immune system generates inflammatory cells that target the lining tissue of the joint (synovium), the cartilage that caps the end of bones and forms the gliding surface of joints, and components of the immune system itself [68]. The immune system also begins to make antibodies against normal proteins, which can inactivate them. In RA, two of these so-called autoantibodies are commonly made. Rheumatoid factor is an antibody to immunoglobulins, which are proteins that provide immune protection against viruses and bacteria. Antibodies to citrullinated proteins bind specific proteins found in the connective tissue between cells. Both of these antibodies can be measured in clinical laboratories, and are used to aid in the diagnosis of RA. About 80 % of patients with RA have either rheumatoid factor or antibodies to citrullinated proteins detectable in their blood.

Inflammation develops as a consequence of these autoimmune reactions. In the joints, this inflammation causes joint swelling due to fluid accumulation in the joint space, infiltration of the synovium by white blood cells and expansion of blood vessels, and over time, proliferation of the synovial cells. Persistent inflammation can, over weeks to months, lead to loss of mineralization of the surrounding bone, wearing away of the joint cartilage, and eventually erosion of the bone surfaces at the margins of the joints. Persistent joint swelling can also stretch and weaken surrounding ligaments and tendons, resulting in shifting of the joints out of normal alignment. RA is therefore known as a deforming arthritis. This shifting places the joints at mechanical disadvantage, and which along with swelling, can cause weakness.

3.5.2 Clinical Manifestations

RA affects multiple joints simultaneously, with pain, stiffness, and swelling [69]. These symptoms in turn cause problems in using the joints to accomplish movements and tasks, such as walking or getting dressed. RA primarily affects peripheral joints, and less commonly the spine. Small joints of the fingers and hands, and wrists are affected in almost all patients. Knees, ankles, and small joints of the feet and toes are also commonly affected. While other joints are less commonly involved in RA, any synovial joint may be affected. Without treatment, the joint pain and swelling tends to persist and can last weeks or months. Even with treatment, symptoms may at times wax and wane, with “flares” of worsening joint inflammation occurring episodically. A feeling of stiffness, or restricted ease of movement, in and around the joints is common, particularly in the morning or after periods of inactivity. Fatigue is also common during periods of active inflammation, and joint pain may interfere with sleep. Patients often experience depression as a consequence of chronic pain and concern about their future health.

Chronic joint inflammation that leads to cartilage, bone, and ligament damage can result in joint deformities. Common deformities include fixed flexion of the fingers, sideways drifting of the fingers at the knuckles, and inward deviation of the knees and ankles. Muscle weakness may result from both these deformities and from disuse of painful joints. Loss of cartilage can also lead to limited range of motion of the joints, which in severe cases can fuse and become immobile.

The cervical spine is involved in up to 80 % of patients with RA, although symptoms related to the cervical spine may be present in less than one-half of patients [70]. Cervical spine problems are more common later in the course of RA than at the onset. The main symptoms are neck pain, headache at the back of the head, and less commonly, numbness of the arms, hands, or legs. Rarely, instability of the cervical spine as a result of inflammation can cause the vertebrae to impinge on nerve roots or even the spinal cord, causing radiculopathy or myelopathy. Depending on the location of the impingement, serious neurological complications may occur. If the spinal cord is impinged, paralysis may result. If the brainstem is impinged, sudden death may occur. These problems may be provoked by movements that flex or extend the neck, and so raise particular concerns about whiplash injuries in automobile accidents. Inadvertent injuries may also occur during the placement of breathing tubes prior to general anesthesia, which requires the head and neck to be extended. Impingement of major blood vessels at the base of the skull may also occur and cause dizziness, weakness, and vision changes. The Ranawat classification system is commonly used to grade the degree of neurological damage in patients with RA-related cervical spine disease. Class I indicates no neurological deficits. Class II indicates subjective weakness and numbness. Class IIIA represents objective weakness and signs of spinal cord compression but with preserved ability to walk, while Class IIIB represents weakness and signs of cord compression with inability to walk.

Three types of cervical spine involvement are commonly recognized, which are distinguished by the specific areas of the cervical spine that are involved: atlanto-axial

subluxation, atlanto-axial impaction, and subaxial subluxation. Atlanto-axial subluxation is the separation of joint between the atlantis (the common name of C1, the first cervical vertebra) and the axis (the common name of C2, the second cervical vertebra). Inflammation of this joint leads to loosening of the surrounding ligaments, which can permit a dynamic separation of this joint with flexion of the head. With extensive subluxation, the superior part of C2 (known as the dens) can compress the spinal cord when the head is flexed. Atlanto-axial impaction results when bone and cartilage loss between the base of the skull and C1, and between C1 and C2, leads to the superior migration of C2 relative to the skull. In severe cases, part of C2 can penetrate the spinal cord opening at the base of the skull and compress the brainstem. Because the brainstem controls vital functions such as respiration, compression may result in death. Subaxial subluxation is the malalignment of vertebrae below C2, due to chronic erosive joint inflammation and ligament instability. Atlanto-axial subluxation is the most common cervical spine abnormality, occurring in up to 50 %. Atlanto-axial impaction occurs in up to 40 %, while subaxial subluxation occurs in 10–20 %. The thoracic spine and lumbar spine are typically not affected by RA.

Although RA primarily affects the joints, other parts of the body may be affected by inflammation due to RA, including the lungs or lung linings, the heart lining, the outer surface of the eye, and blood-forming elements in the bone marrow. Vasculitis, or inflammation of the blood vessels, may also occur.

The diagnosis of RA is based on a compatible clinical presentation, inflammation in many small joints on both the right and left sides, and the presence of autoantibodies (either rheumatoid factor or antibodies to citrullinated proteins). Blood tests indicating systemic inflammation, such as the C-reactive protein level, are also often elevated. Radiographs that show bone erosions in typical locations can also be helpful, but because these lesions take time to develop, they are often not present at the start of symptoms.

3.5.3 Treatment

The goal of RA treatment is prompt and complete control of joint inflammation, which will lessen symptoms, improve quality of life, and decrease the likelihood of chronic joint damage and associated disability [71]. Medications therefore occupy the central focus in RA treatment. While analgesics and NSAIDs such as naproxen and ibuprofen can help lessen joint pain, they provide only temporary symptom benefit. Corticosteroids can also be beneficial in controlling joint inflammation, but side effects preclude their chronic use. Appropriate treatment requires the long-term use of one or more “disease-modifying” medications, which over time provide for more sustained control of inflammation and the potential to decrease the development of joint damage [72]. Methotrexate, taken weekly in low doses, is the most commonly used disease-modifying medication, based on evidence of sustained efficacy and generally good tolerability. Hydroxychloroquine, sulfasalazine, and leflunomide are other disease-modifying medications that can be used alone or in

conjunction with methotrexate. Biologic medications, which are antibodies developed to block key mediators of inflammation such as tumor necrosis factor-alpha or interleukin-6, are also effective in controlling inflammation and slowing joint damage. Biologics are often added when conventional disease-modifying medications have proven to be insufficient at controlling joint pain and swelling. For most patients, treatment is needed for years or decades, although slow tapering of medications is often possible as the inflammation comes under control.

Physical therapy and occupational therapy can help improve joint function and range of motion. Joint replacement surgery or joint fusion surgery is indicated when dysfunction or persistent pain of damaged joints limits the patient's ability to do daily activities. These surgeries are very effective in relieving pain and restoring functional ability. Treatment of cervical spine involvement includes traction to help relieve pressure on the impinged nerves or spinal cord, surgery to decompress the area by removing excess synovial tissue, and surgical fusion of the vertebrae to stabilize regions of subluxation. Cervical spine surgery is often effective in providing at least partial pain relief and preventing worsening of the neurological problems. However, existing neurological damage may not reverse with surgery. Recovery from quadriplegia is uncommon and the survival of these patients is low [73].

3.5.4 Imaging

Plain radiographs of peripheral joints are very useful in the diagnosis of RA, as well as helping to distinguish other types of arthritis that may have clinical features that mimic RA [74]. In early RA, radiographs may be normal or show only prominent shadows of the joint linings or excess joint fluid. Osteopenia next to the joints may also be visible. Tell-tale bone erosions at the margins of the joints are the most specific radiographic sign of RA, and occur in up to 60 % of patients. Radiographs can also demonstrate joint space narrowing due to cartilage loss, bony fusion, and bone malalignment or subluxations. In the cervical spine, radiographs can adequately show each of the three main types of involvement, although films taken with both neck flexion and extension may be needed to reveal dynamic atlanto-axial subluxation (Fig. 12). Radiographs are useful in planning surgical approaches and evaluating the results of surgical corrections. Development of new bone erosions and progressive joint space narrowing on radiographs is used in clinical trials to test the efficacy of medications and in clinical practice to monitor patient's responses to medications.

Diagnostic ultrasound has been increasingly used to detect thickening of the joint linings and other signs of joint inflammation, such as enhanced Power Doppler signals, which may help in diagnosis [75]. Improvement or resolution of these features can also be used to assess remission and response to treatment. Erosions of bone are also visible on ultrasound, but the time needed for examination may limit its use for assessing progression of erosions. Ultrasound can also be used to guide the injection of medications into a joint.

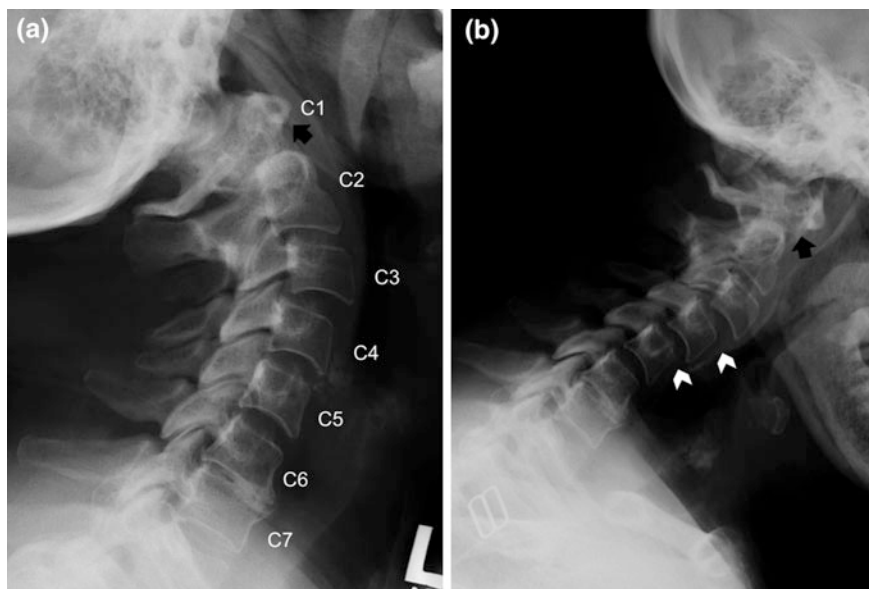


Fig. 12 Plain radiographs of the cervical spine showing atlanto-axial subluxation and subaxial subluxation in a patient with rheumatoid arthritis. The lateral views of the cervical spine were taken with neck extension (a) and flexion (b). In the flexion position, a separation of anterior arch of C1 from the dens of C2 (arrow) is revealed. This is not observed in the extension position (arrow), indicating the presence of dynamic atlantoaxial subluxation. Subaxial subluxation (arrowheads) is also present at C3–C4 and C4–C5

MRI can also demonstrate synovial thickening and excess joint fluid related to RA, as well as bone erosions. In addition, bone marrow edema on MRI may indicate inflammation not otherwise appreciated. However because of its expense and the fact that most information can be obtained by other modalities, MRI is not often used in clinical practice for imaging the peripheral joints in RA. However, MRI is valuable in imaging the cervical spine, particularly in detailing areas of spinal cord or nerve root compression. Computed tomography is not often used, because the necessary structural information can in most instances be obtained by radiography or MRI.

3.6 Juvenile Idiopathic Arthritis

Juvenile idiopathic arthritis is the most common type of arthritis in children, but is rare, affecting 10,000–60,000 children in the United States. Among several subtypes, three are most common: pauci-articular, polyarticular, and systemic-onset subtypes. The pauci-articular subtype, which typically affects girls under the age of 5, presents with inflammation in 4 or fewer joints, most often the knees, ankles, or

elbows. Over time, the arthritis tends to resolve, although in some patients, it may persist and affect additional joints. The polyarticular subtype affects older girls, involves 5 or more joints at onset, and mimics adult RA. Patients with the systemic-onset subtype have not only arthritis but fever, skin rashes, blood cell abnormalities, and liver inflammation. Treatment of juvenile idiopathic arthritis generally follows that of adult RA.

Cervical spine inflammation occurs in up to 70 % of patients with juvenile idiopathic arthritis, and affects patients with each subtype. Neck pain and limited range of motion are the most common associated symptoms. While atlanto-axial subluxation and subaxial subluxation occur, the most common cervical spine abnormality in juvenile idiopathic arthritis is fusion of the facet joints [76]. This fusion often extends for the entire length of the cervical spine, with consequent inability to freely move the head and neck.

Radiographs are useful to detect cervical spine involvement, and MRI may be helpful to identify areas of potential neurological impingement.

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