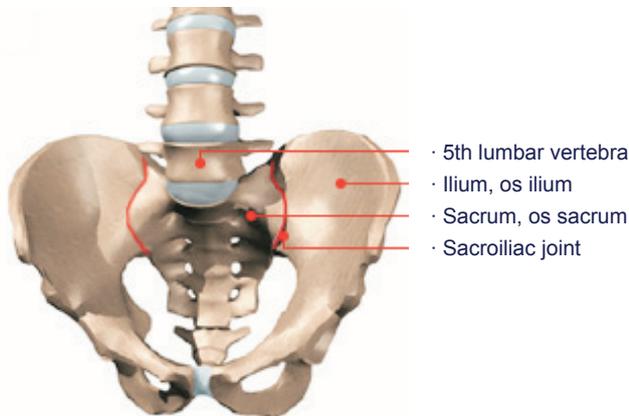


What is ankylosing spondylitis?

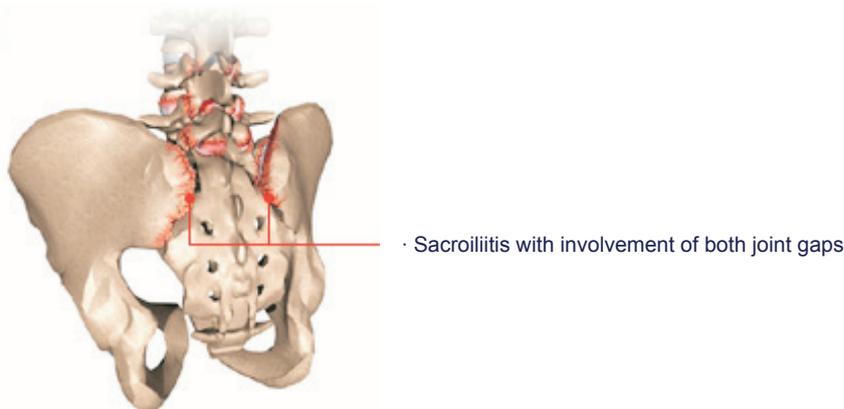
Ankylosing spondylitis is a chronic inflammatory rheumatic disease from the group of seronegative spondylarthropathies. It has an intermittent course, usually with onset in the sacroiliac joints (joints of the sacrum and ilium). In the spinal column, the disease causes ascending destructive inflammatory changes in the vertebral joints, affecting entire sections of the spine. The longitudinal structures of the ligamentous apparatus of the spinal column are also calcified, resulting in ascending ankylosis (rigidification) of the spine.

Men are affected more frequently than women, with onset in most patients between the ages of 15 and 40. Inflammatory changes are also frequently found in joints in the extremities, as are inflammatory irritations of the bony insertions of tendons, ligaments and joint capsule (enthesiopathies). Eye and heart involvement is also common.

- Pelvis and lumbar spine from the front, sacroiliac joints, connection of ilium and sacrum properly developed



- Pelvis and lumbar spine from the rear, sacroiliitis with pronounced inflammatory changes and deposition of syndesmophytes



How does this disease develop?

The initial cause of the inflammatory processes is still unknown, though studies have shown that 95% of the patients with this disease exhibit the human leukocyte antigen B27 (HLA-B27), supporting the conclusion that genetics play a role in its pathogenesis.

HLA antigens are immunoglobulins located in the cell membranes. They play a central role in the human immune system, because they can differentiate between the body's own proteins and foreign proteins and can therefore send signals to the immune system as to which foreign substances (antigens) have to be attacked and destroyed.

Patients with ankylosing spondylitis frequently also suffer from infections of the gastrointestinal and urogenital tracts caused by Klebsiellae – nonmotile, encapsulated bacteria that can cause pneumonia, meningitis, and blood poisoning (sepsis), in addition to other infections.

Klebsiellae possess microbial O and K antigens, foreign proteins that induce the production of antibodies (immune defense substances) in the human organism.

These facts lead to the supposition that a potential cause of the disease could be a cross-reaction between the body's own and bacterial antigens in the immune systems of HLA-B27-positive patients suffering from Klebsiellae infections. This initiates an autoimmune process in which the body's own immune system attacks and damages healthy structures such as the vertebral joints and vertebral bodies.

What examinations are done?

1. Rheumatological case history

A review of a specifically rheumatological medical history can provide valuable information as a basis for an initial tentative diagnosis with a few specific questions:

- Where is the source of the pain?
 - In the joints?
 - In soft tissues?
 - In the spinal column?
- How has the disease developed over time?
 - Acute start or gradual worsening?
 - Intermittent episodes with phases of remission and worsening?
 - Does the pain exhibit a typical pattern over the day?
- Is there a specific pattern of affected joints?
 - Are large or small joints more typically affected?
 - Is only one joint affected, or several?
 - Do the symptoms move from one joint to another?
- Since rheumatic conditions also frequently affect organ systems, it makes sense to note any abnormalities in the following areas:
 - Kidneys and efferent urinary tract (cystourethral inflammations, balanitis, previous STDs)?
 - Gastrointestinal tract (diarrhea, admixture of blood)?
 - Cardiovascular system
 - Lungs

- Skin (psoriasis, nodular changes, swellings, ulcers)?
- Eye symptoms (burning, vision problems, foreign-body sensation, dryness, redness)?
- Fever (bouts of fever, chills)?
- Neurological symptoms

2. Physical examination

- Inspection

Every physical examination should cover all organ systems.

We will limit our focus in what follows to the most important clinical examinations in cases of suspected rheumatic disease.

- Skeletal malpositions, asymmetries or deformities?
- Normal leg axes?
- Joints (mobility, joint effusions, redness, swelling?)
- Muscles (too little/too much, (=atrophy/hypertrophy), normal strength development?)
- Normal posture and movement?
- Skin and mucosa (skin changes, psoriasis, nodular changes, fluid accumulation)?

- Palpation

- Muscles: muscle tone (tonus) raised or reduced, myogeloses (hardened muscles), trigger points (pressure points from where a spreading pain can be induced)?
- Pain induction (pressure, percussion, tension, compression pain)?
- Pain induction around the insertions of tendons, ligaments and joint capsules (enthesopathy)?
- Tendons and bursae (inflammatory changes)?
- Joints (effusion, mobility, capsule thickening, grating noises)?
- Thorax (respiratory movements normal, can compression pain be stimulated)?

- Functional tests - specific spinal column functional tests:

- Active and passive mobility tests of the spinal column (flexion, extension, stretching, lateral inclination)
- Finger-floor distance (measurement of overall spinal mobility)
- Schober's sign (measurement of mobility of the lumbar spine)
- Ott's sign (measurement of mobility of the thoracic spine)
- Occiput-wall distance (measurement of extent of thoracic kyphosis)
- Chin-sternum distance (measurement of cervical spine mobility)
- Tests for sacroiliac joint involvement:
 - Three-phase test
 - Forward flexion phenomenon
 - Mennell's sign

- Other functional tests include:

- Measurement of joint mobility with the neutral zero method
- Measurement of crude strength in arms and legs
- Joint stability testing

3. Instrumental diagnostics

- Conventional x-rays

Since the onset of ankylosing spondylitis usually manifests in the sacroiliac joints, the first radiological changes appear here in the form of blurred joint contours, erosive bony defects and bone densification (sclerotization) in the vicinity of the joints. In advanced stages of the disease, the ossification (ankylosing) of the joint becomes visible.

As the disease progresses further, bony bridge elements (syndesmophytes) that connect the individual vertebra can be seen in all vertebral segments, further stiffening the spinal column. The ankylosed spinal column is often referred to as a “bamboo spine” in the advanced stage.

- Pelvis and lumbar spine showing slight degenerative changes



- Sacroiliitis with ossification of the sacroiliac joints, lumbar spine ankylosed - “bamboo spine”



X-rays can also reveal additional destructive inflammatory changes that result from the transformation of the vertebrae by spondylodiscitis (inflammation of vertebra and disc) and ossification of the ligamentous structures of the spinal column.

- Andersson's lesions (defects in the vertebral endplates, sign of spondylodiscitis)
- Romanus lesions, sign of anterior spondylitis
- “Shining corners” at anterior vertebral margins caused by sclerosing
- Ossification of the vertebral joints and costovertebral articulations

- Vertebral body deformations (box and barrel-shaped vertebrae)
- Signs of segmental instability: With the increasing stiffening of vertebral segments interrupted by segments that are not yet stiffened, signs of degeneration and instability such as combined rotation and slippage of vertebrae, pseudospondylolisthesis (forward slippage of vertebrae), and osteochondrosis are discernable
- Sagittal images of the cervical spine reveal instabilities of the upper cervical spine (atlantoaxial instability).

· **Magnetic resonance tomography (MRT) and computer tomography (CT)**

With these technologies, clear images can be obtained of the bony changes in the sacroiliac joints and adjacent soft tissues.

In the spinal column, edemas or cysts (accumulations of fluid), bony necroses (areas of destroyed bone tissue), the spinal cord, and soft tissues can be readily evaluated.

· **Skeletal scintigraphy**

In the early stages of the disease, this method can be used to confirm a diagnosis of ankylosing spondylitis, but only in combination with the clinical and conventional radiological findings.

4. Laboratory diagnostics

- Detection of HLA-B27 antigens
- White blood cell (leukocyte) count, blood sedimentation rate and measurement of C-reactive protein as signs of an inflammation.
- Rheumatoid factor is always negative ("seronegative spondyloarthritis")

What criteria are used to confirm a tentative diagnosis of ankylosing spondylitis?

Due to the varying course and appearance of this disease, and the similarity of its symptoms to those of other diseases, it is difficult to define a definitive evaluation scheme that would allow for the reliable diagnosis of the disease. Therefore, different criteria and grades that can be found in all individual findings, in some cases with point scales, facilitate diagnosis.

1. Grading of sacroiliitis

Grade 0: Normal findings

Grade 1: Joint gap blurred with a low level of sclerotization

Grade 2: Erosions, pronounced sclerotization, joint gap irregular and widened

Grade 4: Erosions, joint gap narrowed, joint gap partially or completely ankylosed (ossified)

2. Criteria for inflammatory low back pain

- Gradual onset of disease before age 40
- Pain persists for at least 3 months
- Morning stiffness
- Improvement of symptoms

3. Criteria for early diagnosis of ankylosing spondylitis

- HLA-B27 antigen positive, blood sedimentation rate elevated
- Positive clinical signs from examination of sacroiliac joints
- Restricted mobility of cervical and lumbar spine
- Spontaneous and pressure pain in bony thorax
- Respiratory movements of ribcage restricted

- Signs of joint involvement or enthesiopathies
- Eye symptoms (iritis, iridocyclitis) (iris inflammations)

4. New York criteria, which can first be sensibly applied when the disease has persisted for some time, since the radiological changes in the sacroiliac joints develop over the course of the disease (between 2nd and 10th year of disease).

Clinical criteria:

- Lumbar spine mobility highly restricted
- Acute or early pains in lumbar spine and at lumbosacral transition
- Limitation of chest expansion to the level of 4th intercostal space

According to these criteria, a definite ankylosing spondylitis exists in the presence of a combination of bilateral grade 3 or 4 sacroiliitis together with one of the clinical criteria, a bilateral grade 2 sacroiliitis with clinical criterion 1, or a unilateral grade 3 or 4 sacroiliitis with clinical criteria 2 and 3

What are the symptoms of ankylosing spondylitis?

- Spinal column, thorax and pelvis
 - Sacroiliitis with low back pains
 - Inflammatory back pain
 - Vertebral deformation
 - Deformation and stiffening of the spinal column (bamboo spine)
 - Calcification, mainly of the longitudinal ligamentous structures of the spine
 - Postural changes over the course of the disease due to increasing stiffening of the spinal column: the lumbar spine flattens and the thoracic spine bends to form a hump
 - Reactive osteoporosis (bone atrophy) due to immobility
 - Vertebral fractures

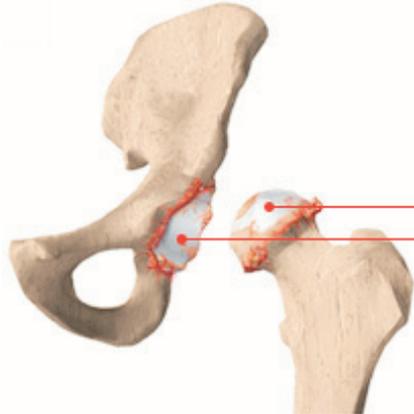
Due to the loss of elasticity and mobility of the spinal column, even slight accident-related traumas may result in vertebral fractures in advanced stages, mainly around the cervicothoracic transition (neck-chest region) and thoracolumbar transition (chest-lower back region). These vertebral fractures are caused by the combination of the existing pathological factors of osteoporosis, lack of elasticity, and the partial stiffening of vertebral segments because the spinal column has lost the capacity to dampen and transmit the forces acting on it. The resulting compression or luxation fractures may lead to neurological dysfunctions or even quadriplegia.

- Spinal column instability in the region of the head-to-cervical spine transition (occipitocervical instability), (atlantoaxial instability)
 - Limitation of thoracic respiration due to ossification and stiffening of costovertebral articulations and rib-sternum connections. In combination with a kyphotic deformation of the thoracic spine ("humpback"), this can lead to pronounced respiratory difficulties.
- Peripheral joints
 - Frequently affecting the major joints knees, hips and shoulders, with painful restriction of movements.

- Normal hip joint

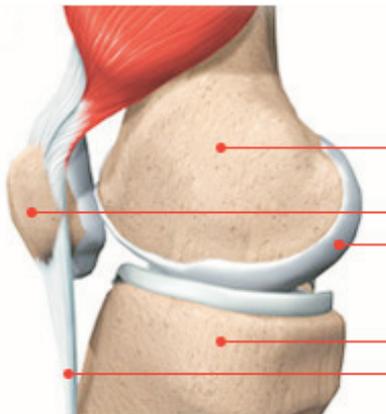


- Hip joint arthrosis with destructive changes in condyle and acetabulum



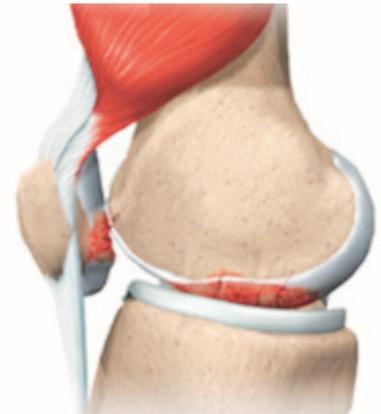
- Cartilage destruction of head (condyle) of femur
- Cartilage destruction of acetabulum

- Knee from the side, normal findings



- Femoral condyles (thigh)
- Kneecap
- Joint cartilage
- Shin bone condyle
- Patellar tendon

- Knee from the side, arthrosis of dorsal surface of kneecap and femoral condyle

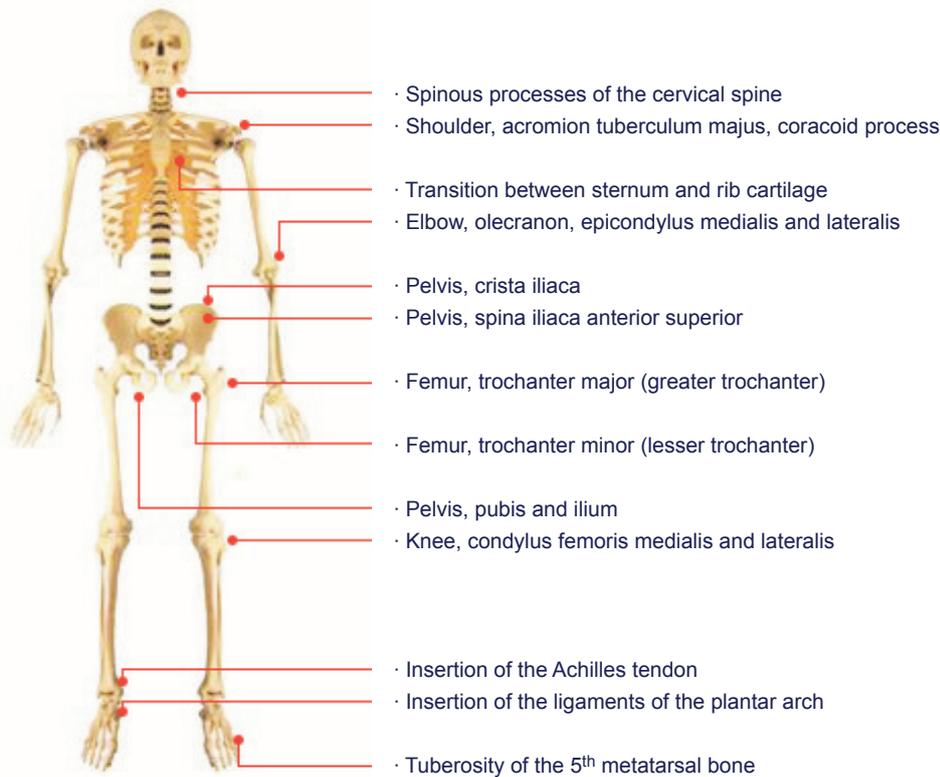


- More rarely: involvement of finger and toe joints, elbow and ankle joints

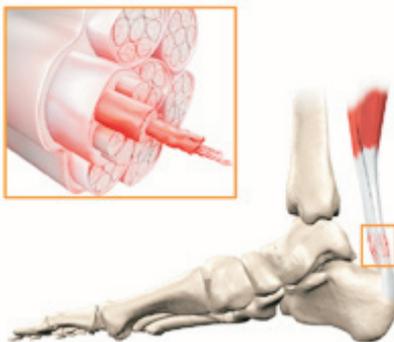
· Enthesiopathies

· With pain and inflammation around tendon and ligament insertions. Here are the most frequent patterns of distribution:

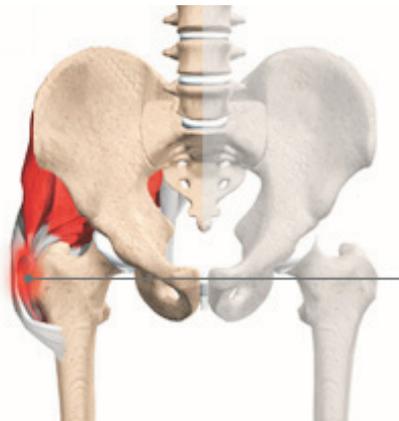
• Localization of enthesiopathies



• Enthesopathy of the Achilles tendon (irritation of tendon insertion)



- Enthesopathy in the area of the greater trochanter at the femur with irritation of the bursa



· Bursitis (subtrochanteric bursitis)

- Other manifestations in organs
 - Cardiac involvement with aortic valve defect (aortic insufficiency), inflammation of the aorta (aortitis), cardiac dysrhythmias and pericarditis.
 - Pulmonary involvement with cystic pulmonary fibrosis
 - Eye involvement with inflammation of anterior chamber of the eye and iris (iridocyclitis)
 - Renal involvement with nephritis and secondary amyloidosis
 - Neurological involvement in advanced stages of disease with spinal cord compression and cauda equina syndrome.

What is the typical course of this disease?

The course of this disease is difficult to predict because of the many different variants. Normally, the disease has an intermittent course for a number of years, but it may also quickly lead to stiffening of the spine with pronounced inflammatory reactions in rare cases. In some cases, only the sacroiliitis manifests without any other major symptoms. Another factor that renders assessment difficult is that an exact diagnosis is often not possible until the disease has persisted for a number of years, since radiological signs of sacroiliitis may not manifest for a number of years.

The inflammation of the sacroiliac joints that occurs initially results in instability, straightening up the pelvis. This static change initiates a “compensatory chain reaction” over the course of the disease. The upright position of the pelvis flattens the curvature of the lumbar spine and the physiological lordosis disappears. The body's center of gravity is shifted in front of the body's central axis, resulting in a compensatory increase in thoracic kyphosis, resulting in a hump, which in turn further increases the thoracic kyphosis with the increasing flaccidity of the back extensor muscles and the shifting of the center of gravity toward the front. In this position, the head and eyes are pointed at the floor, which results a compensatory increase in cervical spine lordosis.

The straightening up of the pelvis overextends the hip joints, which is then compensated by increased flexing of the knee joints. The malposition of the hip and knee joints results in flexion contraction that increases the overall deformation of the spinal column.

Together with the deformity of the thorax, the inflammatory ossification of the sternocostal joints and costovertebral joints results in reparatory problems.

How is ankylosing spondylitis treated?

There is no therapy available to cure this disease.

Conservative therapy is based on a combination of the following therapeutic methods:

- Medical drug treatment
 - Antiphlogistic
 - With NSAR (non-steroid antirheumatics)
 - With corticoids, which cannot be used as long-term medications due to their side effects
 - TNF-alpha blocker (tumor necrosis factor alpha), a new group of medicines that block TNF-alpha, a cytokine that exhibits elevated levels in rheumatic diseases, including ankylosing spondylitis, and which presumably plays a major role in inflammatory joint destruction
 - Injection of the radioactive isotope radium 224 can have a beneficial effect on the inflammatory processes
 - Analgesics
 - Muscle relaxants
 - Treatment with long-term "disease-modifying antirheumatic drugs" (DMARD), e.g. sulfalazine or methotrexate can be used in cases characterized by severe effects in the large joints. Their use is controversial in cases where only the spinal column is affected.
- Active and passive kinesitherapy

Kinesitherapy (motion therapy) must be done regularly and intensively in the form of appropriate exercises, postural and movement training, compensation for existing muscular imbalances, respiratory and endurance training to preserve and improve spinal column and joint mobility.
- Physical therapy with irradiation, massages, electrotherapy, cold and heat applications, etc. helps loosen the muscle and reduce inflammations.
- Other possible treatment methods include homeopathy, phytotherapy, traditional Chinese medicine, neurotherapeutic psychological support with relaxation techniques.
- Surgical therapy of ankylosing spondylitis may be required to treat:
 - Massive deformities of the spinal column:

If the pathological curvatures of the spine are so pronounced that the space available to inner organs such as the lungs is restricted, and the quality of life is greatly reduced due to the bent-over posture, corrective osteotomies can be carried out to reposition the spine.
 - Massive instability of spinal segments:

In cases in which the spine is partially ankylosed, with intervening vertebral segments that are not yet ankylosed, these segments may become unstable.

The destabilized segments are then often surgically rigidified (spondylodesis)
 - In the case of vertebral fractures, surgical stabilization of the fracture is normally achieved by means of dorsoventral methods (access from back and abdomen).
 - If large joints are affected, accompanied by inflammatory destruction, surgical implantation of artificial hip or knee joints may be indicated.

A number of different surgical approaches are used for the corrective repositioning of the spinal column when treating instabilities. The following surgical methods are frequently applied in our department, depending on the specific indications in each individual case:

- Predominant lumbar kyphosis:
 - Pedicle subtraction osteotomy with extensive instrumentation
 - Multisegmental osteotomy acc. to Smith-Peterson (chevron osteotomy) with extensive pedicle instrumentation
- Thoracic kyphosis:
 - Complete vertebral body resection with straightening spondylodesis
- Thoracocervical manifestation:
 - Thoracocervical straightening spondylodesis with pedicle subtraction at TH1
- Upper cervical manifestation:
 - C1/C2 fusion using the Harms technique