Ankylosing Spondylitis

Self study materials for students.
5th year, Internal Medicine, 2nd semester
Topic 6. Ankylosing spondylitis.

6th year, Internal Medicine, Rheumatology circle
Topic 4. Management of patients with back pain and joint syndrome.
Definition

- **Ankylosing spondylitis (AS)** – is a chronic systemic inflammatory disease of the axial skeleton, with variable involvement of peripheral joints and nonarticular structures.

- AS is one of the **seronegative spondyloarthropathies** and has a strong genetic predisposition. It mainly affects joints in the **spine** and the **sacroiliac joint** in the pelvis.

- In severe cases, complete **fusion and rigidity of the spine** can occur.
Synonyms

- Bekhterev (Bechterew’s) disease
- Marie-Strümpell disease
- Bekhterev-Marie-Strümpell disease
What is ankylosing spondylitis?

https://www.youtube.com/watch?v=zXYwMMxqxhs
Epidemiology

- The prevalence ranges from 0.1 to 1% of the population
- Men are affected 3 times more than women
- Commonly develops between the ages of 15 and 40
- Predominant in Caucasians worldwide

Etiology

- Etiology is unknown, but probable etiologic factors are:
  - Genetic predisposition - % of people with AS share the genetic marker HLA-B27
  - Bacterias - Klebsiella pneumoniae and some other Enterobacteriases.
• **Human Leukocyte Antigen (HLA) B27** is a surface antigen encoded by the B locus in the major histocompatibility complex (MHC) on chromosome 6 and presents antigenic peptides to T cells.
• It lies on the surface of WBC.
• HLA-B27 is strongly associated with ankylosing spondylitis, and other associated inflammatory diseases referred to as "spondyloarthropathies".
• More than 100 disease associations have been made, including many ocular diseases and systemic diseases with specific ocular manifestations.
HLA B27

Associated pathologies:

• Ankylosing spondylitis
• Juvenile rheumatoid arthritis (JRA)
• Arthritis related to Crohn's disease or ulcerative colitis
• Psoriatic arthritis
• Reactive arthritis (Reiter's syndrome)
• Uveitis
**HLA B27**

- **HLA-B27 Typing** is a laboratory **immunogenetic PCR blood test** that determines the presence or absence of the HLA B27 alleles.
- Venous blood is been tested.
- Patient shouldn’t smoke for 1 hour before blood collecting.
- Price: Ukraine 6-30 USD, USA 200 USD, India 17-60 USD.
- **Indications:** differential diagnostics of systemic diseases. Most valuable in case of validating ankylosing spondylitis and reactive arthritis, making out it’s prognosis.

- **NB!!!** It’s an **additional** test which helps to validate Ds of AS. **It’s not the main and only investigation!!!**
- **NB!!!** This test is negative in about 10% of patients with AS.

The **Enterobacteriaceae** are a large family of **Gram-negative bacteria** that includes, along with many harmless symbionts, many of the more familiar pathogens, such as:

- *Salmonella*
- *Escherichia coli*
- *Yersinia pestis*
- *Klebsiella pneumoniae*
There are 2 theories:

- **Receptors theory** – HLA B27 is a receptor for etiologic factor (bacteria, virus, etc.). The resulting complex provokes production of cytotoxic T-cells which cause damage to cells with HLA B27 molecule. **So, urinary or bowel infection can be a trigger for AS.**

- **Molecular mimicry theory** – bacterial antigen (or other damaging factor) in complex with other HLA molecule gets similar to HLA B27 properties and is been recognized by cytotoxic T-cells as HLA B27 or decreases the immune reaction at pathologic peptide (immunological tolerance).
In both cases **autoimmune inflammatory process** is a result. It has features:

- Usually starts with affection of **sacroiliac joints**, then **intervertebral and costovertebral joints** are involved (rarely – peripheral joints).
- Characterized by active **fibrosis** with further **ossification and calcification**, and **ankylosis** as result.
Pathomorphology

- **Enthesitis** - the site of ligamentous attachment to bone is the primary site of pathology. The early lesions consist of subchondral granulation tissue, infiltrates of lymphocytes and macrophages in ligamentous and periosteal zones, and subchondral bone marrow edema.

- **Synovitis** - may progress to pannus formation with islands of new bone formation.

- **Ostitis** – with fibrosis and ossification.

- **Ankylosis**
Pathomorphology

Normal spine

Early ankylosing spondylitis

Advanced ankylosing spondylitis

Inflammation

Fusion
Sites of affection

- Sacroiliac joints
- Intervertebral joints
- Costovertebral joints
- Brachial (shoulder) joints
- Coxofemoral (hip) joints
- Knee joints
- Ankle joints
- Small joints of hands

Symptoms (early AS)

1. Pain in sacroiliac and lower back regions:
   - permanent; dull
   - worsens in rest; in the morning; nocturnal
   - reliefs in motion; in the afternoon

2. Buttock pain:
   - irradiates into posterior surface of hip
   - migrates from left to right gluteus
3. Lower back stiffness:
   • in the morning, for $\geq 30$ minutes
   • reliefs after activity, warm shower

4. Chest pain:
   • mimicries intercostal neuralgia and intercostal muscles myositis
   • worsens in coughing, sneezing, deep breathing
5. Stiffness and tenderness of back muscles.

6. Flattening of lumbar lordosis

7. Bilateral sacroilitis.
Symptoms (early AS)

8. **Enthesopathies** – pain in the site of ligamentous attachment to bone:
   - iliac crests
   - trochanters
   - spinous processes of vertebrae
   - costovertebral joints

9. **Extra-articular manifestations** – usually eyes affection (*anterior uveitis*); bilateral, acute onset, lasts for 2-3 months, registered in 30% of patients.
Symptoms (advanced AS)

1. Pain in different segments of spine.
2. Question mark posture
3. Atrophy of back muscles.
4. Decreased thorax excursion.
5. Decreased articulations in spine.
6. Ankylosis of sacroiliac and intervertebral joints.
7. Cutaneous lesions – that are identical to pustular psoriasis
8. Cardiovascular system involvement:
   • aortitis
   • aortic insufficiency
   • pericarditis, myocarditis


10. Urinary system involvement
    • amyloidosis
    • IgA-nephropathy

11. Gastrointestinal system involvement
    • ulcerative colitis
    • Crohn’s disease
Question mark posture, or suppliant posture - loss of lumbar lordosis, fixed kyphosis, compensated extension cervical spine, protruberant abdomen.
Question mark posture

Extra articular manifestations

- **Ocular** (anterior uveitis)
- **Cardiovascular** (aortitis, myocarditis, AV-block)
- **Gastrointestinal** (colitis, enteritis)
- **Cutaneous** (pustular psoriasis)
- **Pulmonary** (fibrosis)
- **Renal** (amyloidosis)

Ocular manifestations

- **Anterior uveitis (iritis, iridocyclitis)** – is an inflammation of the front part of the eye, between the cornea and the lens.
- Appears in 20-30% of patients with AS.
- **Symptoms**: eye pain, sensitivity to light, eye redness, blurred vision, spots in field of vision.
- Usually resolves within 2–3 months without residual visual impairment.
- **Complications**: hypopion, synechiae, cataract and glaucoma.
- **Treatment**: steroid, antibiotic and miotic eye drops, usage of sunglasses.

Cardiovascular manifestations

• May include:
  1. Aortitis
  2. Aortic insufficiency
  3. Pericarditis
  4. Myocarditis
  5. AV-blocks

• Registered in about 33% of patients with AS.

• **Investigations:** ECG, echocardiography, CT.

• All these conditions should be treated by cardiologist.

Aortic insufficiency

Gastrointestinal manifestations

- Inflammatory bowel diseases (IBD) - is a group of inflammatory conditions of the colon and small intestine, which include:

  1. Crohn’s disease
  2. Ulcerative colitis

- Diagnosed in 5-10% of patients with AS.

Gastrointestinal manifestations

• **Symptoms:** abdominal pain, vomiting, diarrhea, rectal bleeding, severe internal cramps, weight loss, anemia.

• **Complications:** toxic megacolon, bowel perforation, colorectal cancer, intestinal obstruction, fistulas, abscesses, malabsorption and malnutrition.

![Images of Healthy Colon, Ulcerative Colitis, and Crohn's Disease](http://www.athersys.com/images/IBDFigure1.jpg)
Gastrointestinal manifestations

• **Investigations:** stool analysis, colonoscopy with biopsy.

• **Treatment:** steroids, immunesuppressants, antibiotics, TNF inhibitors, surgery, fecal bacteriotherapy.

**NB!** NSAIDs are prohibited in case of IBD!!!
Psoriasis is a chronic autoimmune disease characterized by patches of abnormal skin (typically red, itchy, and scaly) that may vary in severity from small and localized to complete body coverage.

There are 5 main types: plaque, guttate, inverse, pustular, and erythrodermic.

Pustular psoriasis associates with AS.

Occurs in 10-25% of patients with AS.

Dermatologist’s assistance is needed.
Cutaneous manifestations

Pustular psoriasis usually exists as a large red area covered with green tender pustules (blisters) that are 1-2 mm diameter.
Pulmonary manifestations

• Apical (upper lobe) fibrosis – is a rather prevalent complication of a large number of pathologies.

• **Symptoms:**
  productive/non-productive cough, dyspnea.

• Develops in up to 50% of patients with AS.

Check for tuberculosis!!!
Renal manifestations

- **Renal amyloidosis** – renal deposits of amyloid, especially in glomerular capillary walls, which may cause albuminuria and the **nephrotic syndrome**.

- **IgA nephropathy** - deposition of the IgA antibody in the glomerulus, the most common variant of **nephritic syndrome**.

- Met in 10-35% of patients with AS.

- **Complication**: chronic renal failure.

- Cooperation with **nephrologist** is needed.
Nota Bene!!!

- Uveitis without joint syndrome = Uveitis
- Joint syndrome + Uveitis = AS
- Aortitis without joint syndrome = Aortitis
- Joint syndrome + Aortitis = AS
- IBD without joint syndrome = IBD
- Joint syndrome + IBD = AS

... and so on.
Complications

- Functional insufficiency (ankylosis)
- Spinal fractures (osteoporosis)
- Cauda equina syndrome - is a rare complication that occurs when nerves at the bottom of spine become compressed. Causes pain or numbness in lower back and buttocks, weakness in legs (can affect ability to walk), urinary incontinence or bowel incontinence.
A large number of different specialists may be needed for management of AS patients.
Teamwork

...or sometimes one may be enough.
Forms of the disease

- **Central** – affection of only spine and sacroiliac joints.
- **Rhizomelic** – affection of spine, shoulder and hip joints.
- **Peripheral** – affection of both axial and peripheral joints (knee, ankle, etc.)
- **Scandinavic** – affection of spine and hand joints (mimicries rheumatoid arthritis)
- **Visceral** – affection of joints and internal organs.
Mobility measurement

1. Lumbar mobility
   • Modified Schober test (lumbar flexion test)
   • Finger-to-floor distance (Tomayer test)
   • Lumbar lateral flexion

2. Thoracic mobility
   • Chest expansion

3. Cervical mobility
   • Occiput-to-wall distance (Forestier test)
   • Tragus-to-wall distance
   • Cervical rotation

4. Hip mobility
   • Intermalleolar distance
• Patient standing upright
• Two marks are made on the patient's back: one at the level of the sacral dimples (at the fifth lumbar spinous process) and the other 10 cm above.
• The patient then bends forward as far as possible (ie, attempts to touch toes with knees extended), and the distance between the two marks is again measured.
• Normally the overlying skin will stretch to 15 cm
• Values less than this can be indicative of reduced lumbar mobility.
Modified Schober test

• In this test marks are made 5 cm below and 10 cm above the sacral dimples.

• The distance between these marks should increase from 15 cm to at least 20 cm with lumbar flexion.

• The distance less than 5 cm is abnormal.
Modified Schober test

https://www.youtube.com/watch?v=B9RaFB5BwrQ&index=1&list=PLB376ABEA66A984D
Finger-to-floor distance

- Expression of spinal column mobility when bending over forward
- Measured distance is between the tips of the fingers and the floor when the patient is bent over forward with knees and arms fully extended.
Lateral lumbar flexion

• Patient stands with heels and buttocks touching the wall, knees straight, shoulders back, outer edges of feet 30 cm apart, feet parallel.

• The patient bends laterally as much as he can

• Measure minimal fingertip-to-floor distance in full lateral flexion without flexion, extension or rotation of the trunk or bending the knees.

• The difference between start and endpoint is recorded

• Normally >10 cm.
Lateral lumbar flexion

https://www.youtube.com/watch?v=c-IeFZkPEoE&index=2&list=P LB376ABEAA66A984D
Chest expansion

- Measured as the difference between maximal inspiration and maximal forced expiration in the fourth intercostal space in males or just below the breasts in females.
- Normal chest expansion is $\geq 5$ cm.
Chest expansion

Normal values depending on age and sex.

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Chest expansion

https://www.youtube.com/watch?v=SumtVr5c1Qg&list=PLB376ABEAA66A984D&index=3
Occiput to wall distance

- Patient stands, with heels and buttocks against the wall; the head is placed back as far as possible, keeping the chin horizontal.
- Patient extends his neck maximally in an attempt to touch the wall with the occiput.
- Normally = 0.
Tragus to wall distance

• Patient stands, with heels and buttocks against the wall.
• The head is placed back as far as possible, keeping the chin horizontal.
• Normally <15 cm.
Tragus to wall distance

https://www.youtube.com/watch?v=9-SvI4disNE&index=6&list=PLB376ABEAA66A984D
Cervical rotation

- Patient supine, head in neutral position, forehead horizontal.
- If necessary head on pillow or foam block to allow this.
- Gravity goniometer / bubble inclinometer placed centrally on the forehead.
- Patient rotates head as far as possible, keeping shoulders still, ensure no neck flexion or side flexion occurs.
- Normally 70-90°
Cervical rotation

https://www.youtube.com/watch?v=t7Z47hxrducI&list=PLB376ABEAA66A984D&index=4
• Patient stands with legs separated as far as possible.
• The distance between the medial malleoli is measured.
• Normally >100 cm.
Intramalleolar distance

https://www.youtube.com/watch?v=-MSzN8jPrHk&index=5&list=PLB376ABEAA66A984D
Tests for sacroiliitis

- Pelvic compression test
- Fabere test
- Gaenslen Test
Pelvic compression test

- Test irritability by compressing the pelvis with the patient prone.
- Sacroiliac pain will be lateralised to the inflamed joint.
Pelvic compression test

https://www.youtube.com/watch?v=ux8G2pNhQQs&list=PLik7Tzimeyml_Fd8aTceYUp6YNTjzk1Rq
Fabere test

• FABER test (Fabere test, Patrick test, Figure Four test) is performed by having the tested leg flexed, abducted and externally rotated.
• If pain occurs anteriorly on the same side of the body → hip joint disorder.
• If pain occurs posteriorly on the opposite side of the body → sacroiliac joint disorder.
https://www.youtube.com/watch?v=p1jo3puFDAU
Gaenslen test

• The non-tested leg is kept in extension, while the tested leg is placed in maximal flexion.
• The examiner places one hand on the anterior thigh of the non-tested leg and the other hand on the knee of the tested leg to apply a flexion overpressure.
• The extended leg may also be placed off the table to create a greater force.
• A positive test occurs if it produces low back pain.

http://www.e-rheumatology.gr/sites/default/files/SDS-Sacroiliac-Gaenslen-test.gif
https://www.youtube.com/watch?v=GT23jJ4k4NQ&index=2&list=PLik7Tzimeyml_Fd8aTceYUp6YNTjkz1Rq
Laboratory tests

- **CBC:** increased ESR, sometimes – hypochromic anemia and leucocytosis.

- **Biochemistry:** increased level of $\alpha$-2-globulines and $\gamma$-globulines, seromucoid, sialic acid, CRP.

- **Rheumatoid factor** in blood – negative.

- **HLA-B27 Typing** – positive in about 90% of cases.

- **Others** – depending on extra articular manifestations and complications.
Instrumental tests

- **X-ray** – main diagnostic method
- **Scyntygraphy**
- **CT-scan, MRI**
- **Others** - depending on extra articular manifestations and complications.
X-Ray Grading of SI joints

- **Grade 0:** normal
- **Grade I:** some blurring of the joint margins – suspicious (A)
- **Grade II:** minimal sclerosis with some erosion (B)
- **Grade III:**
  - definite sclerosis on both sides of joint
  - severe erosions with widening of joint space with or without ankylosis (C)
- **Grade IV:** complete ankylosis (D)

http://www.remedicajournals.com/UIControls/ImageOpen.axd?aaid=7000
Bamboo spine

• **Bamboo spine** occurs as a result of vertebral body fusion by marginal syndesmophytes. It is often accompanied by fusion of the posterior vertebral elements as well.

• Typically involves the thoracolumbar and or lumbosacral junctions and predisposes to unstable vertebral fractures.
Bamboo spine

- The outer fibres of the annulus fibrosus of the intervertebral discs ossify, which results in the formation of marginal syndesmophytes between adjoining vertebral bodies. The resulting radiographic appearance therefore is that of thin, curved, radio-opaque spicules that completely bridge adjoining vertebral bodies.

- There is also accompanying squaring of the anterior vertebral body margins with associated reactive sclerosis of the vertebral body margins (shiny corner sign).

http://1.bp.blogspot.com/_QeK6h6J8gEo/SxILouJOUlI/AAAAAABYkA/hdt3AhCyJek/s1600/ASSpinepic.jpg
Bamboo spine

0 Normal
1 Erosion
1 Sclerosis
1 Squaring
2 Syndesmophyte
2 Syndesmophyte
3 Complete bridging
3 Complete bridging
Modified New York Criteria (1984)

**Clinical Criteria**
- Low back pain, > 3 months, improved by exercise, not relieved by rest
- Limitation of lumbar spine motion, sagittal and frontal planes
- Limitation of chest expansion relative to normal values for age and sex

**Radiologic Criteria**
- Sacroiliitis grade $\geq 2$ bilaterally
  - OR
  - Sacroiliitis grade 3 – 4 unilaterally

**Definite AS** if radiologic criterion present plus at least one clinical criteria

**Probable AS** if:
- Three clinical criterion
- Radiologic criterion present, but no signs or symptoms satisfy clinical criteria
ASAS Criteria (2010)

Sacroiliitis on imaging
AND
≥ 1 SpA feature

OR

HLA-B27 positive
AND
≥ 2 other SpA features

SpA features
- inflammatory back pain
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn’s / colitis
- good response to NSAIDs
- family history of SpA
- HLA-B27
- elevated CRP

Sacroiliitis on imaging
- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
- definite radiographic sacroiliitis according to modified New York criteria
Treatment

1. Regime
2. Drug therapy:
   • NSAIDs
   • Steroids
   • DMARDs
   • Anti-TNF drugs
3. Physiotherapy
4. Surgical treatment
• **Regular exercises** – swimming, yoga.

**NB!** Contact sports are NOT recommended.

• **Hard bed**

• **Posture** – sit/walk straight.

• **Diet** – rich with Calcium, avoid overweight.
• **Indomethacin (Indocin)** – 25mg 3 times per day, up to 150 mg per day.

• **Diclofenac (Cataflam, Voltaren-XR, Zorvolex)** – 25-50 mg 3 times per day.

• **Ibuprofen (Motrin, Advil)** – 200 mg 3 times per day.

 Steroids

• Used when NSAIDs non-effective.

• Prednisone – 5-60 mg per day (1 mg/kg/day).

• Hydrocortisone – 20-240 mg per day.

• Pulse therapy – prednisone IV 1000 mg 1 time per day for 3 days.

http://predexpress.com/prednisone.jpg,
DMARDs

• Extremely effective in case of peripheral form of AS.

• Sulfasalazine – 2-3 g per day.

• Methotrexate – 7.5 – 20 mg 1 time per week.
TNF inhibitors

- **TNF inhibitors** - are pharmaceutical drugs that suppresses the physiologic response to tumor necrosis factor (TNF), which is part of the inflammatory response.

- **Advantages:** high specificity, selectivity; decreased risk of immunosuppression.

- **Disadvantages:** high price, increased oncological risk.

NB! The global market for TNF inhibitors in 2008 was **$13.5 billion** and **$22 billion** in 2009.
TNF inhibitors

- **Indications:** rheumatoid arthritis, ankylosing spondylitis, inflammatory bowel disease, psoriasis.
- **Side effects:** lymphomas, infections, congestive heart failure, demyelinating disease, a lupus-like syndrome, induction of auto-antibodies, injection site reactions.
TNF inhibitors

- **Golimumab (Simponi)** – SC 50 mg every month.

- **Adalimumab (Humira, Exemptia)** – SC 40 mg 1 time per 2 weeks.

- **Infliximab (Remicade, Remsima, Inflectra)** – IV drop 5 mg/kg once, repeat in 2 weeks, then – in 6 weeks and perform every 6-8 weeks.
Physiotherapy

- Exercises
- Massage
- Heat procedures
Surgical Treatment

• **Spine osteotomy** is a surgical procedure in which a section of the spinal bone is cut and removed to allow for correction of spinal alignment.

• Usually needed for correction of severe deformed, rigid and fixed spinal deformity.

• The three main types of osteotomy are:
  1. Smith-Petersen Osteotomy (SPO)
  2. Pedicle Subtraction Osteotomy (PSO)
  3. Vertebral Column Resection Osteotomy (VCR)
Surgical Treatment

• **Smith-Petersen Osteotomy (SPO)** - is recommended in patients in whom a relatively small amount of correction (10-20° for each level) is required.

• A section of bone with posterior ligament and facet joints are removed from the back of the spine causing the spine to lean more toward the back.

• SPO may be performed at one or multiple locations along the spine to restore lordosis.
Surgical Treatment

- **Pedicle Subtraction Osteotomy (PSO)** - is recommended in patients in whom a correction of approximately 30° is required mainly at the lumbar level.

- PSO involves all three posterior, middle, and anterior columns of the spine.

- A posterior element and facet joints (similar to a SPO) and a portion of the vertebral body along with the pedicles are removed.

- PSO allows for more correction of the lordosis than SPO.
Surgical Treatment

- Vertebral Column Resection Osteotomy (VCR) - involves the complete removal of a single or multiple vertebral bodies.

- It allows for maximum correction that can be achieved with any spinal osteotomy.

- It introduces a large defect in the spine, so the spinal fusion is also performed over these levels for reconstruction (autograft, structural allograft or metal cage).
Prognosis

http://www.painneck.com/images/ankylosing-spondylitis-symptoms.jpg
Thank you

http://www.brettsanders.me/wp-content/uploads/2015/01/bamboo_texture1595.jpg