

Rheumatoid arthritis

LECTURE IN INTERNAL MEDICINE FOR V COURSE STUDENTS

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Plan of the Lecture

- Definition
- Epidemiology
- Risk factors
- Etiology
- Mechanisms
- Classification
- Clinical investigation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic and treatment guidelines



Definition

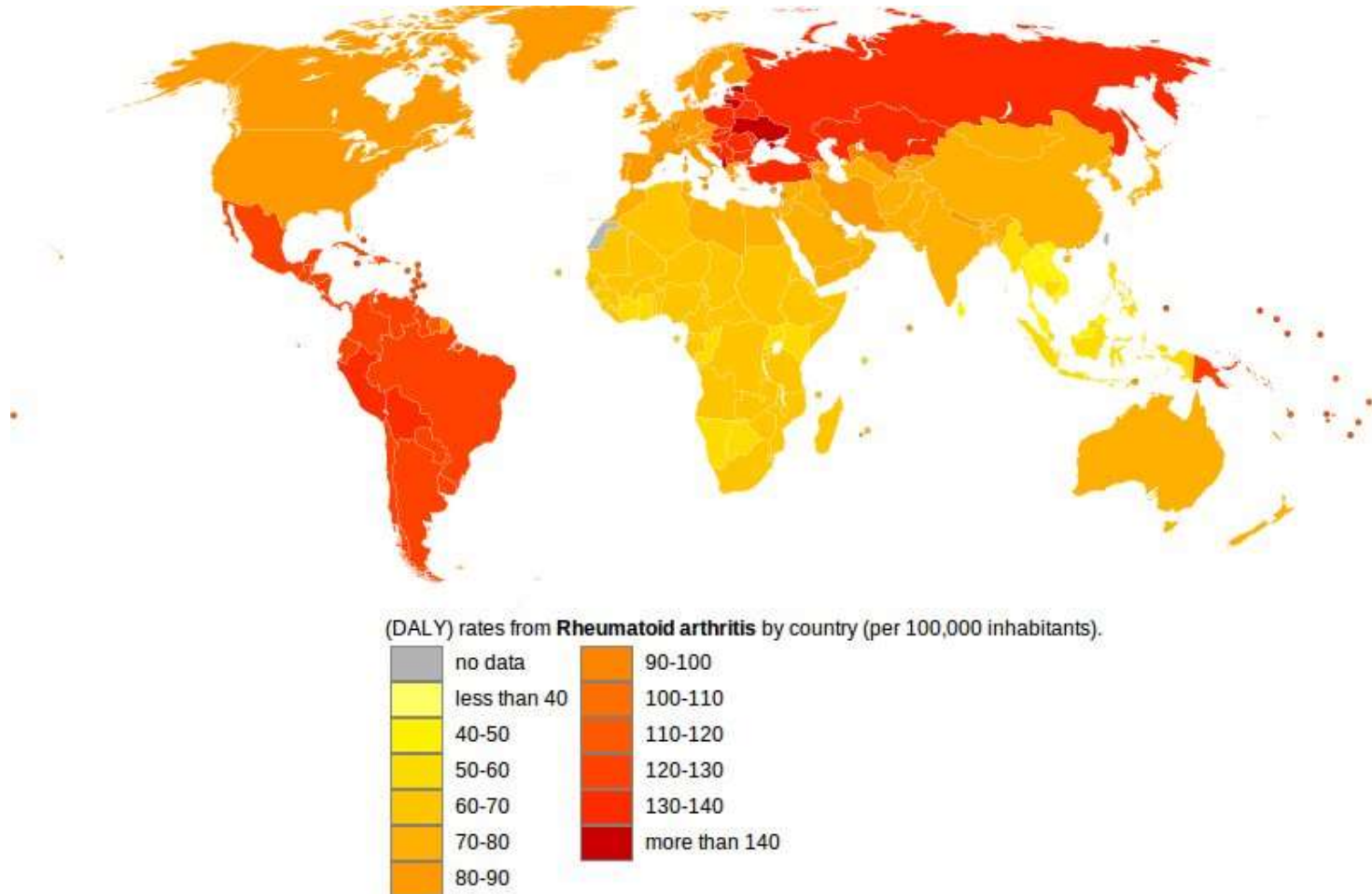
Rheumatoid arthritis (RA) is the most common long-lasting autoimmune inflammatory disorder that primarily affects joints typically involved on both sides of the body with erosions of the cartilage and bone sometimes causes joint deformity, but can also affect other organs with significant negative impact on the ability to perform daily activities, including work and household tasks, and health related quality of life, and it increases mortality.

Epidemiology

- Worldwide, the annual incidence of RA is approximately 3 cases per 10,000 population, and the prevalence rate is approximately 1%, increasing with age and peaking between the ages of 35 and 50 years.
- RA is uncommon under the age of 15 and from then on the incidence rises with age until the age of 80.
- Women are affected three to five times as often as men, but sex differences diminish in older age groups.
- There may be a link between fetal microchimerism (in which fetal cells are present in the maternal circulation) and RA.

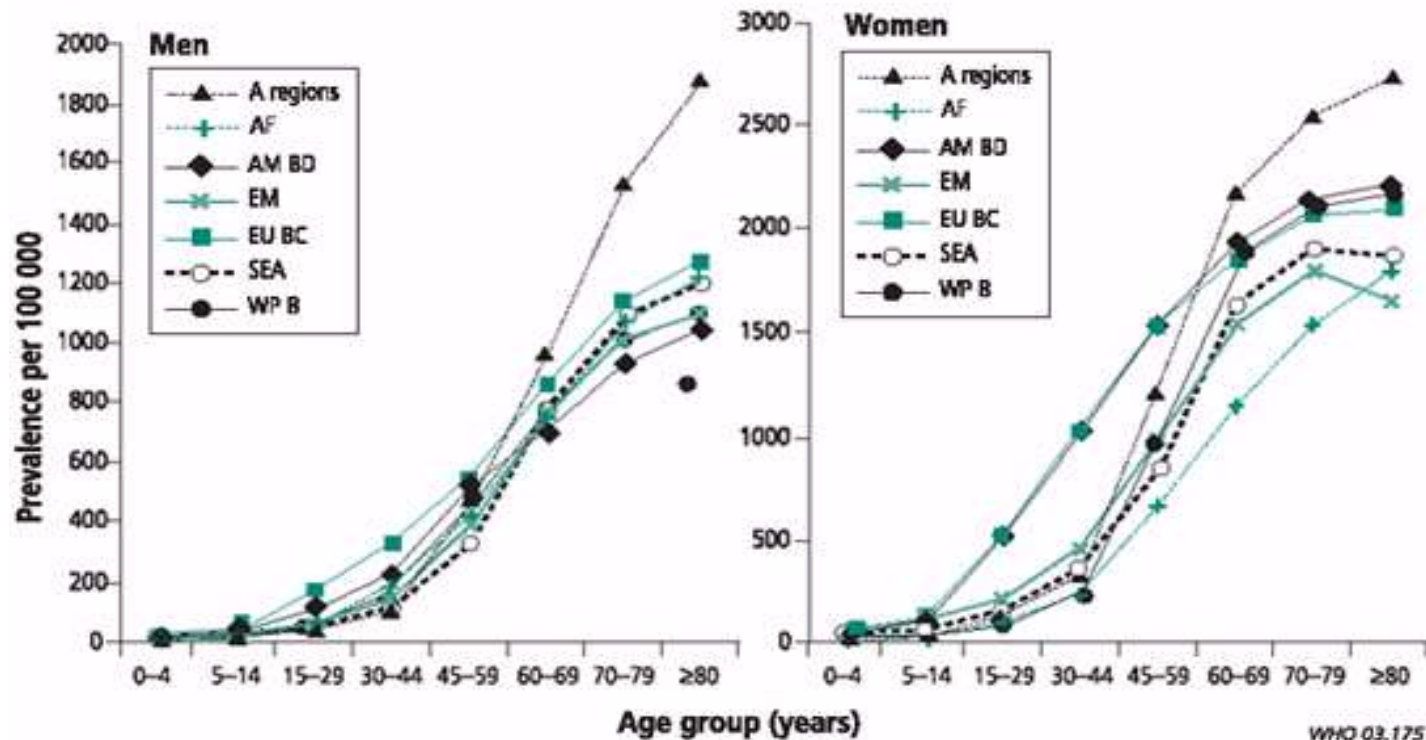
Epidemiology

(Rates from RA by country)



Epidemiology

(Prevalence of RA by Age, Sex, and Region)



A regions – developed countries everywhere, AF – sub-Saharan Africa, AM BD - developing countries in the Americas, EM – countries in the Eastern Mediterranean and North African regions, EU BC – developing countries in Europe, SEA – countries in South-east Asia, WP B – countries in the Western Pacific region.

Risk Factors and Etiology

- Age and sex: the incidence of RA is to three times higher in women than men.
- Genetics: specific HLA class II genotypes are associated with increased risk of developing RA.
- Modifiable: reproductive hormonal exposures, tobacco use, dietary factors, and microbial exposures.
- Oral contraceptives (OC).
- Hormone Replacement therapy (HRT).
- Live Birth History: women who have never had a live birth have a slight to moderately increased risk of RA.
- Breastfeeding (RA is less common among women who breastfeed).
- A truncated menstrual history.
- Early Life Exposures (e.g., maternal smoking doubled the risk of children developing RA as adults).
- Decreased physical Activity.

Risk Factors and Etiology

(Accent on Genetic Factors)

- Genetic factors account for 50% of the risk for developing RA.
- About 60% of RA patients carry a shared epitope of the human leukocyte antigen (HLA)-DR4 cluster, which constitutes one of the peptide-binding sites of certain HLA-DR molecules associated with RA also carries this shared epitope and confers risk.
- Genes other than those of the major histocompatibility complex (MHC) are also involved, and results from sequencing genes of families with RA suggest the presence of several resistance and susceptibility genes, including *PTPN22* and *TRAF5*.
- More significant prevalent RA in women than in men suggests that genomic imprinting from parents participates in its expression.
- Epigenetics is the change in DNA expression that is due to environmentally induced methylation and not to a change in DNA structure.

Risk Factors and Etiology

(Accent on Infectious Agents)

Infectious agents as potential causes of RA:

- *Mycoplasma* organisms,
- Epstein-Barr virus (EBV),
- Rubella virus.
- This suggestion is indirectly supported by the following evidence:
- Periodontopathic bacteria, including *Porphyromonas gingivalis*.

Risk Factors and Etiology

(Accent on Hormonal Factors)

- Sex hormones may play a role in RA, as evidenced by the disproportionate number of females with this disease, its amelioration during pregnancy, its recurrence in the early postpartum period, and its reduced incidence in women using oral contraceptives.
- Hyperprolactinemia may be a risk factor for RA.

Risk Factors and Etiology

(Accent on Immunologic Factors)

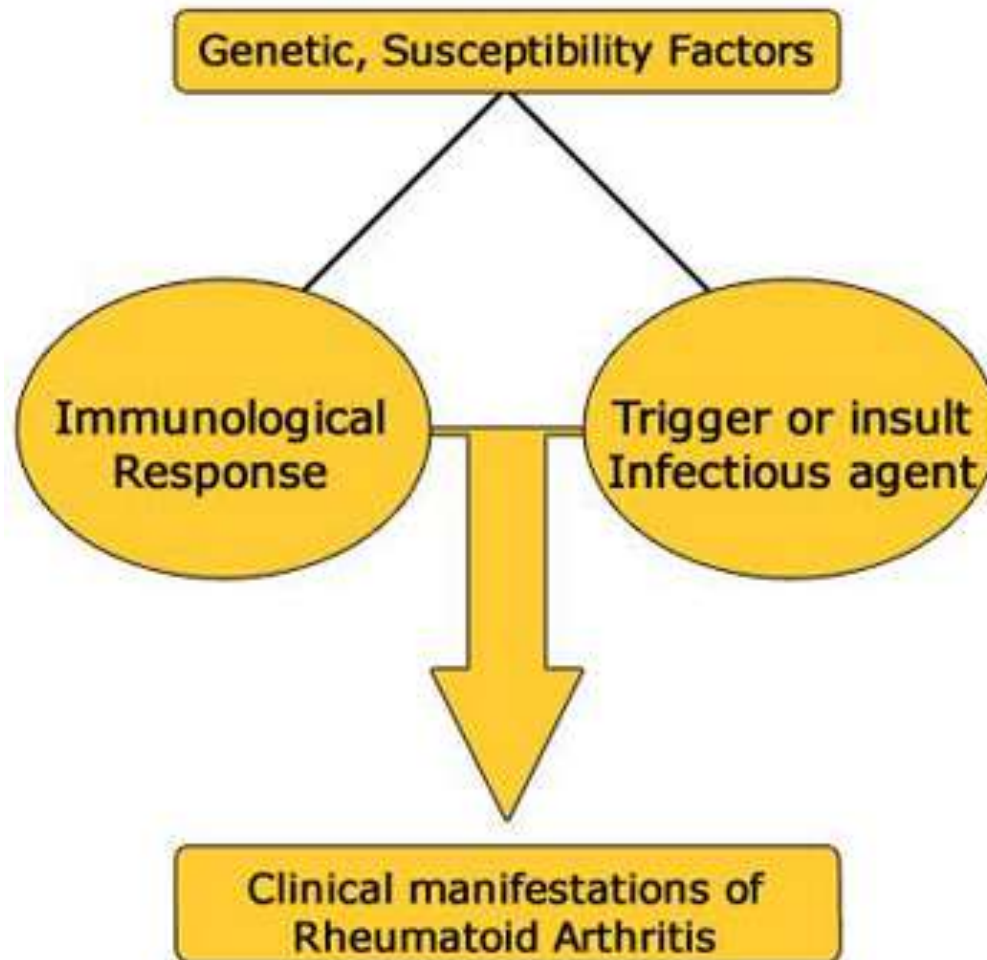
- All of the major immunologic elements play fundamental roles in initiating, propagating, and maintaining the autoimmune process of RA.
- The exact orchestration of the cellular and cytokine events that lead to pathologic consequences (e.g., synovial proliferation and subsequent joint destruction) is complex, involving T and B cells, antigen-presenting cells (e.g., B cells, macrophages, and dendritic cells), and various cytokines.
- Aberrant production and regulation of both proinflammatory and anti-inflammatory cytokines and cytokine pathways are found in RA.
- The major difference between RA and other forms of inflammatory arthritis, such as psoriatic arthritis, lies not in their respective cytokine patterns but, rather, in the highly destructive potential of the RA synovial membrane and in the local and systemic autoimmunity.

Mechanisms

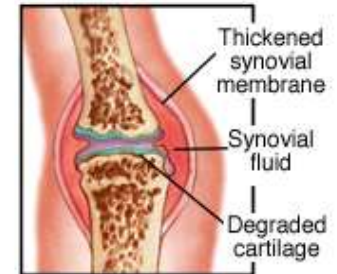
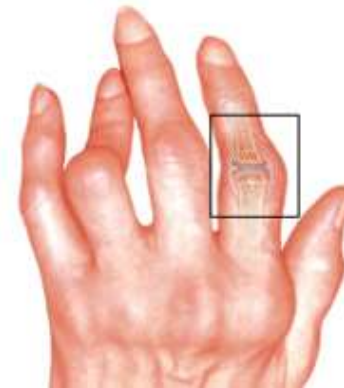
- Mechanisms of RA are not completely understood.
- An external trigger (e.g., cigarette smoking, infection, or trauma) that triggers an autoimmune reaction, leading to synovial hypertrophy and chronic joint inflammation along with the potential for extra-articular manifestations, is theorized to occur in genetically susceptible individuals.
- Synovial cell hyperplasia and endothelial cell activation are early events in the pathologic process that progresses to uncontrolled inflammation and consequent cartilage and bone destruction.
- Inflammation and exuberant proliferation of the synovium (i.e., pannus) leads to destruction of various tissues, including cartilage (see the image below), bone, tendons, ligaments, and blood vessels.
- Although the articular structures are the primary sites involved by RA, other tissues are also affected.

Mechanisms

(The Development of Rheumatoid Arthritis)



Mechanisms (Joint Degradation)



Classification

(International Classification of Diseases (ICD))

Arthropathies (M00-M25)

Inflammatory polyarthropathies (M05-M14)

M05 Seropositive rheumatoid arthritis: M05.0 Felty syndrome (Rheumatoid arthritis with splenomegaly and leukopenia; M05.1† Rheumatoid lung disease (J99.0); M05.2 Rheumatoid vasculitis; M05.3† Rheumatoid arthritis with involvement of other organs and systems (rheumatoid: carditis (I52.8), endocarditis (I39.), myocarditis (I41.8), myopathy (G73.7), pericarditis (I32.8), polyneuropathy (G63.6); M05.8 Other seropositive rheumatoid arthritis; M05.9 Seropositive rheumatoid arthritis, unspecified

M06 Other rheumatoid arthritis: M06.0 Seronegative rheumatoid arthritis; M06.1 Adult-onset Still disease; M06.2 Rheumatoid bursitis; M06.3 Rheumatoid nodule; M06.4 Inflammatory polyarthropathy; M06.8 Other specified rheumatoid arthritis; M06.9 Rheumatoid arthritis, unspecified

Clinical Investigation

(Signs and Symptoms: Joints)

- RA typically manifests with signs of inflammation, with the affected joints being swollen, warm, painful and stiff.
- Most commonly involved are the small joints of the hands, feet and cervical spine, but larger joints like the shoulder and knee can also be involved.
- The joints are often affected in a fairly symmetrical fashion, although the initial presentation may be asymmetrical.
- Increased stiffness early in the morning is often a prominent feature of the RA and typically lasts for more than an hour; gentle movements may relieve symptoms in early stages of the disease.
- As the pathology progresses the inflammatory activity leads to tendon tethering and erosion and destruction of the joint surface, which impairs range of movement and leads to deformity.
- Specific deformities include ulnar deviation, boutonniere deformity, swan neck deformity, and "Z-thumb" or "Z-deformity", that consists of hyperextension of the interphalangeal joint, fixed flexion and subluxation of the metacarpophalangeal joint (arthritis mutilans).

Clinical Investigation (Ulnar Deviation)



Ulnar deviation, also known as ulnar drift, is a hand deformity in which the swelling of the metacarpophalangeal joints causes the fingers to become displaced, tending towards the little finger. Its name comes from the displacement toward the ulna.

Clinical Investigation (Boutonniere Deformity)



Boutonnière deformity is a deformation of the finger in which the distal interphalangeal joint (DIP joint) is hyperextended, or bent away from the palm, while the proximal interphalangeal joint (PIP joint) is hyperflexed, or bent towards the palm. This results in a deformed finger.

Clinical Investigation (Swan Neck Deformity)



The shape of the finger looks like a Swan's neck. Splints can be used to help control the deformity if it is flexible. If deformity is present for a long enough time the joints may be destroyed and the deformity may become "fixed".

Clinical Investigation (Z-Thumb)



"Z-thumb" or "Z-deformity" consists of hyperextension of the interphalangeal joint, fixed flexion and subluxation of the metacarpophalangeal joint and gives a "Z" appearance to the thumb.

Clinical Investigation

(Signs and Symptoms: Skin)

- The rheumatoid nodule (necrotizing granuloma) is the most common non joint feature and occur in 30% of people.
- The nodule has a central area of fibrinoid necrosis that may be fissured and which corresponds to the fibrin-rich necrotic material found in.
- The typical rheumatoid nodule may be a few mm to a few cm in diameter and is found over bony prominences, or other areas that repeated mechanical stress.
- Nodules are associated with a positive RF titer and severe erosive arthritis; rarely, these can occur in internal organs or at diverse sites on the body.
- Several forms of *vasculitis* occur in RA.
- More severe forms include *livedo reticularis*, which is a network of erythematous to purplish discoloration of the skin caused by the presence of an obliterative cutaneous capillaropathy.
- Other, rather rare, skin associated symptoms include pyoderma gangrenosum, Sweet's syndrome, drug reactions, erythema nodosum, lobe panniculitis, atrophy of finger skin, palmar erythema, diffuse thinning (rice paper skin), and skin fragility (often worsened by corticosteroid use).

Clinical Investigation

(The Rheumatoid Nodule)



Rheumatoid nodules are firm lumps under the skin. They form close to joints affected by rheumatoid arthritis. These bumps can be as large as a walnut or as small as a pea. Not everyone with RA gets them.

Clinical Investigation (Livedo Reticularis)



Livedo reticularis is a purplish-colored lace pattern under the skin. There is no raised or itchy rash on the surface of the skin, but the light and dark areas resemble a net-like pattern.

Clinical Investigation

(Signs and Symptoms: Lungs, Kidneys, Cardiovascular)

- Fibrosis of the lungs and pleural effusions are a recognized response to RA, and consequence of its therapy (e.g., methotrexate and leflunomide).
- Renal amyloidosis can occur as a consequence of chronic inflammation, but RA may affect the kidney glomerulus directly through a vasculopathy or a mesangial infiltrate .
- People with RA are more prone to atherosclerosis, and risk of myocardial infarction and stroke is markedly increased: other possible complications that may arise include: pericarditis, endocarditis, left ventricular failure, valvulitis and fibrosis.

Clinical Investigation

(Signs and Symptoms: Other)

- The eye can be affected in the form of episcleritis, scleritis, or keratoconjunctivitis sicca, which can lead to keratitis and loss of vision.
- Liver problems may be due to the underlying disease process or as a result of the medications used to treat the disease.
- Anemia is by far the most common abnormality of the blood cells which can be caused by a variety of mechanisms.
- A low white blood cell count usually only occurs in people with Felty's syndrome with an enlarged liver and spleen.
- An increased platelet count occurs when inflammation is uncontrolled.
- Peripheral neuropathy and mononeuritis multiplex may occur.
- The most common problem is carpal tunnel syndrome caused by compression of the median nerve by swelling around the wrist.
- Atlanto-axial subluxation can occur, owing to erosion of the odontoid process and/or transverse ligaments in the cervical spine's connection to the skull.
- Constitutional symptoms include fatigue, low grade fever, malaise, etc.

Diagnosis (Imaging)

- X-rays of the hands and feet are generally performed in people with a many joints affected: in RA, there may be no changes in the early stages of the disease, or the x-ray may demonstrate juxta-articular osteopenia, soft tissue swelling and loss of joint space; as the disease advances, there may be bony erosions and subluxation. X-rays of other joints may be taken if symptoms of pain or swelling occur in those joints.
- Other medical imaging techniques such as magnetic resonance imaging (MRI) and ultrasound are also used in RA:
 - High-frequency transducers (10 MHz or higher) have improved the spatial resolution of ultrasound images; these images can depict 20% more erosions than conventional radiography,
 - Color Doppler and power Doppler ultrasound, which show vascular signals of active synovitis depending on the degree of inflammation, are useful in assessing synovial inflammation.

Diagnosis

(Imaging: X-rays - Hands)



Extensive fusion (ankylosis) at both wrists – all of the carpal bones have fused. The patient has had previous joint replacements at the right 2nd, 3rd and 4th MCP joints, while on the left you can see erosions at the MCP joints, with ulnar subluxation.

Diagnosis

(Imaging: X-rays – Elbow)



This patient's elbow has been severely eroded by RA – the olecranon now looks almost like a spoon, the radial head has disappeared, and the joint has become subluxed (partially dislocated) as a result.

Diagnosis

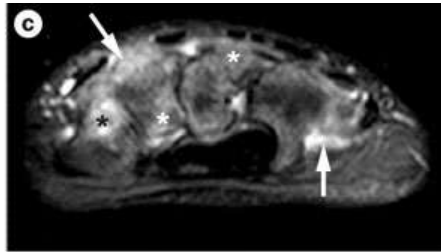
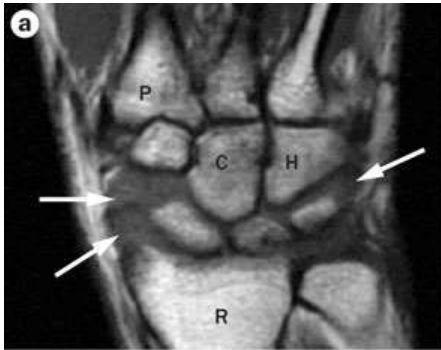
(Imaging: X-rays – Extraskkeletal Manifestations in RA)



A 45 year old female was diagnosed with seropositive rheumatoid arthritis, and lung involvement. X-rays showed right pleural effusion and in upper-middle side of right lung there was 1.6 centimetres mass looked like rheumatoid nodule.

Diagnosis

(Imaging: MRI – Wrist)



a) Areas of inflamed synovium are identified as hypointense signal (arrows);

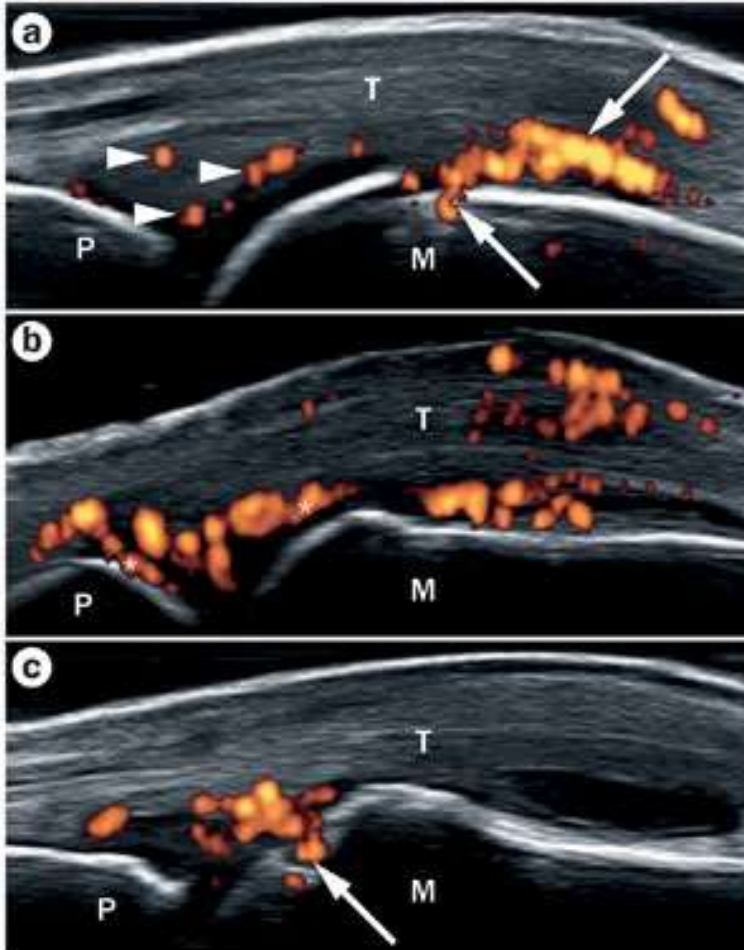
b) Inflamed synovium is identified as hyperintense regions (arrows) and bone marrow edema (asterisks);

C-d) Enhancement of both thickened synovium (arrows) and enhancing, reactive bone marrow edema (asterisks).

Abbreviations: C, capitate; H, hamate; P, first metacarpal; R, radius.

Diagnosis

(Imaging: Power Doppler Ultrasound)



- a) Very early arthritis: the power Doppler signal is distributed at the levels of both the fat pad (arrowheads) and feeding vessel (arrows).
- b) Established disease: the power Doppler signal is located at areas of synovial proliferation that are very close to the bony cortex and metacarpal head hyaline cartilage (*).
- c) Long-standing disease: the power Doppler signal is located within the bone erosion (arrow).

Abbreviations: M, metacarpal bone; P, proximal phalanx; T, finger extensor tendon.

Diagnosis

(Blood Tests)

- When RA is clinically suspected, testing for the presence of RF and anti-citrullinated protein antibody (ACPAs) may be required. A negative RF does not rule out RA; rather, the arthritis is called *seronegative*. RF is also seen in other illnesses, for example Sjögren's syndrome, hepatitis C, systemic lupus erythematosus, chronic infections and atc.
- The most common tests for ACPAs are the anti-CCP (cyclic citrullinated peptide) test, the Anti-MCV assay (antibodies against mutated citrullinated Vimentin), a serological point-of-care test (POCT). This assay combines the detection of rheumatoid factor and anti-MCV for diagnosis of RA and shows a sensitivity of 72% and specificity of 99.7%.
- Other blood tests are usually follows: the erythrocyte sedimentation rate (ESR), C-reactive protein, full blood count, kidney function, liver enzymes and other immunological tests (e.g., antinuclear antibody). Elevated ferritin levels can reveal hemochromatosis, a mimic of RA, or be a sign of Still's disease, a seronegative, usually juvenile, variant of rheumatoid arthritis.

Diagnosis

(2010 Rheumatoid Arthritis Classification: 1)

	Score
Target population (who should be tested?): patients who	
1) have at least one joint with definite clinical synovitis (swelling)*	
2) with the synovitis not better explained by another disease†	
Classification criteria for RA (score-based algorithm: add score of categories A–D a score of ≥6/10 is needed for classification of a patient as having definite RA)‡	
A. Joint involvement§	
1 large joint¶	0
2–10 large joints	1
1–3 small joints (with or without involvement of large joints)**	2
4–10 small joints (with or without involvement of large joints)	3
>10 joints (at least one small joint)‡‡	5
B. Serology (at least 1 test result is needed for classification)‡‡	
Negative RF <i>and</i> negative ACPA	0
Low-positive RF <i>or</i> low-positive ACPA	2
High-positive RF <i>or</i> high-positive ACPA	3
C. Acute-phase reactants (at least one test result is needed for classification)§§	
Normal CRP <i>and</i> normal ESR 0	0
Abnormal CRP <i>or</i> normal ESR 1	1
D. Duration of symptoms¶¶	
<6 weeks	0
≥6 weeks	1

Diagnosis

(2010 Rheumatoid Arthritis Classification: 2)

- * The criteria are aimed at classification of newly presenting patients. In addition, patients with erosive disease typical of rheumatoid arthritis (RA) with a history compatible with prior fulfilment of the 2010 criteria should be classified as having RA. Patients with long-standing disease, including those whose disease is inactive (with or without treatment) who, based on retrospectively available data, have previously fulfilled the 2010 criteria should be classified as having RA.
- † Differential diagnoses differ in patients with different presentations, but may include conditions such as systemic lupus erythematosus, psoriatic arthritis and gout. If it is unclear about the relevant differential diagnoses to consider, an expert rheumatologist should be consulted.
- ‡ Although patients with a score of less than 6/10 are not classifiable as having RA, their status can be reassessed and the criteria might be fulfilled cumulatively over time.
- § Joint involvement refers to any swollen or tender joint on examination, which may be confirmed by imaging evidence of synovitis. Distal interphalangeal joints, first carpometacarpal joints and first metatarsophalangeal joints are excluded from assessment. Categories of joint distribution are classified according to the location and number of involved joints, with placement into the highest category possible based on the pattern of joint involvement.

Diagnosis

(2010 Rheumatoid Arthritis Classification: 3)

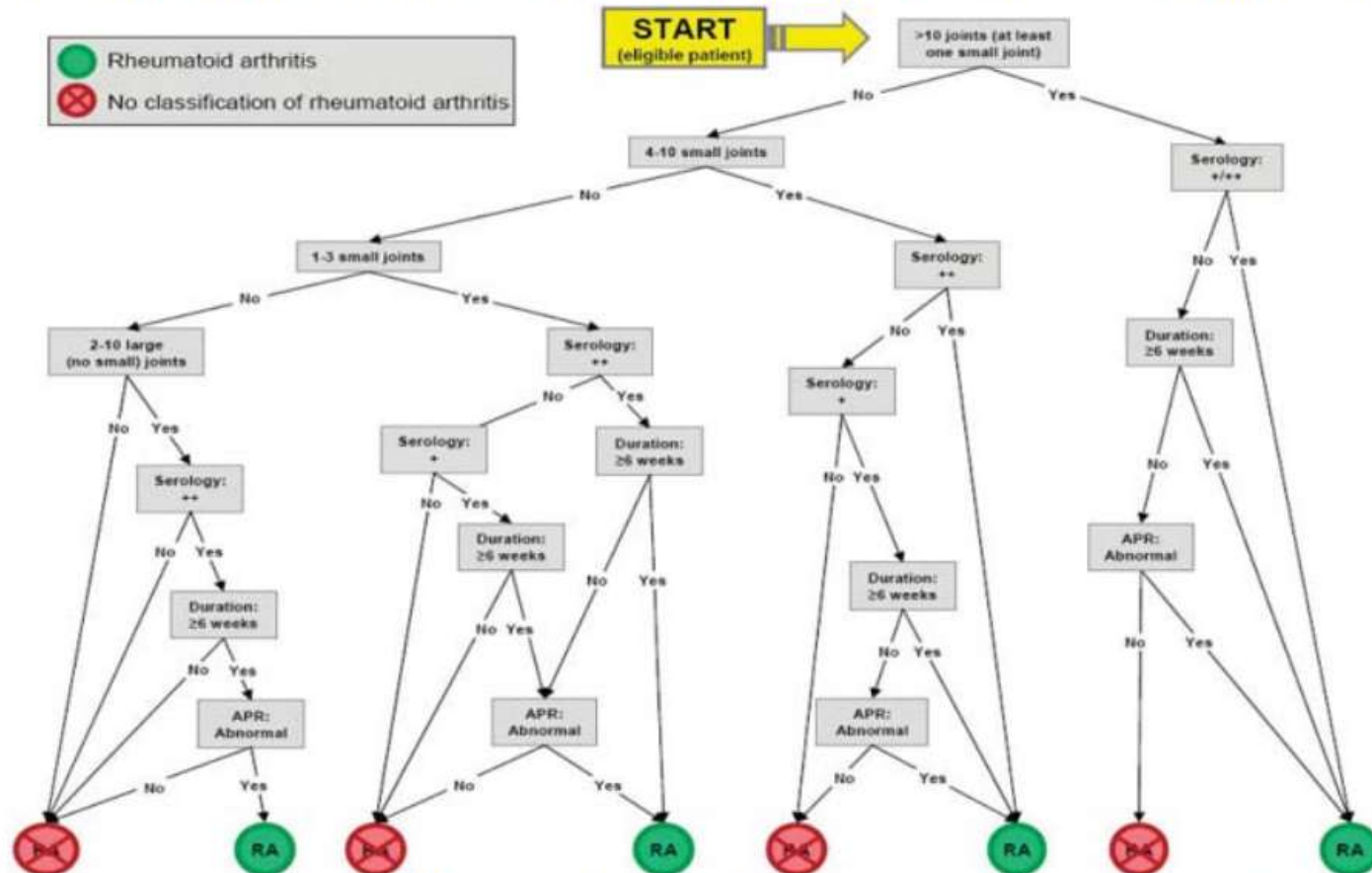
- ¶ 'Large joints' refers to shoulders, elbows, hips, knees and ankles.
- ** 'Small joints' refers to the metacarpophalangeal joints, proximal interphalangeal joints, second to fifth metatarsophalangeal joints, thumb interphalangeal joints and wrists.
- †† In this category, at least one of the involved joints must be a small joint; the other joints can include any combination of large and additional small joints, as well as other joints not specifically listed elsewhere.
- ‡‡ Negative refers to international unit (IU) values that are less than or equal to the upper limit of normal (ULN) for the laboratory and assay; low-positive refers to IU values that are higher than the ULN but three or less times the ULN for the laboratory and assay; high-positive refers to IU values that are more than three times the ULN for the laboratory and assay. When rheumatoid factor (RF) information is only available as positive or negative, a positive result should be scored as low-positive for RF.
- §§ Normal/abnormal is determined by local laboratory standards.
- ¶¶ Duration of symptoms refers to patient self-report of the duration of signs or symptoms of synovitis (e.g., pain, swelling, tenderness) of joints that are clinically involved at the time of assessment, regardless of treatment status.

ACPA, anti-citrullinated protein antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Diagnosis

(Tree Algorithm for classifying Definite RA)

THE 2010 TREE ALGORITHM FOR CLASSIFYING DEFINITE RA (GREEN CIRCLES) OR FOR EXCLUDING ITS PRESENCE (RED CIRCLES) AMONG THOSE WHO ARE ELIGIBLE TO BE ASSESSED BY THE 2010 ACR-EULAR RA CLASSIFICATION CRITERIA



APR = acute-phase response. Serology: + = low-positive for rheumatoid factor (RF) or anti - citrullinated protein antibody (ACPA); serology: ++ = high-positive for RF or ACPA; serology: +/+ = serology either + or ++.

Aletaha D, Neogi T, Silman A, Funovits J, Felson D, et al. 2010 Rheumatoid Arthritis Classification Criteria: An American College of Rheumatology / European League Against Rheumatism Collaborative Initiative. *Arthritis Rheum* 2010;62:2569-81.

Diagnosis

(Monitoring Progression)

- Crystal induced arthritis (gout, and pseudogout).
- Osteoarthritis.
- Systemic lupus erythematosus (SLE).
- Psoriatic arthritis.
- Lyme disease.
- Reactive arthritis (previously Reiter's disease).
- Ankylosing spondylitis.
- Hepatitis C.
- Sarcoidosis, amyloidosis, and Whipple's disease.
- Hemochromatosis.
- Acute rheumatic fever.
- Bacterial arthritis.
- Gonococcal arthritis.

Diagnosis

(Clinical Disease Activity Index (CDAI))

- **CDAI = SJC(28) + TJC(28) + PGA + EGA**
- **SJC(28):** Swollen 28-Joint Count (shoulders, elbows, wrists, MCPs, PIPs, knees)
- **TJC(28):** Tender 28-Joint Count (shoulders, elbows, wrists, MCPs, PIPs, knees)
- **PGA:** Patient Global disease Activity (patient's self assessment of overall RA disease activity on a scale 1-10 where 10 is maximal activity)
- **EGA:** Evaluator's Global disease Activity (evaluator's assessment of overall RA disease activity on a scale 1-10 where 10 is maximal activity)
- **Interpretation**
- **Remission** $\text{CDAI} \leq 2.8$
- **Low Disease Activity** $\text{CDAI} > 2.8 \text{ and } \leq 10$
- **Moderate Disease Activity** $\text{CDAI} > 10 \text{ and } \leq 22$
- **High Disease Activity** $\text{CDAI} > 22$
- A CDAI reduction of 6.5 represents moderate improvement.
- **Deficiencies**
- Does not include the ankles / feet
- Does not include inflammatory markers (although this is what makes it a quick and useful *clinical* tool)

Diagnosis

(Disease Activity Score Calculator for RA)

DAWN VISUAL DAS28 CALCULATOR

DAS 28 - Disease Activity Score Calculator for Rheumatoid Arthritis

Enter Patient ID

Would love to
Click here to
give us your
feedback

Joint Scores

Tender:

Swollen:

To enter joint scores, I prefer

- ☒ Use Mannequin
- ☐ Type totals

Additional Measures

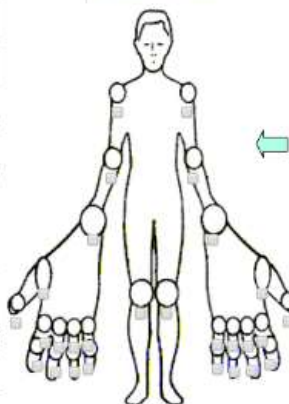
☒ ESR:
mm/hr

☒ CRP:
mg/l

☒ Patient Global Health:
mm

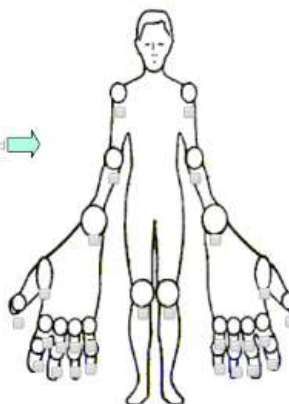
0 - Best Worst
- 100

Tender Joints



Click affected joints

Swollen Joints



Clear all

DAS28

Calculate

FORMULA: $DAS28(4) = 0.56 \cdot \sqrt{t28} + 0.28 \cdot \sqrt{sw28} + 0.70 \cdot \ln(ESR) + 0.014 \cdot GH$

Reference: <http://www.das-score.nl>

Diagnosis (Differential)

- Crystal induced arthritis (gout, and pseudogout).
- Osteoarthritis.
- Systemic lupus erythematosus (SLE).
- Psoriatic arthritis.
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Treatment

(General Principles)

- There is no cure for RA, but treatments can improve symptoms and slow its progress.
- • Treatment of patients with RA should aim for the best care and must be based on a shared decision between the patient and the rheumatologist.
- • Rheumatologists are the specialists who should primarily care for patients with RA.
- • RA incurs high individual, societal, and medical costs, all of which should be considered in its management by the treating rheumatologist.
- Disease-modifying treatment has the best results when it is started early and aggressively.

Treatment

(Lifestyle modification)

- Behavioral modification is a primary consideration in any RA management program.
- Regular exercise is recommended as both safe and useful to maintain muscles strength and overall physical function.
- Specific dietary measures have an effect.
- Occupational therapy has a positive role to play in improving functional ability of patients with RA.
- Home visits and regular monitoring reduce the need for hospitalization and improve life expectancy.

Treatment

(Patient Education)

- Patient education and counseling help to reduce pain, disability, and frequency of physician visits.
- The goal is to satisfy the patient's informational needs regarding the diagnosis, prognosis, and treatment in appropriate detail.
- To understand the patient's perspective, requests, and fears, the physician must employ careful questioning and empathic listening.
- The patient needs to know that the primary physician understands the situation and is available for support, advice, and therapy as the need arises.
- Encouraging the patient to ask questions helps to communicate interest and caring.
- Patient education may represent the most cost-effective intervention for RA.

Treatment

(Start Disease-Modifying Antirheumatic Drugs (DMARDs) as soon as possible (ASAP))

- Start DMARDs as soon as an RA diagnosis is made.
- RA should always be treated with true antirheumatic therapies (DMARDs), both to provide the patient symptomatic relief and to prevent long-term damage.
- Some patients with very mild disease or with multiple contraindications might not be suitable for DMARD therapy.

Treatment

(Target Remission or Low Disease Activity)

- Treatment should focus on reaching remission or low disease activity.
- Improvement in physical functioning and slowing or stopping of structural damage are implicit in the definition of "remission."
- For patients in whom remission cannot be achieved, low disease activity defined by a composite measure is a reasonable treatment goal.
- Clinicians need to train themselves to think in terms of the disease state that the patient has to achieve, and simply achieving any improvement, or having a good feeling about the treatment result, is no longer acceptable.

Treatment

(Target Remission or Low Disease Activity)

- Monitor active disease every 1-3 months.
- If there is no improvement by 3 months from the start of treatment or the target is not reached by 6 months, treatment should be modified.
- Monitoring should be performed as frequently as a patient's disease requires.
- Maximizing treatment efficacy includes reaching an optimal methotrexate (MTX) dose within "a few weeks" and maintaining the maximal dose (25-30 mg/week) for at least 8 weeks.
- Maximal efficacy with most treatments may take up to 6 months to achieve in some patients.

Treatment

(Disease modifying agents: 1)

- DMARDs are a diverse collection of drugs that improve symptoms, decrease joint damage, and improve overall functional abilities.
- DMARDs should be started early as they result in RA remission in approximately half of people and improved outcomes overall.
- The following drugs are considered as DMARDs: methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, monoclonal antibodies (certolizumab, rituximab, tocilizumab, infliximab and etanercept), injectible man-made protein used for treating rheumatoid arthritis abatacept, and interleukin 1 anakinra.
- The most commonly used agent is methotrexate with other frequently used agents including sulfasalazine and leflunomide.
- Sodium aurothiomalate (Gold) and cyclosporin are less commonly used due to more common adverse effects.

Treatment

(Disease modifying agents: 2)

- Methotrexate is the most important and useful DMARD and is usually the first treatment. Adverse effects should be monitored regularly with toxicity including gastrointestinal, hematologic, pulmonary, and hepatic. Side effects such as nausea, vomiting or abdominal pain can be reduced by taking folic acid. The most common undesirable effect is that it increases liver enzymes in almost 15% of people.
- Biological agents should generally only be used if methotrexate and other conventional agents are not effective after a trial of three months. They are associated with a higher rate of serious infections as compared to other DMARDs. They are often used in combination with either methotrexate or leflunomide.

Treatment

(Anti-inflammatory agents)

- NSAIDs reduce both pain and stiffness in those with RA. Generally they appear to have no effect on people's long term disease course and thus are no longer first line agents. NSAIDs should be used with caution in those with gastrointestinal, cardiovascular, or kidney problems.
- Use of methotrexate together with NSAIDS is safe, if adequate monitoring is done.
- Glucocorticoids can be used in the short term for flare-ups, while waiting for slow-onset drugs to take effect. Injection of glucocorticoids into individual joints is also effective. While long-term use reduces joint damage it also results in osteoporosis and susceptibility to infections, and thus is not recommended.

Treatment

(Disease-Modifying Antirheumatic Drugs)

Nonbiologic DMARDS

- Hydroxychloroquine
- Azathioprine
- Sulfasalazine
- Methotrexate
- Leflunomide
- Cyclosporine
- Gold salts
- D-penicillamine
- Minocycline

Biologic DMARDS

TNF-inhibiting

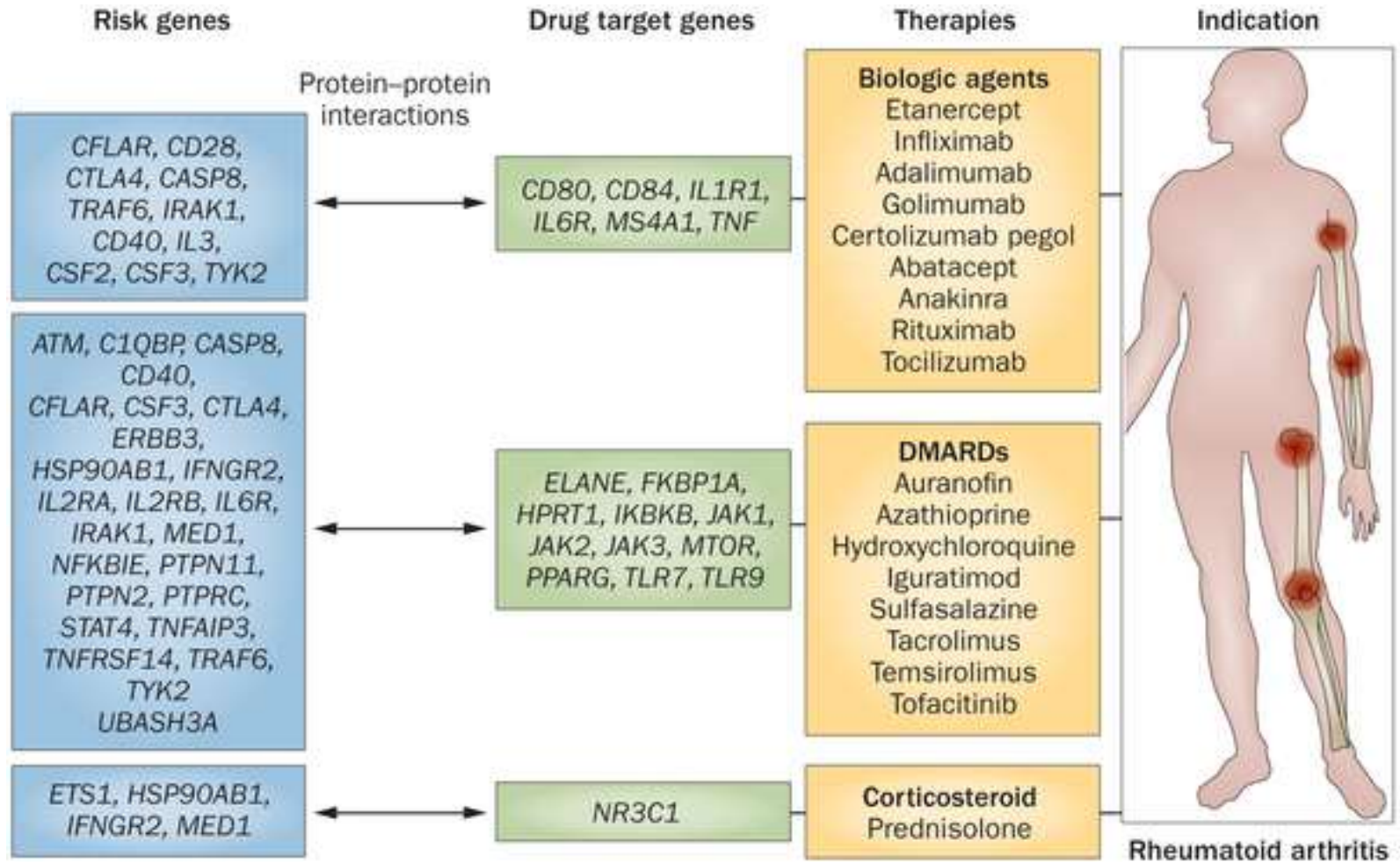
- Etanercept
- Infliximab
- Adalimumab
- Certolizumab
- Golimumab

non-TNF-inhibiting

- Rituximab
- Anakinra
- Abatacept
- Tocilizumab
- Tofacitinib

Treatment

(Risk Genes and Approved RA Drugs)



Treatment

(Surgery)

- In early phases of the disease, an arthroscopic or open synovectomy may be performed. It consists of the removal of the inflamed synovia and prevents a quick destruction of the affected joints.
- Other surgical treatments include tenosynovectomy, tendon realignment, reconstructive surgery or arthroplasty, and arthrodesis.
- Severely affected joints may require joint replacement surgery, such as knee replacement.
- Postoperatively, physiotherapy is always necessary.

Treatment

(Nonpharmacologic, Nonsurgical therapies)

- Heat and cold therapies.
- Orthotics and splints.
- Therapeutic exercise.
- Occupational therapy.
- Adaptive equipment.
- Joint-protection education.
- Energy-conservation education.



Treatment

(Home Care Services)



- In spite of medical treatment, RA often progresses and causes the person to have more and more difficulty in conducting their usual activities of daily living such as bathing or dressing or difficulty with regular homemaking activities such as laundry or routine cleaning.
- Busy families may find it to be challenging to keep up with these needs.
- These families can benefit from the assistance of a home care aide or homemaker.

Prognosis

- The clinical course of RA is generally one of exacerbations and remissions. Approximately 40% of patients become disabled after 10 years, but outcomes are highly variable.
- Poor prognostic factors include persistent synovitis, early erosive disease, extra-articular findings (including subcutaneous rheumatoid nodules), positive serum RF findings, positive serum anti-CCP autoantibodies, family history of RA, poor functional status, socioeconomic factors, elevated acute phase response, and increased clinical severity.

Prophylaxis

- There is no known prevention for the RA other than the reduction of risk factors.
- People with RA have an increased risk of infections and mortality and recommended vaccinations can reduce these risks.
- The killed influenza vaccine should be received annually.
- The pneumococcal vaccine should be administered twice for people under the age 65 and once for those over 65.
- The live-attenuated zoster vaccine should be administered once after the age 60, but is not recommended in people on a tumor necrosis factor alpha blocker.

Abbreviations

ASAP - as soon as possible

ACPA - anti-citrullinated protein antibody

ACR - American College of Rheumatology

anti-CCP - cyclic citrullinated peptide

Anti-MCV assay - antibodies against mutated citrullinated Vimentin

CCP = cyclic citrullinated peptide

CDAI - Clinical Disease Activity Index

CRP - C-reactive protein

DIP or DIJ – distal interphalangeal joints

DMARDs - disease-modifying antirheumatic drugs

EBV - Epstein-Barr virus

ESR - erythrocyte sedimentation rate

IP or IJ - interphalangeal joints

IU - international unit

MCPs - metacarpophalangeal joints

MRI - magnetic resonance imaging

MTX - methotrexate

NSAIDs - nonsteroidal anti-inflammatory drugs
SLE - systemic lupus erythematosus

OC – oral contraceptives

PIP or PIJ – proximal interphalangeal joints

POCT - point-of-care test

RA – rheumatoid arthritis

RF - rheumatoid factor

TNF - tumor necrosis factor

ULN - upper limit of normal

Diagnostic and treatment guidelines

[2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis](#)

[Rheumatoid arthritis in adults: management](#)

[Clinical guideline for the diagnosis and management of early rheumatoid arthritis](#)

[New Rheumatoid Arthritis Management Guidelines: A Quick and Easy Guide](#)

[Rheumatoid Arthritis](#)

[Rheumatoid Arthritis](#)