Rheumatoid arthritis

LECTURE IN INTERNAL MEDICINE FOR V COURSE STUDENTS

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Plan of the Lecture

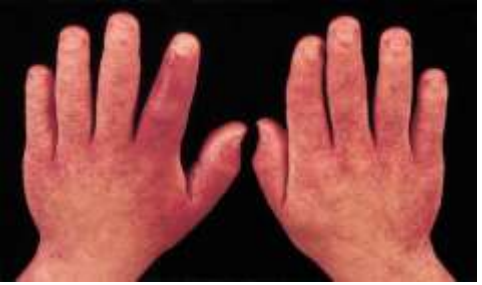
- Definition
- Epidemiology
- Risk factors
- Etiology
- Mechanisms
- Classification
- Clinical investigation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic and treatment guidelines

https://www.verywell.com/rheumatoid-arthritis-explained-with-pictures-190351

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.

rheumatology.org/Portals/0/Files/ACR%202015%20RA%20Guideline.pdf cdc.gov/arthritis/basics/rheumatoid.htm



US MLE TEST

A 35-year-old female presents to her family physician with a complaint of painful joints for the past 2 weeks. She reports symmetric bilateral joint pain in her hands, knees, and ankles. Additionally, the patient states that she experienced a cold-like illness 3 weeks ago that has since resolved. Physical examination is significant for a rash on her hands and feet that is shown in Figure A. Radiographs of the bilateral hands do not show any notable abnormalities. Which of the following is the most likely diagnosis as the cause of this patient's joint pains?

1. Rheumatoid arthritis, 2. Osteoarthritis, 3. Parvovirus B19, 4. Coxsackievirus, 5. Reactive arthritis.

https://www.mommd.com/usmle1to10.shtml

US MLE TEST EXPLANATION

The correct answer is 3. This patient's presentation of symmetric arthritis of the hands, knees, and ankles in the context of a preceding cold-like illness and papular, purpuric rash in a stocking-glove distribution is consistent with a parvovirus B19 infection.

Incorrect Answers:
1: Although rheumatoid arthritis can often be clinically indistinguishable from parvovirus B19 infection, the history of prior cold-like illness and concurrent acral rash make parvovirus B19 infection the more likely, 2: The acuity and widespread distribution of the pain is atypical for osteoarthritis, 4: Coxsackievirus causes hand, foot, and mouth disease; however, it is not associated with development of arthritis, 5: Reactive arthritis (Reiter's syndrome) is a reactive arthritis to bacterial infection that commonly manifests with a triad of arthritis, conjunctivitis, and urethritis.

Epidemiology 1

- 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.

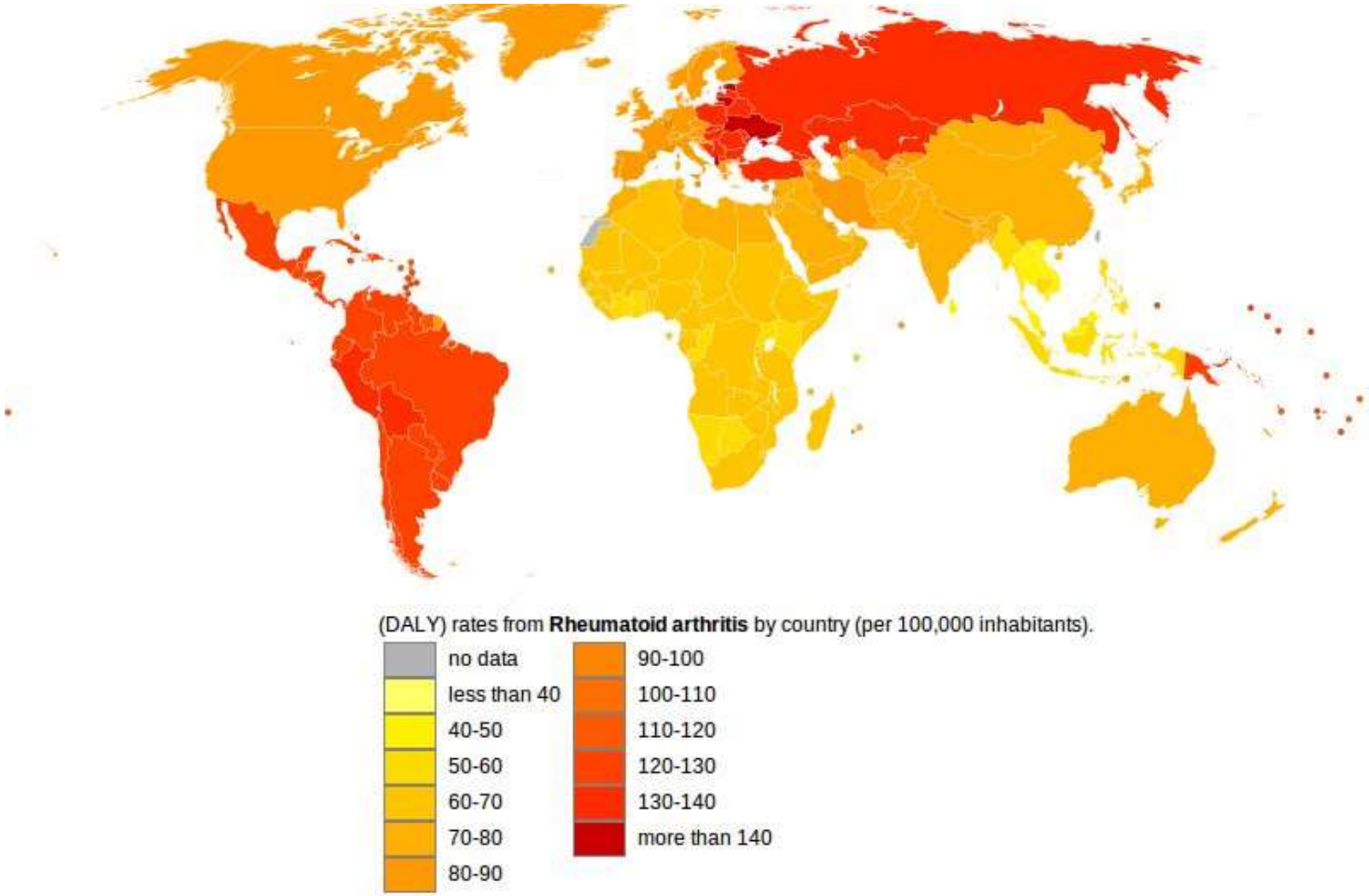
http://emedicine.medscape.com/article/331715-overview#a5 https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Epidemiology

Epidemiology 2

- 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.

http://emedicine.medscape.com/article/331715-overview#a5 https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Epidemiology

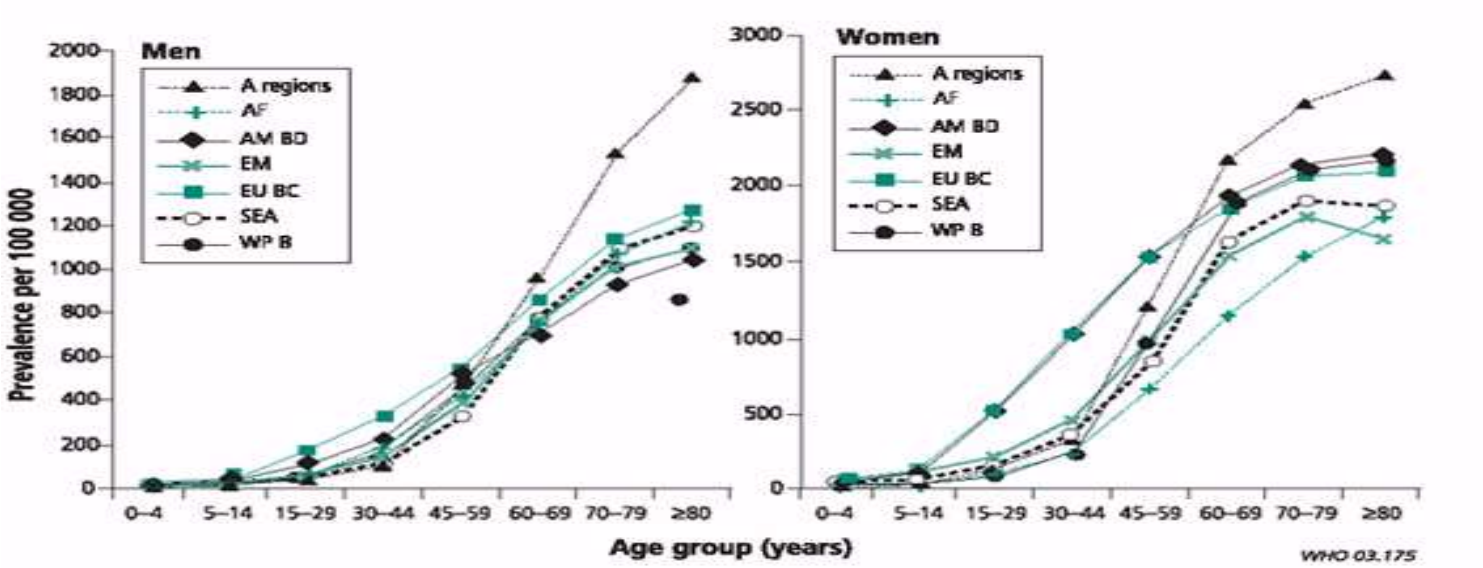
Epidemiology
(Rates from RA by country)



http://buyprovailencheap.org/wp-content/uploads/2013/10/Rheumatoid-arthritis-country.jpg

Epidemiology

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



A regions – developed countries everywhere, AF – sub-Sahar 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.

http://www.scielosp.org/img/revistas/bwho/v81n9/a07fig02.gif

Risk Factors and Etiology 1

- 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).

http://www.cdc.gov/arthritis/basics/rheumatoid.htm

Risk Factors and Etiology 2

- 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.

http://www.cdc.gov/arthritis/basics/rheumatoid.htm

Risk Factors and Etiology
(Accent on Genetic Factors) 1

- 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.

http://emedicine.medscape.com/article/331715-overview#a4

Risk Factors and Etiology
(Accent on Genetic Factors) 2

- 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.

http://emedicine.medscape.com/article/331715-overview#a4

Risk Factors and Etiology
(Accent on Genetic Factors) 3

- Epigenetics is the change in DNA expression that is due to environmentally induced methylation and not to a change in DNA structure.

http://emedicine.medscape.com/article/331715-overview#a4

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*.

http://emedicine.medscape.com/article/331715-overview#a4

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.

http://emedicine.medscape.com/article/331715-overview#a4

Risk Factors and Etiology
(Accent on Immunologic Factors) 1

- 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.

http://emedicine.medscape.com/article/331715-overview#a4

Risk Factors and Etiology
(Accent on Immunologic Factors) 2

- 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.

http://emedicine.medscape.com/article/331715-overview#a4

US MLE TEST

A 52-year-old female with a past medical history of rheumatoid arthritis presents to her primary care physician for complaints of increased swelling in her legs. She also notes her urine to be more "frothy" than usual. On physical exam she is noted to have a blood pressure of 142/90 mmHg. At all prior visits, this patient has had normal blood pressure. A 24-hour urine collection for protein contains 3.8 g. Which of the following is most likely present in this patient's kidney?

1. Immune complex deposits, 2. Amyloid deposition,
3. Thickening of the glomerular basement membrane,
4. Bacterial infection, 5. Normal findings on light microscopy.

https://www.mommd.com/usmle1to10.shtml

US MLE TEST EXPLANATION

The correct answer is 2. The patient in this vignette most likely has secondary nephrotic syndrome as a result of AA amyloid deposition. Amyloidosis is the most probable cause of nephrotic syndrome in patients with rheumatoid arthritis (RA).

Incorrect Answers:
1: Immune complex deposits can be seen with acute post-steptococcal glomerulonephritis, among other conditions, and would not be seen with rheumatoid arthritis, 3: Thickening of the glomerular basement membrane is seen as the first consequence of diabetic kidney disease, 4: This patient has no signs of an upper urinary tract infection, 5: Normal findings on light microscopy is consistent with minimal change disease, not rheumatoid arthritis-associated nephrotic syndrome.

Mechanisms 1

- 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.

http://emedicine.medscape.com/article/331715-overview#a3

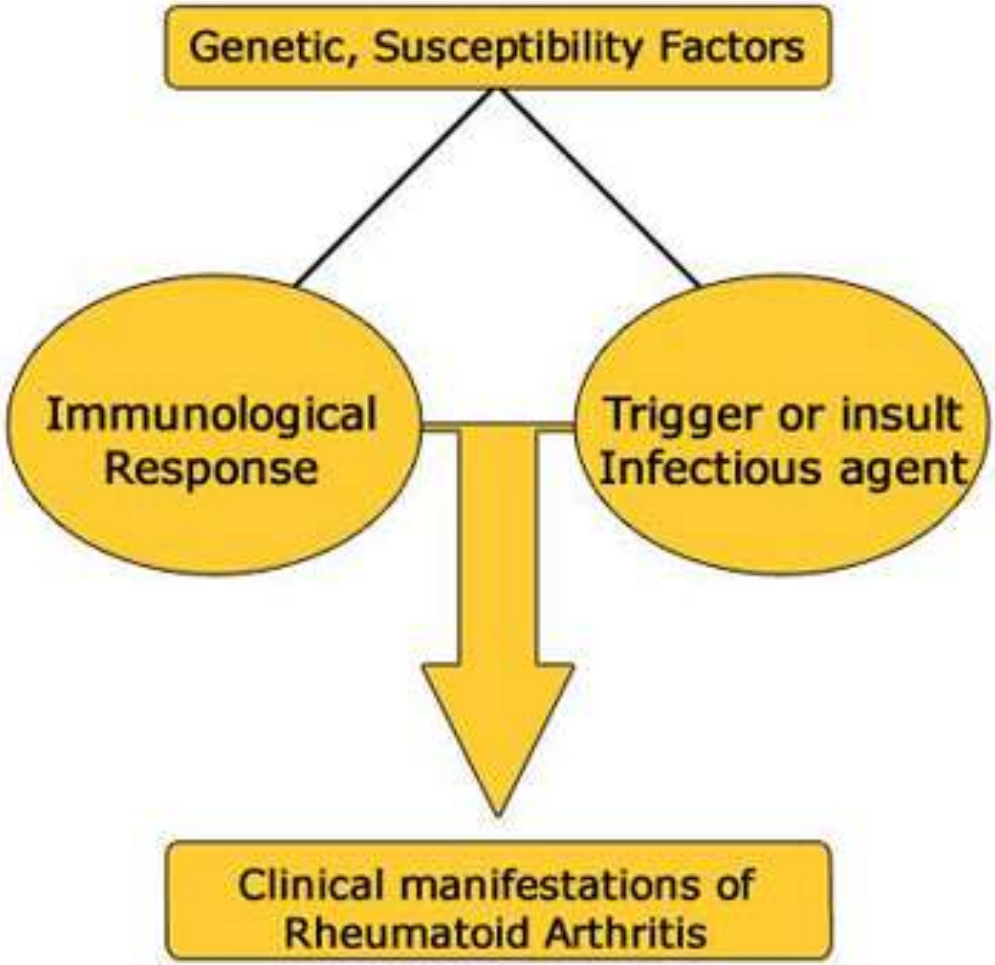
Mechanisms 2

- 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.

http://emedicine.medscape.com/article/331715-overview#a3

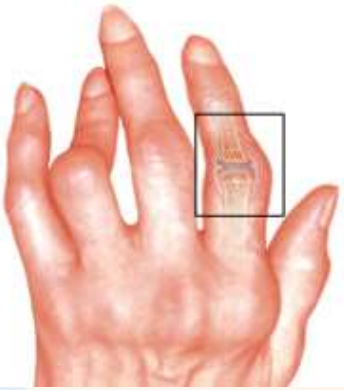
Mechanisms

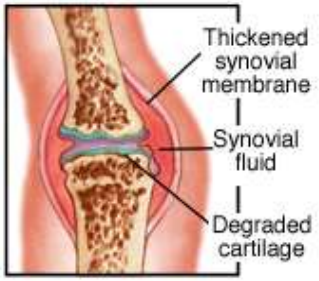
(The Development of Rheumatoid Arthritis)

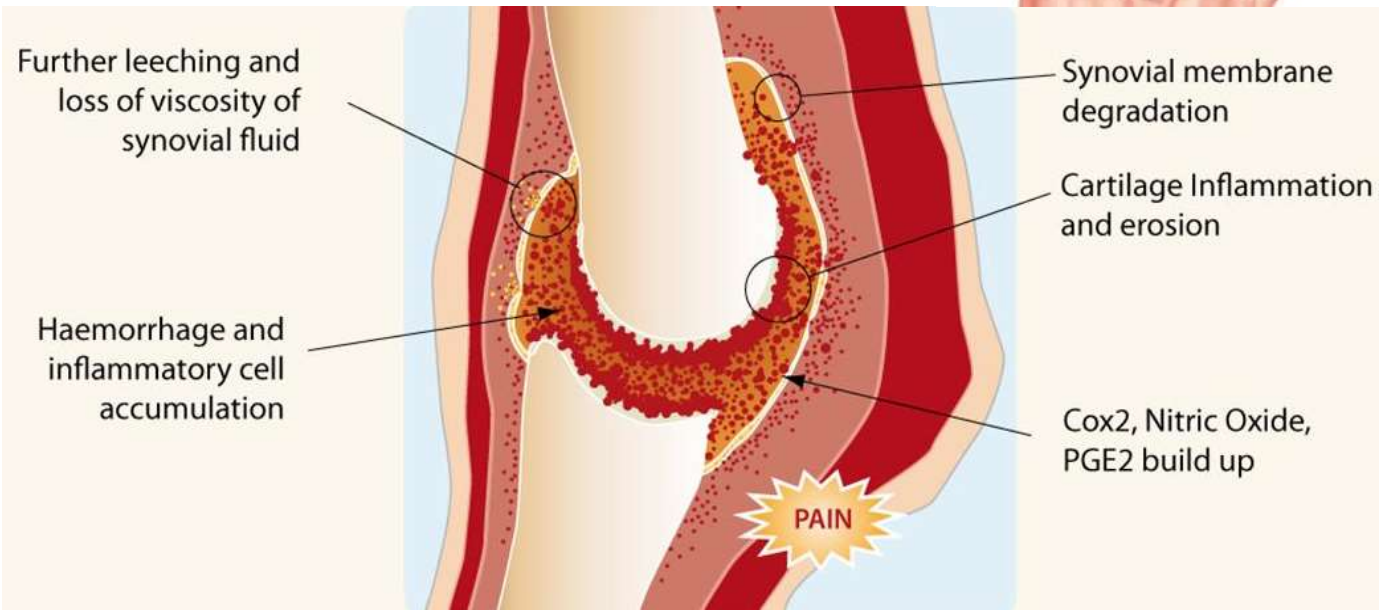


https://www.hss.edu/conditions_an-in-depth-topic-review-of-rheumatoid-arthritis.asp

Mechanisms
(Joint Degradation)







http://www.mayoclinic.org/diseases-conditions/rheumatoid-arthritis/home/ovc-20197388 http://www.jointxl.co.za/index.php/2-uncategorised/11-joint-degeneration-process

Classification

(International Classification of Diseases (ICD)) 1

Arthropathies (M00-M25)

Inflammatory polyarthropathies (M05-M14)

M05 Seropositive rheumatoid arthritis: M05.0 Felty syndrome (Rheumatoid arthritis with splenoadenomegaly 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 (141.8), myopathy (G73.7), pericarditis (I32.8), polyneuropathy (G63.6);

icd10coded.com/cm/ch9/I20-I25/

Classification
(International Classification of Diseases (ICD)) 2

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) 1

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Clinical Investigation
(Signs and Symptoms: Joints) 2

- 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.

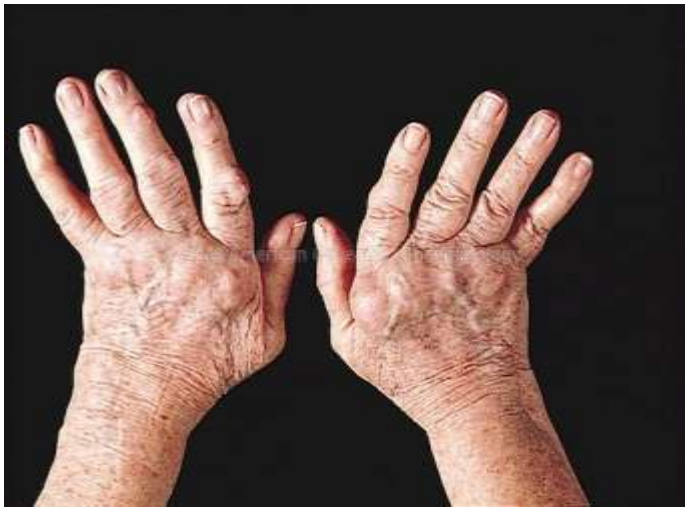
https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Clinical Investigation
(Signs and Symptoms: Joints) 3

- 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 join (arthritis mutilans).

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

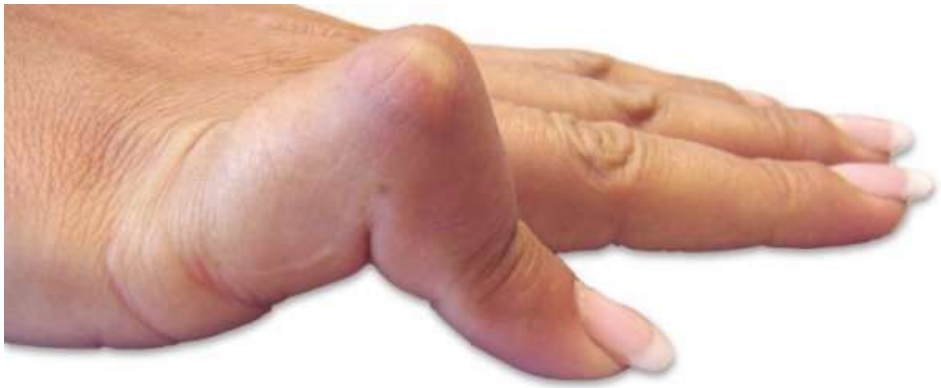
Clinical Investigation
(Ulnar Deviation)



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.

http://america.pink/ulnar-deviation_4582071.html

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.

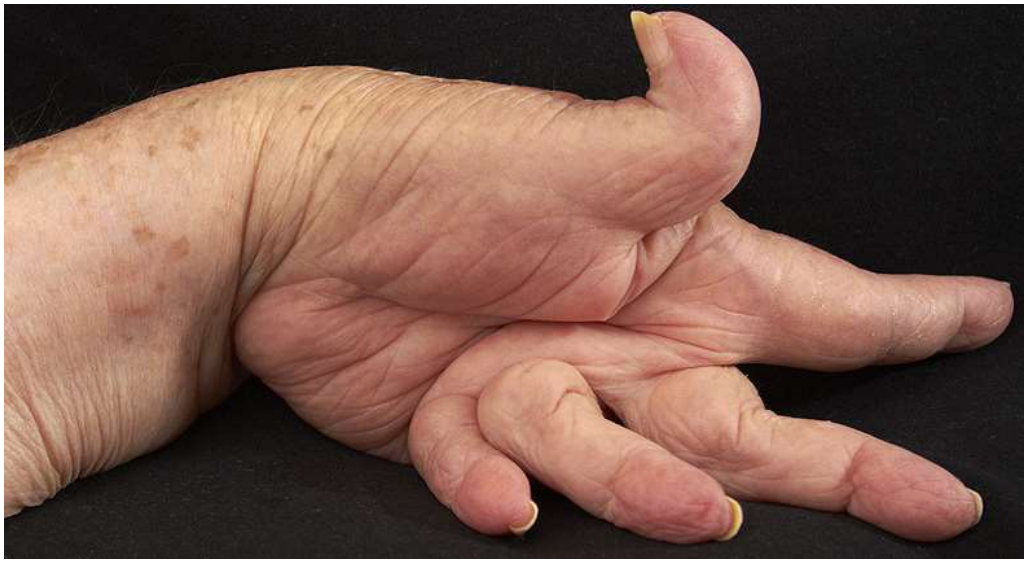
http://www.hand-surgery.eu/en/hand-conditions/boutonniere-deformity

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".

http://www.hand-surgery.eu/en/hand-conditions/boutonniere-deformity

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.

http://medicineinforme.blogspot.com/2015/10/rheumatoid-arthritis-new-medicine-for.html

Clinical Investigation

(Signs and Symptoms: Skin) 1

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Clinical Investigation
(Signs and Symptoms: Skin) 2

- 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.

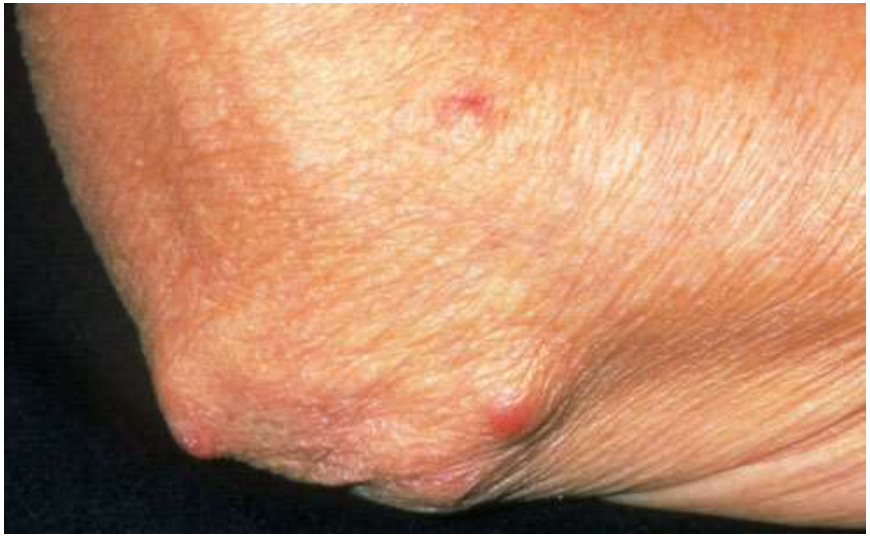
https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Clinical Investigation
(Signs and Symptoms: Skin) 3

- 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).

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

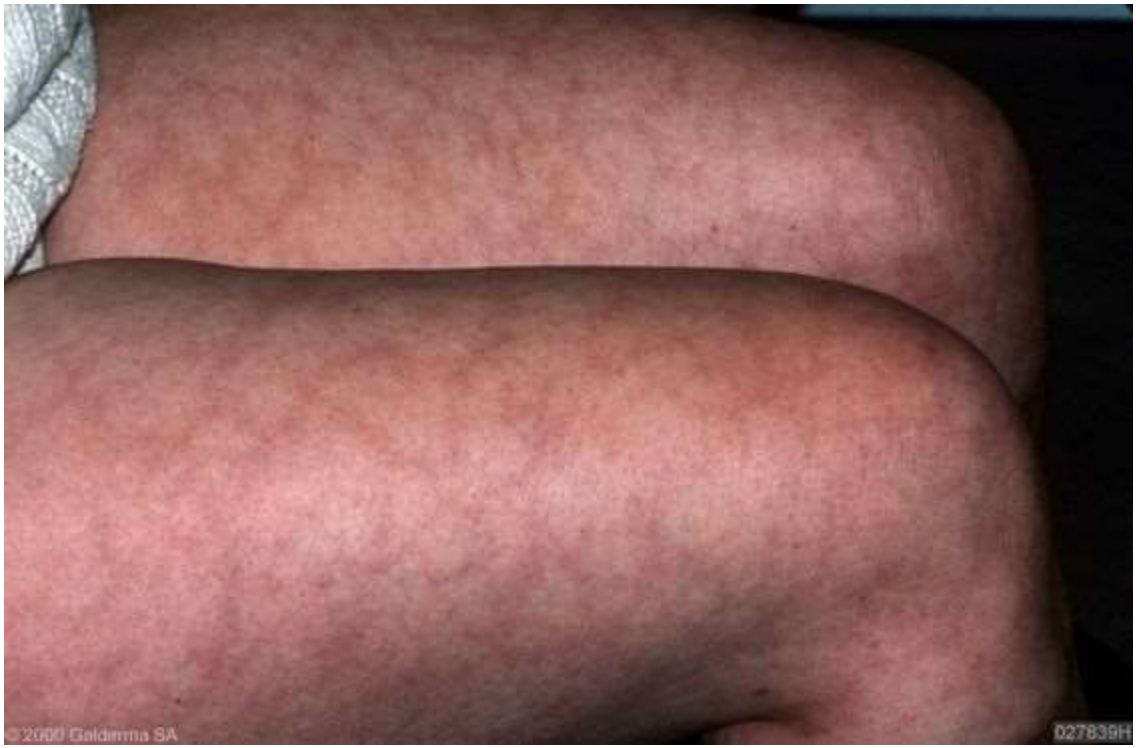
Clinical Investigation
(The Rheumatoid Nodule)



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.

http://www.webmd.com/rheumatoid-arthritis/ss/slideshow-ra-overview

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.

https://s-media-cache-ak0.pinimg.com/564x/10/52/88/105288f9361af0f564e62033336ebb31.jpg

Clinical Investigation

(Signs and Symptoms: Lungs,Kidneys,Cardiovascular) 1

- 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 .

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Clinical Investigation

(Signs and Symptoms: Lungs,Kidneys,Cardiovascular) 2

- , 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Clinical Investigation
(Signs and Symptoms: Other) 1

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Clinical Investigation
(Signs and Symptoms: Other) 2

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Clinical Investigation
(Signs and Symptoms: Other) 3

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

US MLE TEST

A 29-year-old male presents to his primary care physician with complaints of pain with urination, eye dryness, and left ankle and knee pain that has developed over the last several weeks. He reports an illness 3 weeks ago that involved frequent diarrhea as well as nausea and vomiting. This episode resolved without treatment within 2 days. Physical exam shows moderate conjunctivitis; the knee and ankle joints show mild crepitus but no overlying redness or warmth. Which of the following is the best next step in the management of this patient?

1. Prescribe azithromycin and doxycycline, 2. Initiate ibuprofen, 3. Aspiration of the left knee and ankle joints, 4. Initiate PO prednisone, 5. Obtain MRI of the left knee and ankle.

US MLE TEST EXPLANATION

The correct answer is 2. This patient's presentation is consistent with Reiter's syndrome, also known as reactive arthritis. Nonsteroidal anti-inflammatory medications, such as ibuprofen, are the recommended first-line treatment to reduce the pain and inflammation associated with this disease.

Incorrect Answers:
1: Azithromycin and doxycycline would be the correct treatment had the patient suffered from a chlamydial infection that precipitated the reactive arthritis; however, he reports a preceding enteral infection, 3: Aspiration of the joints would be warranted if septic arthritis were suspected; however, there are no clues in the question stem to suggest a diagnosis of septic arthritis, 4: Systemic steroids are indicated for extremely severe or recalcitrant cases of reactive arthritis, 5: MRI is not an appropriate first imaging study.

https://www.mommd.com/usmle1to10.shtml

Diagnosis
(Imaging) 1

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

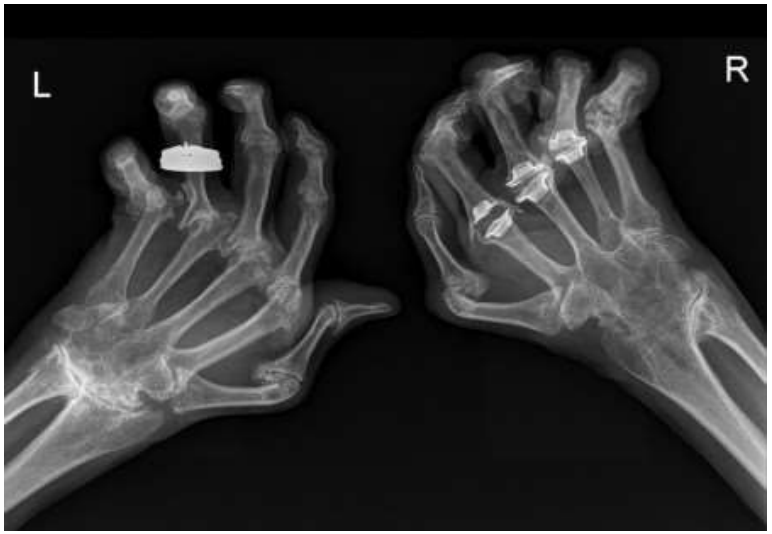
Diagnosis
(Imaging) 2

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Diagnosis

(Imaging: X-rays - Hands)

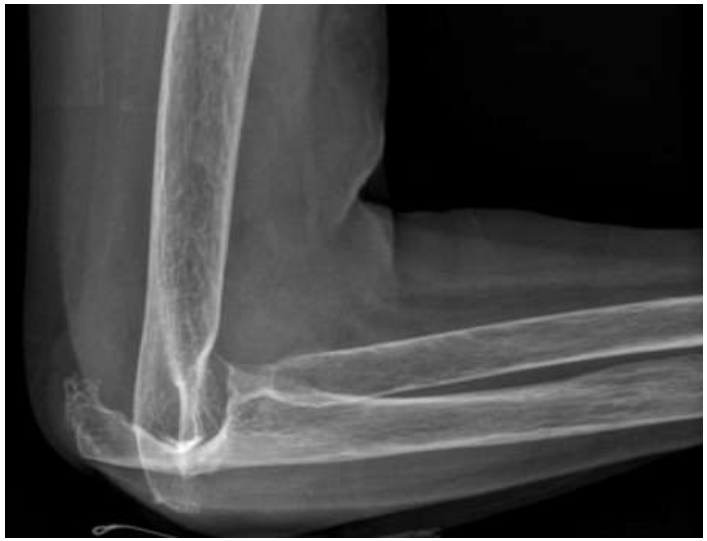


Extensive fusion (ankylosis) at both wrists – all of the carpal bones have fused. The patient has had previous joint replacements at the right 2nd, 3rd and 4th MCP joints, while on the left you can see erosions at the MCP joints, with ulnar subluxation.

http://www.svuhradiology.ie/case-study/rheumatoid-arthritis-hands/

Diagnosis

(Imaging: X-rays – Elbow)

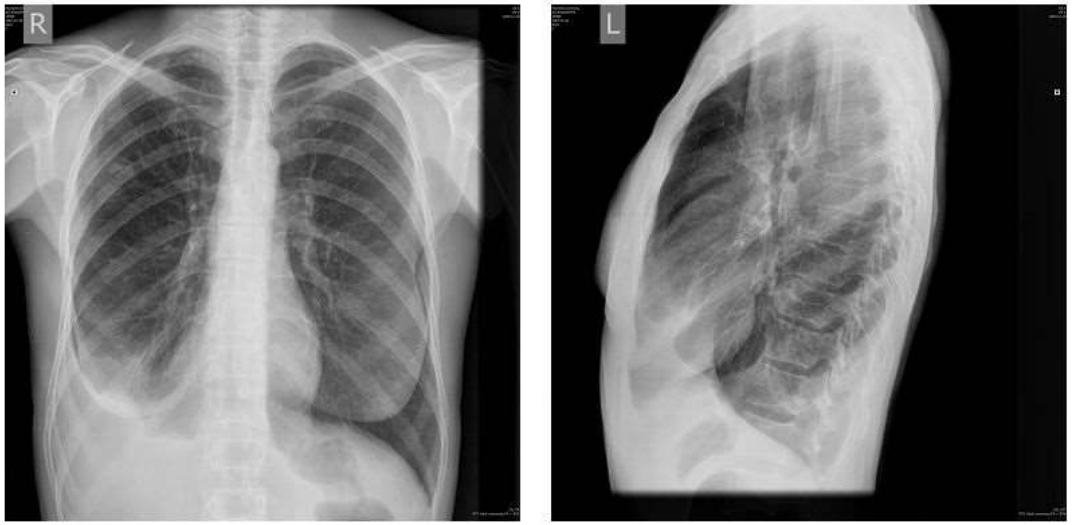


This patient's elbow has been severely eroded by RA – the olecranon now looks almost like a spoon, the radial head has disappeared, and the joint has become subluxed (partially dislocated) as a result.

http://www.svuhradiology.ie/case-study/rheumatoid-arthritis-hands/

Diagnosis

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

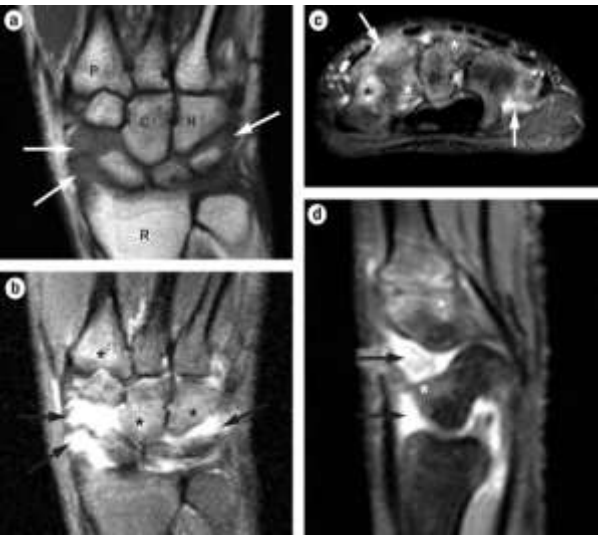


A 45 year old female was diagnosed with seropositive rheumatoid arthritis, and lung involvement. X-rays showed right pleural effusion and in upper-middle side of right lung there was 1.6 centimetres mass looked like rheumatoid nodule.

http://www.intechopen.com/books/innovative-rheumatology/extraskeletal-manifestations-in-rheumatoid-arthritis-clinical-cases

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);

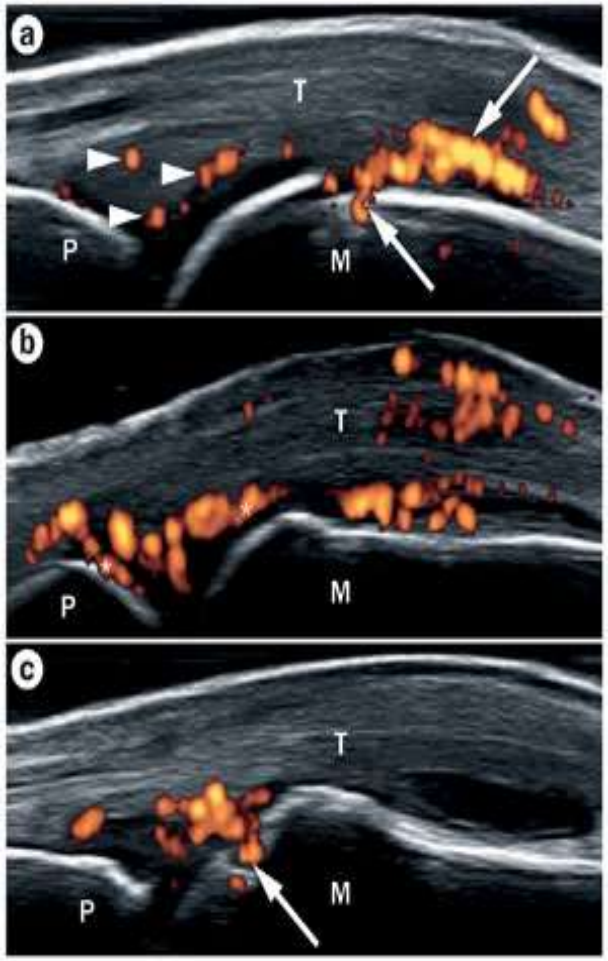
C-d) Enhancement of both thickened synovium (arrows) and enhancing, reactive bone marrow edema (asterisks).

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

http://www.intechopen.com/books/innovative-rheumatology/extraskeletal-manifestations-in-rheumatoid-arthritis-clinical-cases

Diagnosis

(Imaging: Power Doppler Ultrasound) 1

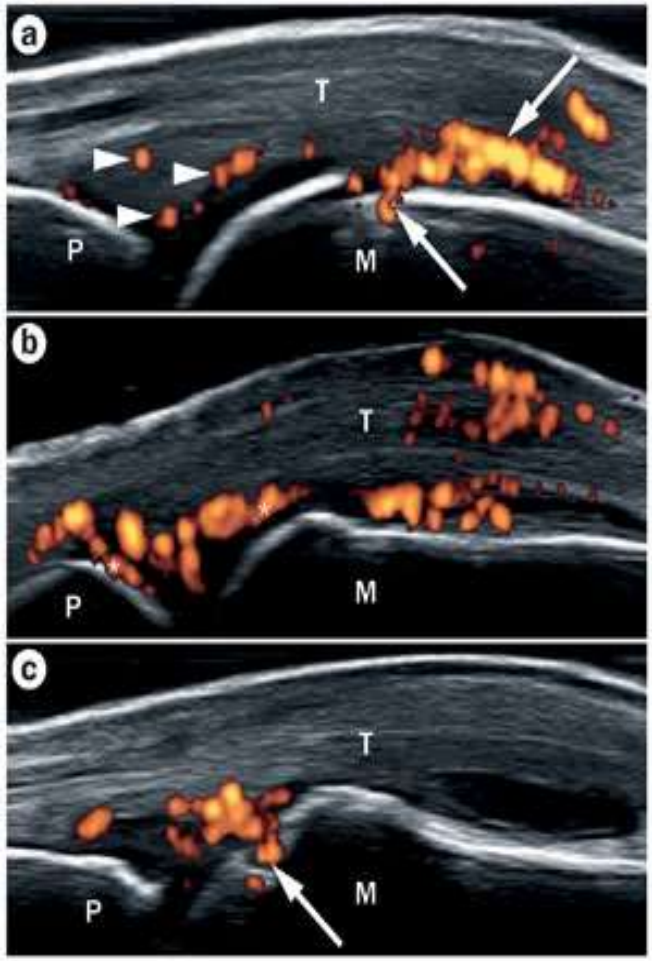


a) Very early arthritis: the power Doppler signal is distributed at the levels of both the fat pad (arrowheads) and feeding vessel (arrows).

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 (*).

http://www.nature.com/nrrheum/journal/v9/n4/fig_tab/nrrheum.2013.39_F1.html

Diagnosis
(Imaging: Power Doppler Ultrasound) 2



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.

http://www.nature.com/nrrheum/journal/v9/n4/fig_tab/nrrheum.2013.39_F1.html

Diagnosis
(Blood Tests) 1

- 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 etc.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Diagnosis
(Blood Tests) 2

- 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%.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Diagnosis
(Blood Tests) 3

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

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 *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive ACPA	3
C. Acute-phase reactants (at least one test result is needed for classification)[§§]	
Normal CRP *and* normal ESR 0	0
Abnormal CRP *or* normal ESR 1	1
D. Duration of symptoms[¶¶]	
<6 weeks	0
≥6 weeks	1

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

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.

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis
(2010 Rheumatoid Arthritis Classification: 3)

- † 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.

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis
(2010 Rheumatoid Arthritis Classification: 4)

- **§** 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.

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis

(2010 Rheumatoid Arthritis Classification: 5)

- ¶ '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.

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis

(2010 Rheumatoid Arthritis Classification: 6)

- ††† 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.

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis
(2010 Rheumatoid Arthritis Classification: 7)

- ‡‡ 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 of 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.

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis

(2010 Rheumatoid Arthritis Classification: 8)

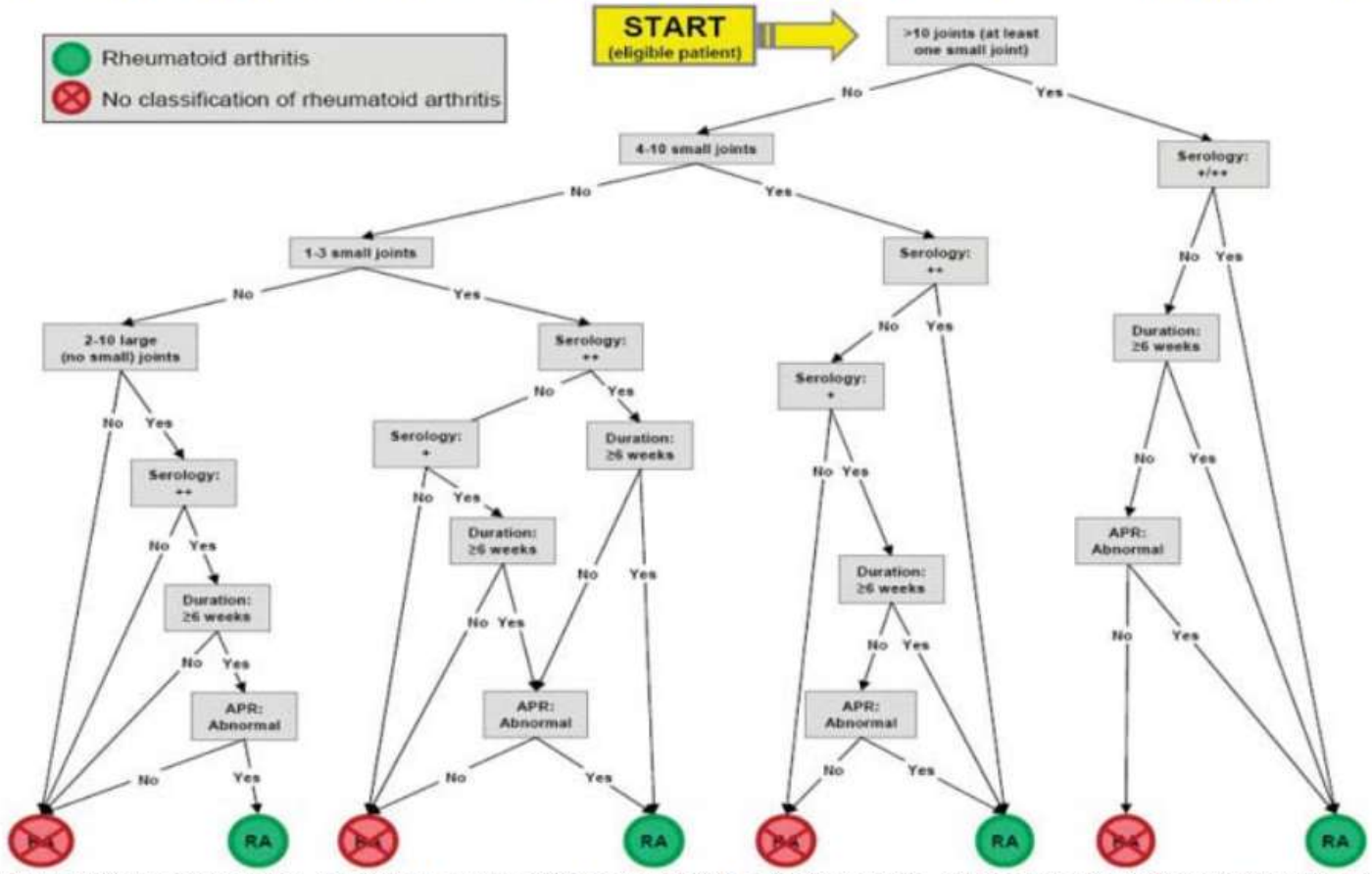
- **§§** Normal/abnormal is determined by local laboratory standards.
- **¶¶** Duration of symptoms refers to patient self-report of the duration of signs or symptoms of synovitis (e.g., pain, swelling, tenderness) of joints that are clinically involved at the time of assessment, regardless of treatment status.

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

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

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.

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis
(Monitoring Progression) 1

- Crystal induced arthritis (gout, and pseudogout).
- Osteoarthritis.
- Systemic lupus erythematosus (SLE).
- Psoriatic arthritis.
- Lyme disease.
- Reactive arthritis (previously Reiter's disease).

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis
(Monitoring Progression) 1

- Ankylosing spondylitis.
- Hepatitis C.
- Sarcoidosis, amyloidosis, and Whipple's disease.
- Hemochromatosis.
- Acute rheumatic fever.
- Bacterial arthritis.
- Gonococcal arthritis.

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis

(Clinical Disease Activity Index (CDAI)) 1

- **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)

http://www.rheumtutor.com/clinical-disease-activity-index-cdai/

Diagnosis

(Clinical Disease Activity Index (CDAI)) 2

- **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** CDAI ≤ 2.8
- **Low Disease Activity** CDAI > 2.8 and ≤ 10
- **Moderate Disease Activity** CDAI > 10 and ≤ 22
- **High Disease Activity** CDAI > 22

http://www.rheumtutor.com/clinical-disease-activity-index-cdai/

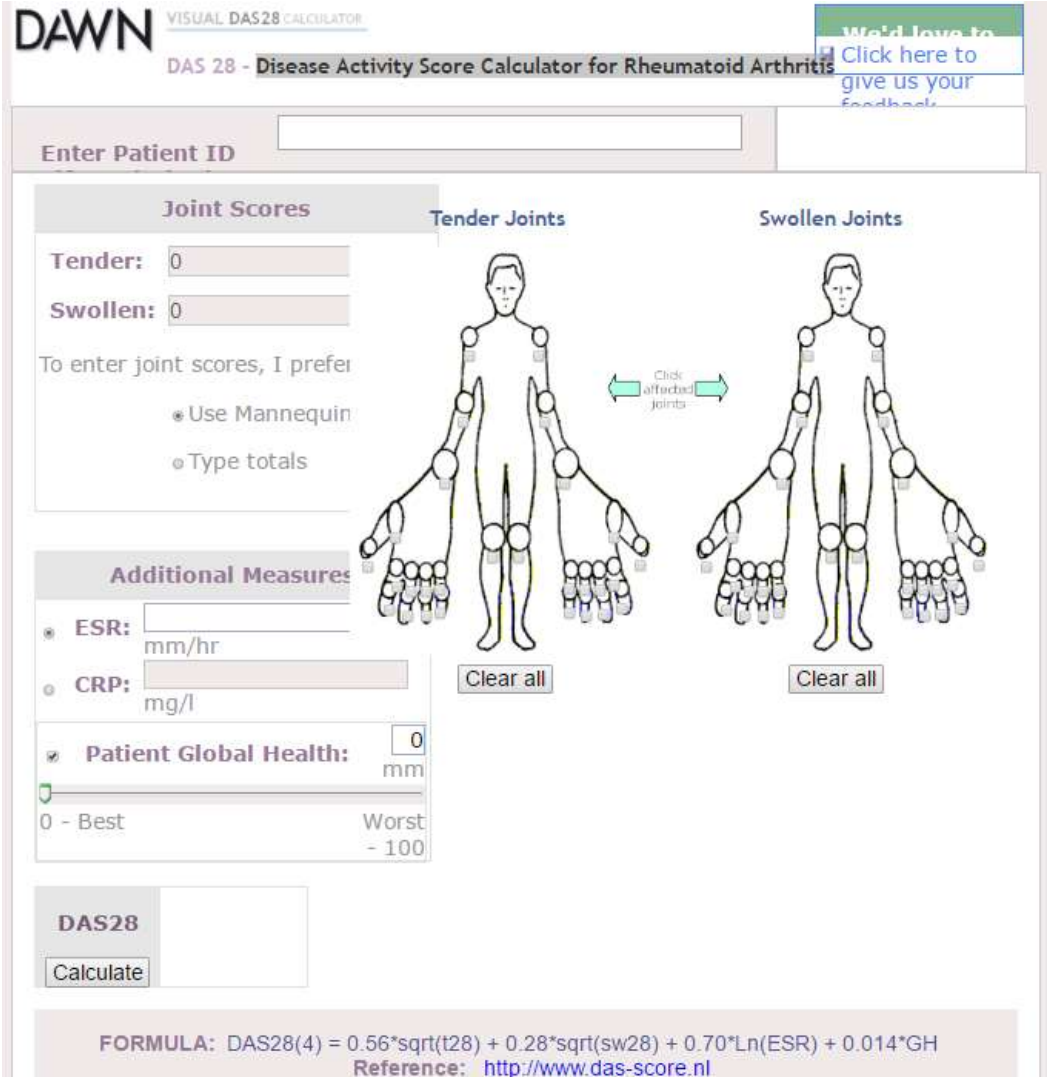
Diagnosis

(Clinical Disease Activity Index (CDAI)) 3

- 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)

http://www.rheumtutor.com/clinical-disease-activity-index-cdai/

Diagnosis
(Disease Activity Score Calculator for RA)



http://www.4s-dawn.com/DAS28/DAS28.html

Diagnosis
(Differential) 1

- Crystal induced arthritis (gout, and pseudogout).
- Osteoarthritis.
- Systemic lupus erythematosus (SLE).
- Psoriatic arthritis.
- Lyme disease.
- Reactive arthritis (previously Reiter's disease).

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Diagnosis
(Differential) 2

- Ankylosing spondylitis.
- Hepatitis C.
- Sarcoidosis, amyloidosis, and Whipple's disease.
- Hemochromatosis.
- Acute rheumatic fever.
- Bacterial arthritis.
- Gonococcal arthritis.

http://www.rheumatology.org/Portals/0/Files/2010%20Rheumatoid%20Arthritis%20Classification_EXCERPT%202010.pdf

Treatment
(General Principles) 1

- 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.

http://www.medscape.com/viewarticle/821404 https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Treatment
(General Principles) 2

- • 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.

http://www.medscape.com/viewarticle/821404 https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Treatment
(Lifestyle modification) 1

- 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.

http://www.rheumatology.org/Portals/0/Files/ACR%202015%20RA%20Guideline.pdf

Treatment
(Lifestyle modification) 2

- 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.

http://www.rheumatology.org/Portals/0/Files/ACR%202015%20RA%20Guideline.pdf

Treatment
(Patient Education) 1

- 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.

http://emedicine.medscape.com/article/331715-overview#a7

Treatment
(Patient Education) 2

- 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.

http://emedicine.medscape.com/article/331715-overview#a7

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.

http://www.medscape.com/viewarticle/821404_2

Treatment
(Target Remission or Low Disease Activity) 1

- 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.

http://www.medscape.com/viewarticle/821404_2

Treatment
(Target Remission or Low Disease Activity) 2

- 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.

http://www.medscape.com/viewarticle/821404_2

Treatment
(Target Remission or Low Disease Activity) 1

- 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.

http://www.medscape.com/viewarticle/821404_2

Treatment
(Target Remission or Low Disease Activity) 2

- 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.

http://www.medscape.com/viewarticle/821404_2

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.

http://www.medscape.com/viewarticle/821404

Treatment
(Disease modifying agents: 2)

- 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.

http://www.medscape.com/viewarticle/821404

Treatment

(Disease modifying agents: 3)

- 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.

http://www.medscape.com/viewarticle/821404

Treatment
(Disease modifying agents: 4)

- 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

http://www.medscape.com/viewarticle/821404

Treatment
(Disease modifying agents: 5)

- 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.

http://www.medscape.com/viewarticle/821404

Treatment
(Anti-inflammatory agents) 1

- 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.

http://www.medscape.com/viewarticle/821404

Treatment
(Anti-inflammatory agents) 2

- 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.

http://www.medscape.com/viewarticle/821404

Treatment
(Disease-Modifying Antirheumatic Drugs)

Nonbiologic DMARDS

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

Biologic DMARDS

TNF-inhibiting

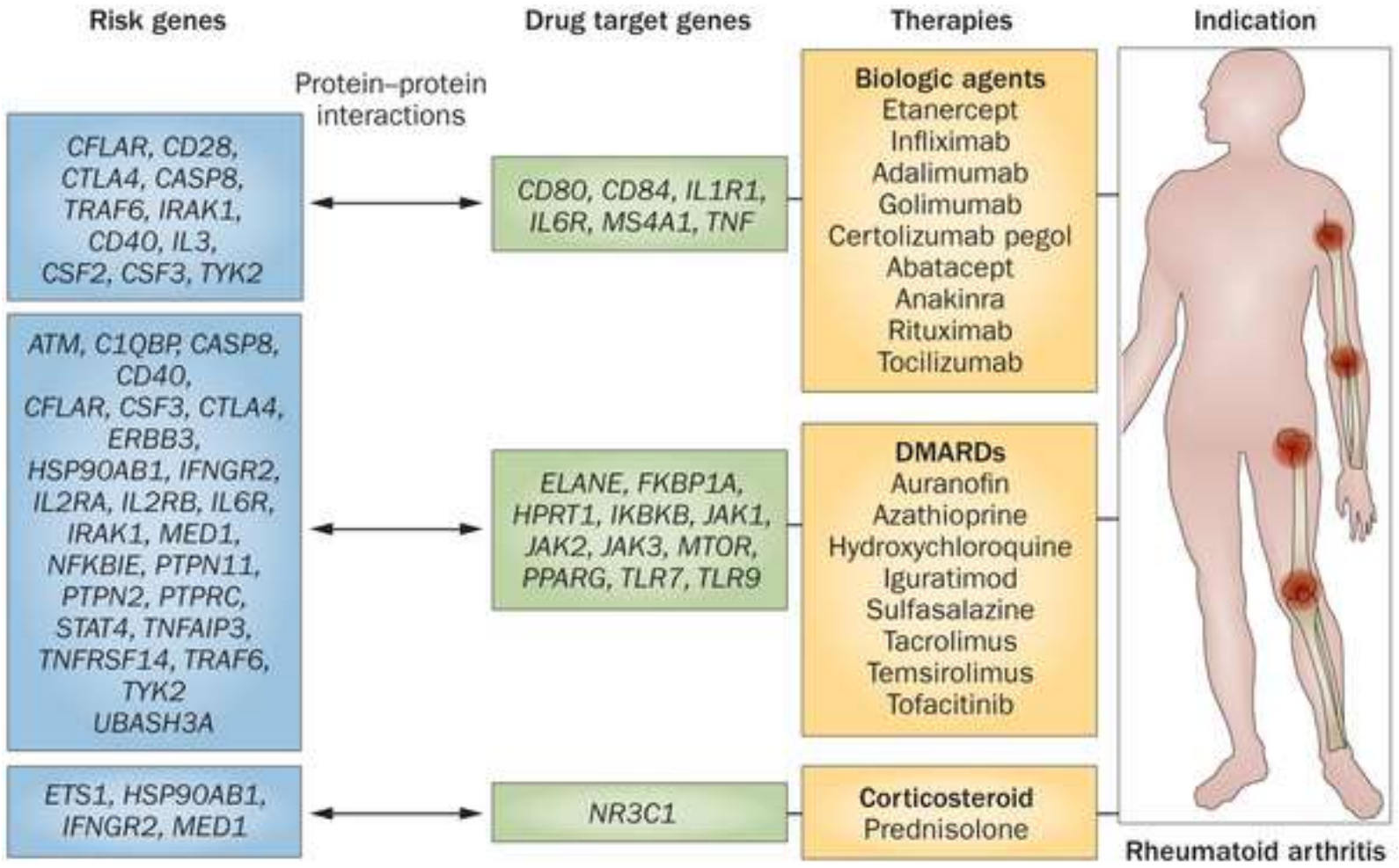
- Etanercept
- Infliximab
- Adalimumab
- Certolizumab
- Golimumab

non-TNF-inhibiting

- Rituximab
- Anakinra
- Abatacept
- Tocilizumab
- Tofacitinib

http://emedicine.medscape.com/article/331715-overview#a1

Treatment
(Risk Genes and Approved RA Drugs)



http://www.nature.com/nrrheum/journal/v11/n6/full/nrrheum.2015.7.html?message-global=remove

Treatment
(Surgery) 1

- 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.

http://www.medscape.com/viewarticle/821404

Treatment
(Surgery) 2

- Severely affected joints may require joint replacement surgery, such as knee replacement.
- Postoperatively, physiotherapy is always necessary.

http://www.medscape.com/viewarticle/821404

Treatment

(Nonpharmacologic, Nonsurgical therapies)

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

http://mymedsupply.com/wp-content/uploads/2015/03/Hot-and-Cold-Therapy-Shoulder.jpg http://emedicine.medscape.com/article/331715-overview#a1

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 theses needs.
- These families can benefit from the assistance of a home care aide or homemaker.

http://www.interimhealthcare.com/services/home-care/information/arthritis

Prognosis

- The clinical course of RA is generally one of exacerbations and remissions. 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, 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.

http://emedicine.medscape.com/article/331715-overview#a6 en.wikipedia.org/wiki/Heart_failure#Prognosis

Prophylaxis 1

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

Prophylaxis 2

- 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.

https://en.wikipedia.org/wiki/Rheumatoid_arthritis#Signs_and_symptoms

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