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# The Complete Guide: Rheumatoid Arthritis



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What is Rheumatoid Arthritis?

Definitions

Stages of Rheumatoid Arthritis

Four Areas of Diagnosis and Special Notes

Treatment

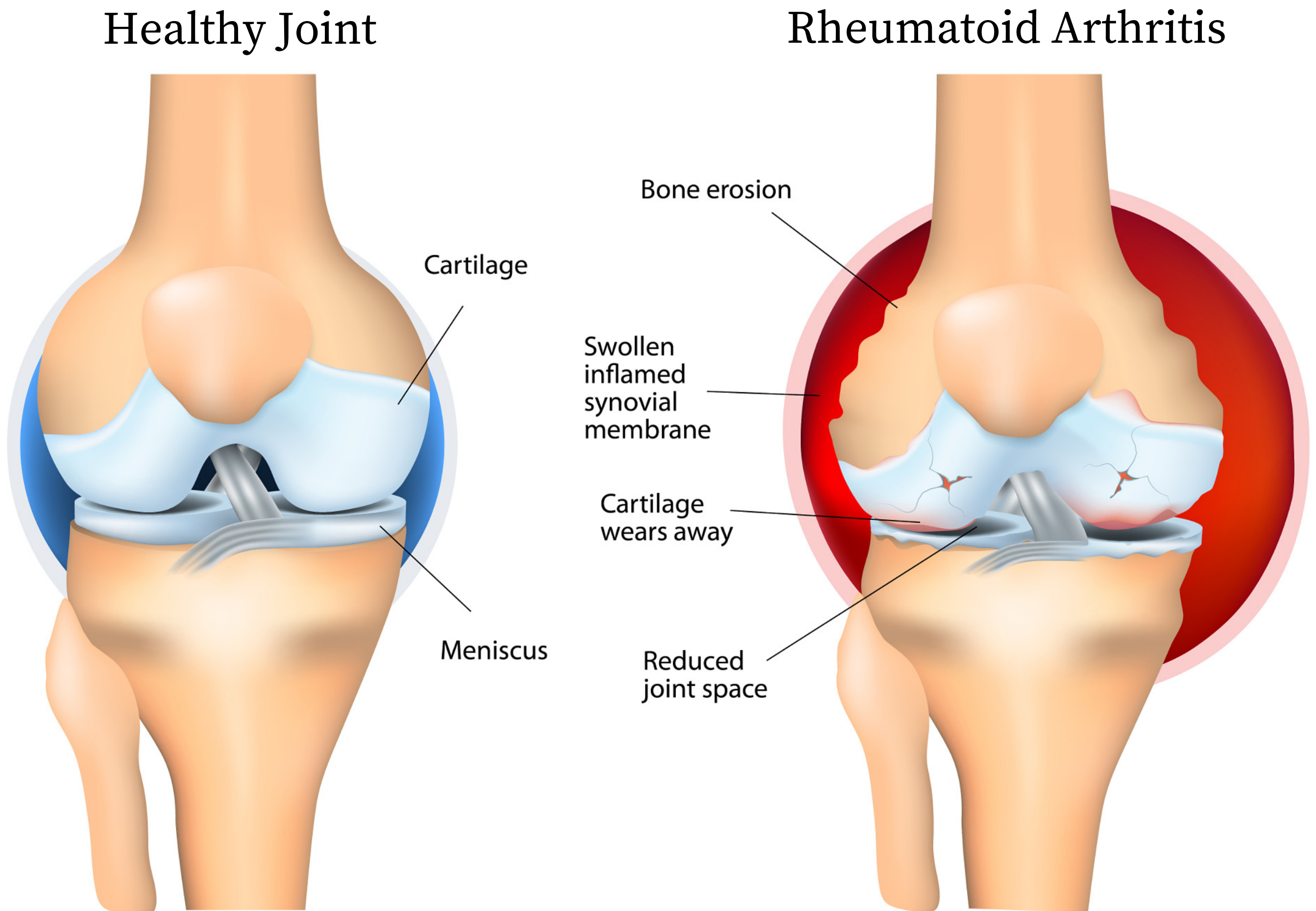
Biomarkers

Frequently Asked Questions



# What is Rheumatoid Arthritis?

Rheumatoid Arthritis is an autoimmune disease affecting the joints. The causes of Rheumatoid Arthritis are genetics (multiple suspects) and infectious agents (multiple suspects).



## Who is affected?

Men and women age 40-50 are most affected by Rheumatoid Arthritis.

## Symptoms may include:

- joint swelling
- tenderness and warmth surrounding joint
- joint pain and stiffness

Over time, multiple joints may be affected by Rheumatoid Arthritis and this results in polyarthrititis.

# Definitions

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**Active RA:** Patient is symptomatic, may or may not be flaring

**Inactive RA:** Patient is asymptomatic

**Flare:** Worsening of a patient's RA symptoms over their baseline symptoms

**Remission:** Recession of symptoms for any given period of time

**Prolonged remission:** Sudden disease onset followed by many consecutive years with no symptoms

**Acute phase:** High levels of inflammation and acute phase in RA is indicated by high levels of the inflammatory biomarkers CRP and ESR (\*see Biomarkers)

**ab:** antibodies

**DMARDs:** Disease-Modifying Antirheumatic Drugs suppress the immune system non-selectively to inhibit joint damage

**Biologics:** Drugs engineered to target specific components of the immune system in order to suppress them and control the overactive immune functions responsible for RA

**Anti-TNFs:** Biologic drugs designed to inhibit RA specific inflammation by blocking Tumor Necrosis Factor, a mediator of the inflammatory response implicated in RA

**Lymphocyte depleting agent:** Refers to biologic Rituximab, a drug designed to inhibit B cell lymphocytes in treating autoimmune disorders like RA and SLE, but not commonly prescribed and typically used in conjunction with methotrexate

**SDAI:** Simplified Disease Activity Index

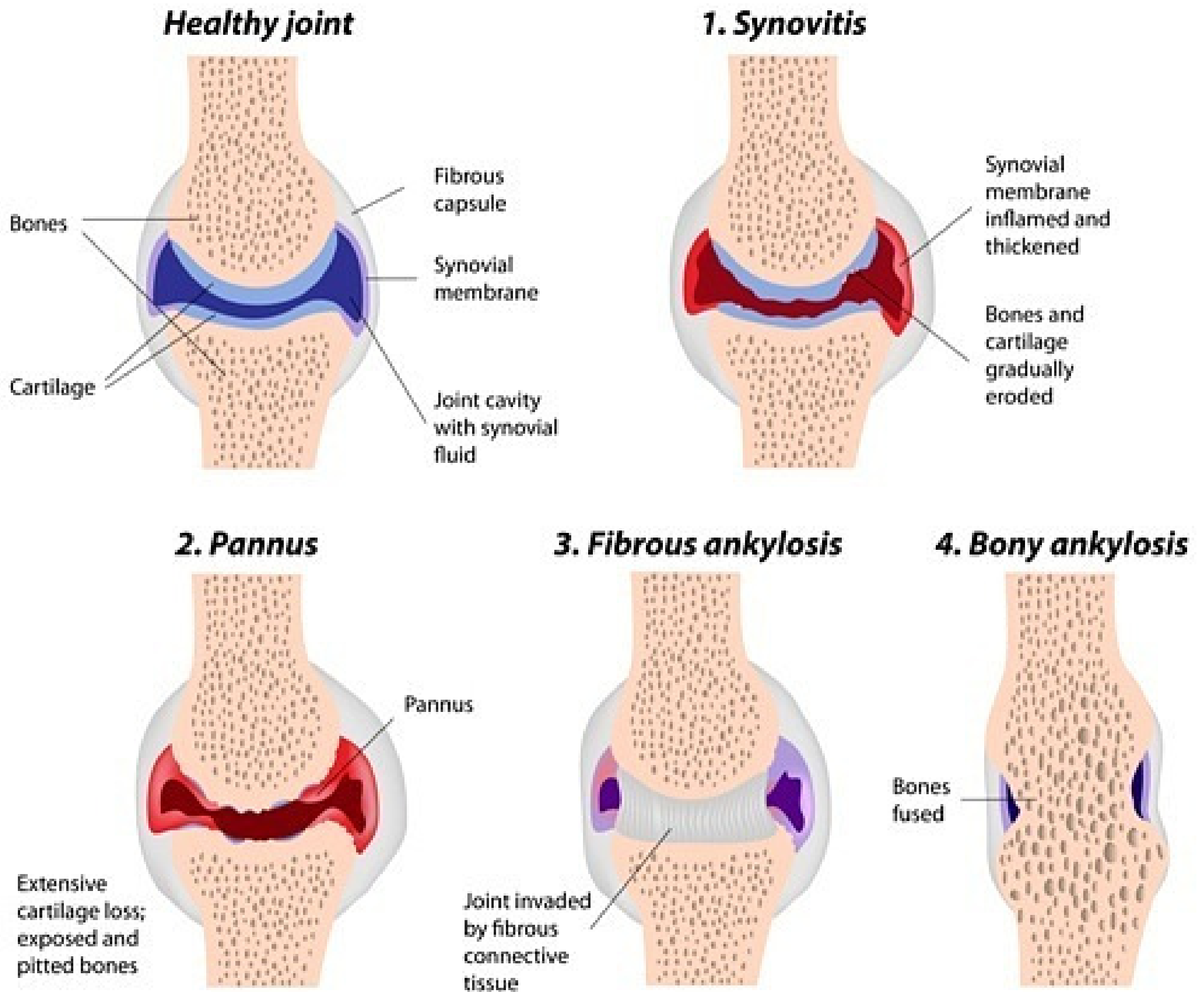
**CDAI:** Crohn's Disease Activity Index

**DAS:** Disease Activity Score

**DAS28:** 'disease activity score' and the number 28 refers to the 28 joints that are examined in the assessment



## Stages of Rheumatoid Arthritis



Early Stage = Patient has evidence of inflammation for no more than 6 months. Treatment is aimed to protect joints and control inflammation

Persistently Active = Patient has evidence of inflammation for 6 to 12 months and may have irreversible joint damage. Treatment goals are same as Early Stage RA.

End Stage = Patient has little or no inflammation but severe joint damage and loss of function. Treatment aims to reduce pain and additional joint damage.

# Four Areas of Diagnosis

## Joint Involvement

The first stage covers joint involvement, designating the metacarpophalangeal joints, proximal interphalangeal joints, the interphalangeal joint of the thumb, second through fifth metatarsophalangeal joint and wrist as small joints, and shoulders, elbows, hip joints, knees, and ankles as large joints:

- Involvement of 1 large joint gives 0 points
- Involvement of 2–10 large joints gives 1 point
- Involvement of 1–3 small joints (with or without involvement of large joints) gives 2 points
- Involvement of 4–10 small joints (with or without involvement of large joints) gives 3 points
- Involvement of more than 10 joints (with involvement of at least 1 small joint) gives 5 points

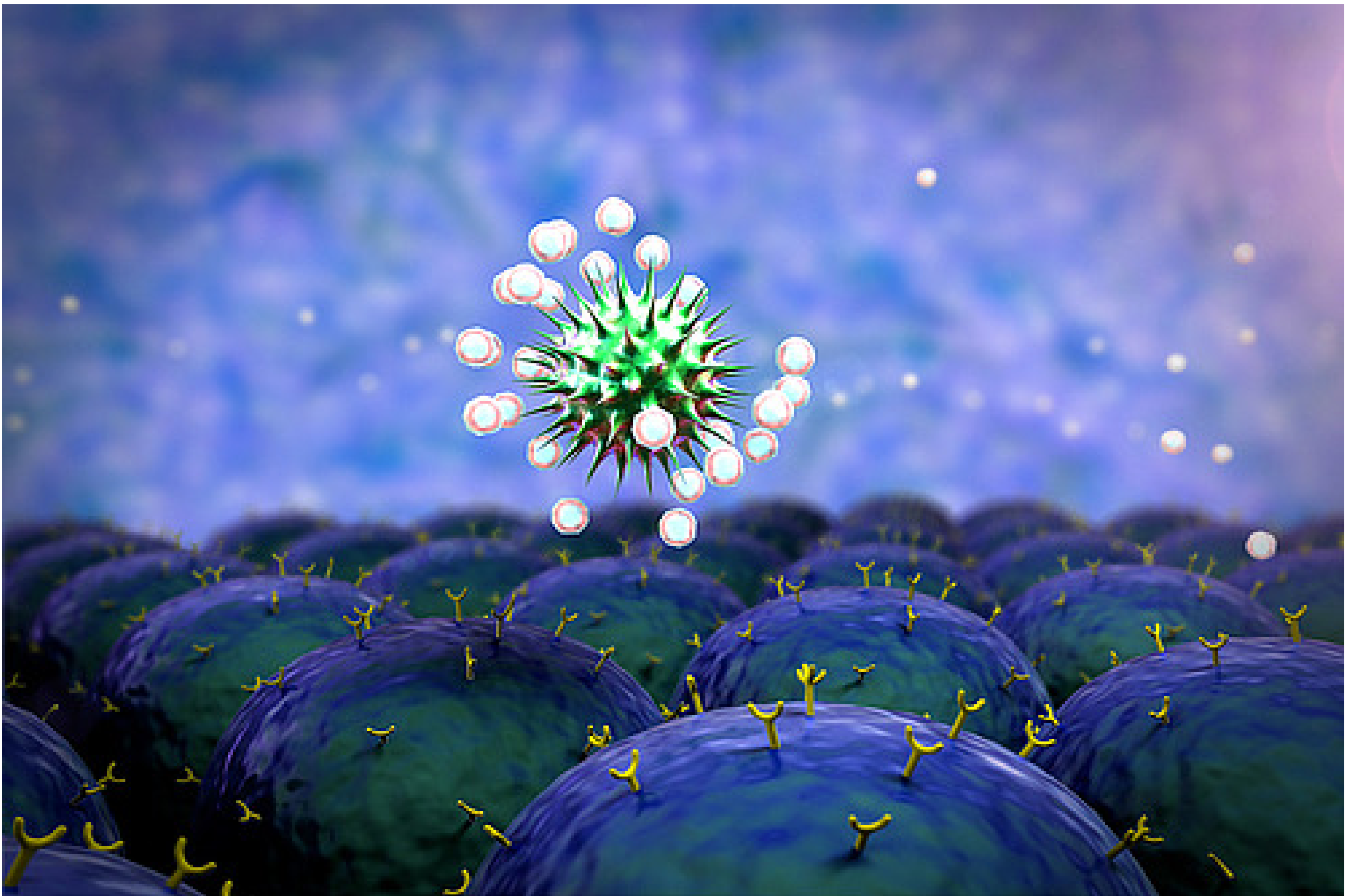
# Four Areas of Diagnosis

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## Serological Parameters

The second stage includes the Rheumatoid Factor (RF) as well as ACPA. "ACPA" stands for "anti-citrullinated protein antibody":

- Negative RF and negative ACPA gives 0 points
- Low-positive RF or low-positive ACPA gives 2 points
- High-positive RF or high-positive ACPA gives 3 points





# Four Areas of Diagnosis

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## Acute Phase Reactants

This area includes:

- 1 point for elevated erythrocyte sedimentation rate (ESR) or elevated C-Reactive Protein (CRP) value



### **Special Note:**

Required: 4+ of these 7 criteria existing for at least 6 months :

- (1) morning stiffness for at least 1 hour
- (2) swelling of 3+ joints simultaneously
- (3) 1+ swollen area in wrist, hand or finger
- (4) symmetric arthritis
- (5) rheumatoid nodules
- (6) high rheumatoid factor blood level
- (7) X-ray indication of involved joint damage



# Four Areas of Diagnosis

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## Duration of Arthritis

This area includes:

- 1 point for symptoms lasting six weeks or longer



### Special Note:

Diagnosing RA is very difficult. The average time between onset of symptoms & diagnosis is about 9 months. RA shares symptoms with other diseases (gout, fibromyalgia, SLE, synovitis) making diagnosis tricky. Physicians will normally perform complete blood test (CBC), careful history and physical exam, and X-ray analysis to confirm a diagnosis.

# Prognosis

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## Poor prognosis factors

- Persistent synovitis
  - Early erosive disease
  - Extra-articular findings (including subcutaneous rheumatoid nodules)
  - Positive serum RF findings
  - Positive serum anti-CCP autoantibodies
  - Carrier ship of HLA-DR4 "Shared Epitope" alleles
  - Family history of RA
  - Poor functional status
  - Socioeconomic factors
  - Elevated acute phase response (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP])
- Increased clinical severity



# Treatment

Analgesics	Analgesics is a standard type of treatment and acetaminophen is the drug used for this treatment. The dosage is 500 - 1000mg per day and the side effects may include itching, rash, and jaundice.
NSAIDs	NSAIDs is a primary form of treatment and ibuprofen, naproxene, celebrex, are the drugs most commonly associated with this type of treatment. The dosage varies. Side effects may include internal bleeding, kidney damage, and liver damage.
Steroids	Steroids are another primary form of treatment. Prednisone is often prescribed at a dosage of 10mg/day for the highest points. Side effects may include anxiety, insomnia, and abdominal pain.
DMARDs	DMARDs is a secondary type of treatment that uses Methotrexate, sulfasalazine, and hydroxychloroquine. The dosages for these drugs are as follows: Methotrexate: 15-30mg/week, Sulfasalazine: 2-3g/day Hydroxychloroquine: 400-600mg/day. Side effects may include kidney damage, heart attack, stroke, and brain damage.
Biologics	Another secondary form of treatment is Biologics. The treatment generally includes: Enbre l (TNF), Humira (TNF), Kineret (IL-1), and Remicade (TNF). The dosage is as follows: Humira: 40mg every 2 weeks Kineret: 100mg/day, Enbrel: 50 mg/week, Remicade: 3-10mg every 4-8 wks. Side effects may include: pain at injection site, infections, cough, and headache.

# Biomarkers

**Rheumatoid Factor (RF)**

The normal/negative level is 20-30 IU/mL Levels over normal indicate autoimmunity, specifically RA.

**C-reactive protein (CRP)**

The normal/negative level is 5-6 mg/mL Levels over normal indicate RA.

**Anti-cyclic citrullinated peptide (anti-CCP)**

The normal/negative level is <20 IU/mL Levels over normal indicate RA.

**Erythrocyte Sedimentation Rate (ESR)**

The normal/negative level is 20mm/hr Levels over normal indicate inflammatory disorder.

**Alpha-1-antitrypsin (AAT)**

The normal/negative level is 170-230 mg/dL Levels over normal indicate RA.

**IgM**

The normal/negative level is 50-220 mg/dl Levels over normal indicate RA.





# FAQ's

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**What are the lines of treatment for RA?**

The answer depends on the severity of an individual patient's RA. If diagnosed early and at a relatively juvenile stage, the first line of treatment is anti-inflammation via NSAIDs and steroids. If the RA progresses to a more advanced stage – or was already advanced at time of diagnosis – the first line of treatment are DMARDs and/or biologics.

**What are the most common drugs given for RA?**

Besides analgesics and NSAIDs, which vary greatly from patient-to-patient, the most commonly given drug to treat RA at this time is methotrexate. Of the biologics, Humira, Enbrel and Simponi compete for the title of most commonly used.

Only 10% of RA patients are on NSAID treatment alone.

**What is TNF?**

Tumor Necrosis Factor (TNF) is a type of protein known as a “cytokine” that is involved in the inflammatory reactions of RA. TNF-blockers are biologic drugs designed to bind to TNF and thereby inhibit it from instigating inflammation. TNF-blockers include:

Eternacept/Enbrel, Infliximab/Remicade, Adalimumab/Humira, Golimumab/Simponi, Abatacept/Orencia, Certolizumab/Cimzia, Tocilizumab/Actemra.

What is RF?

Rheumatoid Factor (RF) is an antibody directed against the body's own tissue. It plays a role in many inflammatory reactions, including those of RA but also including many others. 70-80% of RA patients have high RF levels. A high RF level is anything above 20 IU/ml. RF can exist in any antibody form: IgA, IgG, IgE, IgM and/or IgD. Amount of RF generally correlates to severity of the disease.

What about RA indices?

This table summarizes the 4 main indices used in research to assess RA.

Validity of SDAI and CDAI in RA/ D. Aletaha & J. Smolen

Table I. Elements of composite indices and their potential contributions\* to the total index.

Elements	SDAI	CDAI	DAS	DAS28
Number of swollen joints	Simple count (0-28)	Simple count (0-28)	More extensive joint counts (0-2.86)	Simple count, square root transformed (0-1.48)
Number of tender joints	Simple count (0-28)	Simple count (0-28)	Ritchie Index: graded joint counts; square root transformed (0-4.77)	Simple count; square root transformed (0-2.96)
Acute phase reactants	CRPin mg/dL (0.1-10.0)	–	ESR, log transformed (0.23-1.51)**	ESR, log transformed (0.49-3.22)**
Patient global health	–	–	VAS in mm (0-0.72)**	VAS in mm (0-1.40)**
Patient global disease activity	VAS in cm (0-10.0)	VAS in cm (0-10.0)	–	–
Evaluator global disease activity	VAS in cm (0-10.0)	VAS in cm (0-10.0)	–	–
Total index	No immediate scoring due to CRP; simple calculation possible (0.1-86.0)	Immediate scoring possible; simple calculation possible (0-76.0)	No immediate scoring due to ESR; calculator required (0.23 – 9.87)	No immediate scoring due to ESR; calculator required (0.49-9.07)

\*Based on the transformation and weighting of individual elements according to the formula of the respective index; assumed ranges are 2 to 100mm/h for ESR, and 0.1 to 10mg/dLfor CRP.  
\*\*The DAS and DAS28 formulae have also been modified to include CRPinstead of ESR, and to substitute the patient global health by a constant. These versions are less commonly used and not well validated.

Aletaha, D. and J. Smolen. The Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI): A review of their usefulness and validity in rheumatoid arthritis. Clinical and Experimental Rheumatology (2005): 100-108.



# FAQ's

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**How are Mild, Moderate and Severe Active RA defined?**

There is no clear consensus on this issue; however, the general guidelines followed by physicians are:

Mild RA = A person with Mild RA has some of these symptoms: joint pain, inflammation of 3+ joints w/ no inflammation in other tissues, negative RF test, elevated ESR or CRP levels, and no bone and/or cartilage damage

Moderate RA = A person with Moderate RA has a combination of these symptoms: 6-20 inflamed joints w/ no inflammation in other tissues, elevated ESR or CRP levels, positive RF test or positive anti-CCP test, and no bone and/or cartilage damage

Severe RA = A person with Severe RA has one or more of these symptoms: 20+ persistently inflamed joints w/ inflammation in other tissues, rapid loss of functional ability, elevated ESR or CRP levels, anemia related to chronic illness, low blood albumin level, positive RF test, and bone and/or cartilage damage

**What is the typical washout period between RA medications?**

Biologics: no washout period. Methotrexate: 3 to 6 months, but in many cases doctors will switch medications immediately.

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**Conversant Healthcare Systems, Inc. (Conversant Bio)**  
601 Genome Way, Suite 1200, Huntsville, AL 35806  
(866) 838-2798 phone  
[www.conversantbio.com](http://www.conversantbio.com)

To find out how we can help with your research needs, email us at [sales@conversantbio.com](mailto:sales@conversantbio.com)

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