Rheumatoid Arthritis

Media backgrounder

What is Rheumatoid Arthritis (RA)?

- Rheumatoid arthritis (RA) is a chronic autoimmune disease characterised by inflammation in the synovium (lining of the joints), which causes joint damage, chronic pain, stiffness, swelling and fatigue.1,2
- RA often affects the hands or wrists, but can also affect the elbows, shoulders, neck, knees, hips, feet and ankles, resulting in a limited range of motion and decreased joint function,1,3 impairing daily life.
- It is a systemic disease which means that disease progression can affect the whole body and internal organs.1
- The cause of RA is unknown.1 However, a lot is known about the mechanisms that cause the inflammation in RA.
- RA occurs when white blood cells build up inside joints causing inflammation with the release of cytokines (signalling molecules).
- These molecules attach themselves to the thin synovium causing pain, joint swelling, and joint damage.4
- RA can last a lifetime3 and, although there is no cure for RA, early treatment and management of the disease can delay disease progression for many years.

Prevalence & Incidence

- RA affects up to 1% of the world’s population,5 including more than 2.9 million people in Europe.6
- The disease is more common in women (who account for 75% of patients diagnosed with RA) than in men.3
- People might be more susceptible to developing RA as a result of genetics or environmental factors such as previous injury, infection and smoking.7 RA occurs more frequently in developed countries5 but all ethnic groups are at risk.3
- Many people who are diagnosed with RA are of working age.6 Although the disease often begins in middle age and increases in prevalence amongst older people, young adults can also develop RA.3

Causes & symptoms of RA

- The cause of RA is not yet known.1 However, it seems that people who inherit certain genes are more susceptible than others to the disease.4
It is thought that T-cells play an important part in the development of the disease. When T-cells are activated, they interact with B-cells, which can produce cytokines and enzymes that will progressively destroy bone and cartilage.  

Symptoms of RA include joint swelling, pain, morning joint stiffness, poor sleep, fatigue and loss of weight.

What is the impact of RA?

- Joint damage caused by rheumatoid arthritis may lead to loss of movement resulting in poorer quality of life, inability to work, higher medical costs and potential surgery.
- 89% of patients with RA have reported detrimental effects on income, leisure activity and social independence.
- Over half of people with rheumatoid arthritis have to give up their job within six years of being diagnosed because of their disease.
- Many people with RA experience some degree of depression and/or anxiety.
- There is an increase in morbidity and mortality among RA patients.

What are the current, approved treatment options?

- Early diagnosis is particularly important if RA is to be managed effectively.
- A variety of treatments currently exist for RA:
  - **Analgesics** – painkillers which are useful as an addition to more specific drugs to relieve pain.
  - **Nonsteroidal anti-inflammatory drugs (NSAIDS)** – can be effective at controlling pain and stiffness. Signs and symptoms can be improved, however, they do little to slow the structural progression and the long-term disability associated with RA.
  - **Corticosteroids** – exhibit a powerful effect on reducing inflammation, however managing side effects can be problematic if given in high doses over a long period of time.
  - **Disease-modifying anti-rheumatic drugs (DMARDs)** – appear to slow down disease progression by suppressing the inflammation in the joints. DMARDs may be classified in two ways:
    - Conventional DMARDs, for example methotrexate and sulfasalazine
    - Biological DMARDs, which include abatacept, rituximab, adalimumab, etanercept, infliximab and tocilizumab, golimumab, certulizumab. A number of sub-categories of biological DMARDs exist:
      - T-cell selective co-stimulation modulator (e.g. abatacept) – modulates one of the two signals that activates T-cells, which play a major role in the development of RA
      - Anti-TNFα (e.g. adalimumab, certolizumab, etanercept, golimumab and infliximab) – targets a protein called tumour
necrosis factor, which increases inflammation when excess amounts are present in the blood or joints

- B-cell depletion (e.g. rituximab) – removes B-cells which make antibodies which are involved in the inflammatory process in RA.
- Anti-interleukin (IL)-6 monoclonal antibodies (e.g. tocilizumab) – blocks the action of the IL-6 protein which is involved in the development of immunological and inflammatory reactions related to RA
Adaptive and Innate Immune Processes within the Joint in Rheumatoid Arthritis
Mechanisms That Contribute to Clinically Observed Long-Term Complications in Patients with Rheumatoid Arthritis

Liver
- Acute-phase response (CRP)
- Iron redistribution (hepcidin)

Fat
- Free fatty acid
- Adipocytokines
- TNF-α
- Interleukin-6

Muscle
- Insulin resistance

Bone
- Low bone mineral density
- Fractures

Blood vessels
- Complement immune complexes
- Interleukin-6
- TNF-α
- Atherogenesis
- Myocardial infarction
- Stroke

Brain
- SERT
- HPA axis
- Low stress tolerance
- Depression

Liver:
- Lipid particles altered
- Proinflammatory HDL phenotype
- Total cholesterol decreased
- Small LDL increased

Bone:
- Low bone mineral density

Brain:
- SERT
- HPA axis
- Low stress tolerance
- Depression
References


