RHEUMATOID ARTHRITIS

A long-term autoimmune disorder that primarily affects joints.

Related Diagnoses:
Klinefelter syndrome

About Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic, autoimmune, and complex inflammatory disease leading to bone and cartilage destruction.

It typically results in warm, swollen, and painful joints. Pain and stiffness often worsen following rest. Most commonly, the wrist and hands are involved, with the same joints typically involved on both sides of the body. The disease may also affect other parts of the body. This may result in a low red blood cell count, inflammation around the lungs, and inflammation around the heart. Fever and low energy may also be present. Often, symptoms come on gradually over weeks to months.

While the cause of rheumatoid arthritis is not clear, it is believed to involve a combination of genetic and environmental factors. The underlying mechanism involves the body's immune system attacking the joints. Inflamed joints are infiltrated by a population of cellular and mediators of the immune system, such as T cells (a type of white blood cells), B cells (a type of white blood cells), macrophages (a type of white blood cells), cytokines, and prostaglandins (PGs). This results in inflammation and thickening of the joint capsule. It also affects the underlying bone and cartilage.
The diagnosis is made mostly on the basis of a person's signs and symptoms. X-rays and laboratory testing may support a diagnosis or exclude other diseases with similar symptoms.

When RA is clinically suspected, testing for the presence of rheumatoid factor (RF, a non-specific antibody) and ACPAs (measured as anti-CCP antibodies) may be required. A negative RF or CCP antibody does not rule out RA; rather, the arthritis is called seronegative. This is the case in about 15-25% of people with RA. During the first year of illness, rheumatoid factor is more likely to be negative with some individuals converting to seropositive status over time.

The goals of treatment are to reduce pain, decrease inflammation, and improve a person's overall functioning. Combating rheumatoid arthritis normally consists of medicinal interventions, lifestyle changes, and conservative treatments to manage symptoms and provide pain relief for patients. In more severe cases of rheumatoid arthritis, surgery is indicated.

**Associated diseases**

**Anemia**

Anemia is a decrease in the total amount of red blood cells or hemoglobin (the molecule in red blood cells that carries oxygen) in the blood.

Anemia is a relatively common feature of RA. It has been shown that treatment significantly improves hemoglobin level. In patients with persistent anemia (anemia that persist for 6 months and longer), an erythropoietin (a protein that controls a red blood production) therapy may be considered.

**Amyloidosis**

Amyloidosis is a rare disease that occurs when a substance called amyloid builds up in organs. Secondary amyloidosis occurs during chronic inflammation such as in patients with RA, who have long and very active aggressive course of disease.

The diagnosis of secondary amyloidosis is based on histological examination of tissue from fat tissue, upper gastro intestinal duct or rectum. The most common presentation in amyloid is renal. Renal involvement in RA patient with amyloidosis is approximately 90% of all. Almost every patient with renal involvement has proteinuria (the presence of excess proteins in the urine).

The amyloid can be also present in spleen and liver. However, even severe damage of liver and spleen is usually without symptoms. Heart involvement
occurs in 10% patients with RA.

**Sjögren's syndrome**

Sjögren’s syndrome (SS) is a chronic autoimmune inflammatory disease that affects lacrimal and salivary glands causing mucous dryness. The symptoms are related to diminished lacrimal and salivary gland function. SS can cause also systemic manifestations.

**Osteoporosis**

Local osteoporosis occurs in RA around inflamed joints. It is postulated to be partially caused by inflammatory cytokines (a broad and loose category of small proteins that are important in cell signaling). More general osteoporosis is probably contributed to by immobility, systemic cytokine effects, local cytokine release in bone marrow and corticosteroid therapy.

**Complications**

**Rheumatoid vasculitis**

Rheumatoid vasculitis (an inflammation of blood vessels) is a rare but most serious systemic complication of rheumatoid arthritis. It typically affects small and medium-size vessels. It occurs almost exclusively in patients with seropositive nodular RA who suffer from RA for at least 10 years and is associated with poor prognosis. 40% of patients die within 5 years as well as significant mortality due to both organ damage from vasculities and consequences of the treatment.

**Cardiovascular diseases**

People with RA are more prone to atherosclerosis (hardening of the arteries), and risk of myocardial infarction (heart attack) and stroke is markedly increased. Other possible complications that may arise include: pericarditis (an inflammation of the thin saclike membrane surrounding heart), endocarditis (inflammation of the inner layer of the heart).

**Complications during pregnancy**

More than 75% of women with rheumatoid arthritis have symptoms improve during pregnancy but might have symptoms worsen after delivery. Methotrexate and leflunomide (drugs used as a treatment of rheumatoid arthritis) are teratogenic (harmful to foetus) and not used in pregnancy.
It is recommended women of childbearing age should use contraceptives to avoid pregnancy and to discontinue its use if pregnancy is planned.

**Risk factors**

Although the cause of RA remains unclear, it is believed that both genetic and environmental factors contribute to its development and progression.

A family history of RA increases the risk around three to five times; as of 2017 it was estimated that genetics may account for between 40 and 65% of cases of seropositive RA, but only around 20% for seronegative RA.

One major environmental risk factor is smoking. Smoking increases the risk of developing classical RA. Other potential environmental risk factors include a low alcohol intake and oral contraceptive use.

No infectious agent has been consistently linked with RA and there is no evidence of disease clustering to indicate its infectious cause, but periodontal disease (an inflammatory condition of the gum and bone support surrounding the teeth) has been consistently associated with RA.

### Impact on fertility

The impact of rheumatic disease on fertility and reproduction can be remarkable. Many disease-related factors can influence patients’ sexual functioning, perturb fertility and limit family planning.

**Female fertility**

As such, issues regarding family planning and pregnancy are an important part of the management of these patients. Not only does pregnancy itself cause physiologic and immunologic changes that impact disease activity, but also women with RA face the additional challenges of reduced fecundity and worsened pregnancy outcomes.

Women with rheumatic diseases have a lower number of births, a reduced period of reproduction and a longer inter-pregnancy interval with difficulties in achieving subsequent pregnancy, in comparison with healthy controls. Many female rheumatoid arthritis (RA) patients attempting to conceive have a time to pregnancy longer than 12 months. During this period RA often cannot be treated optimally.
Anti-Müllerian hormone (AMH), produced by ovarian granulosa cells, is a well-established marker of ovarian reserve (a term that is used to determine the capacity of the ovary to provide egg cells that are capable of fertilization). Common RA treatment could negatively impact ovarian reserve. This can lead to irregular ovulation, which is crucial moment for conception.

Decreased libido, or infrequent sex due to pain and fatigue are other possible explanations of reduced fertility in women with rheumatoid arthritis. Delivery by cesarean section has been demonstrated to be more common among women with RA across multiple cohorts with wide-ranging geographic locations.

Male fertility

In men, acute flares of rheumatoid arthritis can temporally reduce sperm count and function thus causing erection problems and decreased libido. The reproduction potential of male patients is impaired by the disease directly in the testicular tissue or by immunosuppressive therapy. The evaluation of male subjects should rely on careful medical history, complete physical examination, semen analysis and sexual hormone profile.

In optimally treated patients, fertility is probably normal. For both genders, treatment improves symptoms affecting sexual function symptoms, but also may have side effects.

Drug treatment is probably the main factor for gonadal dysfunction. Some drugs can cause reversible infertility, such as nonsteroidal anti-inflammatory drugs in women and sulfasalazine/methotrexate in men whereas irreversible (permanent) infertility is occasionally observed after treatment with alkylating agents (cyclophosphamide-CYC and chlorambucil) in both genders. When fertility is an issue, alkylating agents should be used at lowest possible dose and alternative therapies (such as azathioprine or mycophenolate mofetil) must be considered.

Anti-rheumatic pharmacological treatment can also have a crucial role in this field. Proper counseling, preferably provided by a multidisciplinary team of rheumatologists, obstetricians, gynecologists and neonatologists, is recommended for patients taking anti-rheumatic drugs, not only at the beginning, but also during the course of treatment.

Prevention
It is not possible to prevent the disease itself, but there are some methods to relieve the pain in acute stage of disease.

Patients with rheumatoid arthritis often have joint deformity and severe pain manifesting in the great toe, heel, and lesser toe. This can impact gait and functional mobility. Patients with RA can be prescribed foot orthoses or specialist footwear to combat these issues, and receive education for care of skin and nails.

The use of splints (Pic. 1) may be able to provide relief for a rheumatoid patient in acute stage of the disease. Splints may allow functional position to give rest to involved joints. Splinting can provide pain relief, reduce inflammation, increase range of motion, and prevent deformities.

Physical therapists can employ the use of assistive devices for patients with RA to improve functional ability and independence in daily activities. Appropriate assistive devices that benefit patients range from work chairs, rolling walkers, canes, and reachers. Research suggests reasons for using assistive devices also reduce amount of load placed on the joint, reduce pain, fatigue and inflammation.

### Symptoms

#### Joints

Arthritis of joints involves inflammation, joints become swollen, tender and warm, and stiffness limits their movement. With time, multiple joints are affected (polyarthritis). Most commonly involved are the small joints of the hands, feet and neck spine, but larger joints like the shoulder and knee can also be involved. Synovitis (occurs when the synovial membrane which lines and lubricates the knee joint, becomes inflamed) can lead to tethering of tissue with loss of movement and erosion of the joint surface causing deformity and loss of function.

The fingers may suffer from almost any deformity depending on which joints are most involved.

#### Skin

The rheumatoid nodule (Pic. 2), which is sometimes in the skin, is the most common non joint feature. They occur in 30% of people who have RA.
The typical rheumatoid nodule may be a few millimetres to a few centimetres in diameter and is usually found over bony prominences, such as the elbow, the heel, the knuckles, or other areas that sustain repeated mechanical stress.

**Lungs**

Fibrosis of the lungs (Pic. 3) is a recognized complication of rheumatoid arthritis. It is also a rare but well-recognized consequence of therapy (for example with methotrexate and leflunomide).

Caplan's syndrome describes lung nodules in individuals with RA and additional exposure to coal dust. Exudative pleural effusions are also associated with RA.

**Eyes**

Common is the indirect effect of keratoconjunctivitis sicca, which is a dryness of eyes and mouth caused by lymphocyte infiltration of lacrimal and salivary glands. When severe, dryness of the cornea can lead to keratitis and loss of vision.

**Liver**

Liver problems in people with rheumatoid arthritis may be due to the underlying disease process or as a result of the medications used to treat the disease. A coexisting autoimmune liver disease, such as primary biliary cirrhosis or autoimmune hepatitis may also cause problems.

**Neurological symptoms**

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. Clumsiness is initially experienced, but without due care, this can progress to quadriplegia (paralysis caused by illness that results in the partial or total loss of use of all four limbs and torso).

**Constitutional symptoms**

Constitutional symptoms including fatigue, low grade fever, malaise, morning
stiffness, loss of appetite and loss of weight are common systemic manifestations seen in people with active RA.

**Therapies**

**Self therapy**

**Exercise**

With rheumatoid arthritis described as a chronic autoimmune disorder, the consequences to joint surfaces and increased morbidity make patients susceptible to loss of muscle mass, range of motion and diminished aerobic endurance.

An exercise program is essential to prevent joint destruction and combat the symptoms associated with the disease, but comes with a multitude of challenges (Pic. 4, 5).

Those who are diagnosed with RA may be unsure of beginning an exercise regimen due a lack of confidence in abilities and the pain it may cause.

In a review article on the benefits of exercise in this patient population, it is shown that assistance from instructors and social interaction boost motivation for involvement in regular exercise routines. This is where physical therapists play a very important role.

Since the marker of this disease is joint destruction, the most important benefit to note is the impact exercise has on improving joint health. During the course of the disease, tendon sheaths, ligaments and cartilage can be affected and exercise can maintain their integrity. Range of motion and flexibility deficits that hinder a patient's productivity can be improved with regular exercise, and combat RA-related fatigue.

**Diet**

Proper diet is an essential part of maintenance of the disease, as well as adequate rest. Some evidence supports omega-3 fatty acids and gamma-linolenic acid in RA.

**Tai Chi, Yoga and Pilates**
Tai Chi, Yoga, and Pilates are also effective disciplines that can increase range of motion, flexibility, strength, and cardiovascular endurance without putting a large amount of force on joint surfaces.

**Conventional medicine**

The pharmacotherapy is focused on inflammatory reduction, because this condition cannot be cured, only slowed and mitigated. Surgery to repair, replace, or fuse joints may help in certain situations. The most commonly used other therapy in combating rheumatoid arthritis are thermotherapy and cryotherapy.

**Pharmacotherapy**

The genetic make-up of an individual drives how he/she responds to drugs. Genetic variations may correlate with enhanced efficacy of the drug or may make the individual highly susceptible to adverse drug reactions.

The primary treatment is usually disease-modifying anti-rheumatic drugs (DMARDs), which reduce synovitis and systemic inflammation. Biological agents, such as antibodies that block tumour necrosis factor (TNF), have been used to treat RA patients who have failed to respond to treatment with conventional DMARDs.

**Surgical therapy**

Especially for affected fingers, hands, and wrists, synovectomy (removal of synovial tissue) may be needed to prevent pain or tendon rupture when drug treatment has failed. Severely affected joints may require joint replacement surgery, such as knee replacement. Postoperatively, physiotherapy is always necessary.

**Other therapy**

**Thermotherapy**

Therapy modalities can increase blood flow and elasticity of tissues and can be applied as hot packs, paraffin wax, or hydrotherapy. During a flare up of rheumatoid arthritis, a patient may prefer cryotherapy over thermotherapy to cool the joint down, attempt to numb the pain and control inflammation. A cold-pack, ice chips, ice
massage or nitrogen spray can be applied to areas where calming inflammation and pain are desired.

**Transcutaneous electrical nerve stimulation**

Transcutaneous electrical nerve stimulation (TENS) is a therapeutic intervention indicated for pain control and muscle stimulation. While the literature on the use of TENS in patients with rheumatoid arthritis is rather conflicting, it can be supported using the modality for this patient population as TENS does not cause any adverse side effects.

**Assisted reproduction**

There are many risks for pregnancy in rheumatoid arthritis patients. Successful pregnancy is possible after assisted reproductive technology (ART).

Assisted reproductive technology (ART) is the technology used to achieve pregnancy in procedures such as fertility medication, artificial insemination, in vitro fertilization and surrogacy.

IVF and ART generally start with stimulating the ovaries to increase egg production. Most fertility medications are agents that stimulate the development of follicles in the ovary. Examples are gonadotropins and gonadotropin releasing hormone. After stimulation, the physician surgically extracts one or more eggs from the ovary, and unites them with sperm in a laboratory setting, with the intent of producing one or more embryos. Fertilization takes place outside the body, and the fertilized egg is reinserted into the woman's reproductive tract, in a procedure called embryo transfer.

Compelling evidence suggests that an abnormally functioning maternal immune system often leads to poor reproductive performance. Failure of proper function of immunologic interaction during implantation has been implicated as a cause of recurrent miscarriage, late pregnancy fetal loss, IVF failure and infertility.

Women with risk factors such as a positive personal or family history of autoimmune disorders such as rheumatoid arthritis need proper evaluation because immunologic problems may lead to implantation failure.

The selective use of immunotherapy (heparin/aspirin, immunoglobulin G, corticosteroid therapy) has enabled to achieve
successful pregnancies in-patients who had previously suffered repeated IVF failures.

Among women with older reproductive age, with history of repetitive abortions or genetic disorders, genetic analysis is highly recommended. The PGS/PGD allows studying the DNA of eggs or embryos to select those that carry certain damaging characteristics. It is useful when there are previous chromosomal or genetic disorders in the family, within the context of in vitro fertilization programs.

The rate of success for IVF is correlated with a woman’s age. More than 40 percent of women under 35 succeed in giving birth following IVF, but the rate drops to a little over 10 percent in women over 40.

**Find more about related issues**

**Diagnoses**

**Klinefelter syndrome**
The set of symptoms that result from two or more X chromosome in males.
Learn more at: [www.fertilitypedia.org/therapy/diag/klinefelter-syndrome](http://www.fertilitypedia.org/therapy/diag/klinefelter-syndrome)

**Therapies**

**Egg donation**
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: [www.fertilitypedia.org/edu/therapies/egg-donation](http://www.fertilitypedia.org/edu/therapies/egg-donation)

**ICSI**
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: [www.fertilitypedia.org/edu/therapies/icsi](http://www.fertilitypedia.org/edu/therapies/icsi)

**Sperm donation**
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: [www.fertilitypedia.org/edu/therapies/sperm-donation](http://www.fertilitypedia.org/edu/therapies/sperm-donation)
Splint allows each finger to be individually aligned.

A 48-year old female diagnosed with seropositive rheumatoid arthritis. She has numerous rheumatoid nodules.

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.

An illustration of hand exercise techniques.

Standard IVF
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: www.fertilitypedia.org/edu/therapies/standard-ivf
Pic
Severe techniques of body stretching.

Sources

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