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A DETAILED REVIEW ON RHEUMATOID ARTHRITIS (RA)

Snehal Ashok Naik*, Sakshi Vasant Parhad , Rohit Sushil Bairagi

Anuradha College Of Pharmacy, Chikhli, Dist – Buldana (MS) India 443201
Author[1]: naiksnehal32@gmail.com

ABSTRACT

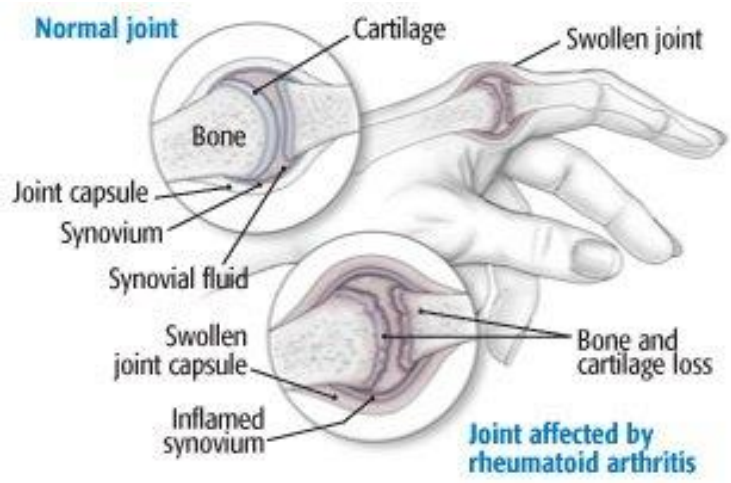
Rheumatoid arthritis is chronic, systemic , inflammatory , disorder that primiarily affect small peripheral joints. The average annual incidence of RA in united State is 0.5 per 1000 person per year. Female : male ratio is 3:1 . Onset of disease occur at ranging 20-60 yrs old . It is multifactorial & heterogenous disease having contribution of both genetic (50-60 %) & environmental factor. Dignosis of RA include morning stiffness at least one hour before maximal improvement, arthritis of 3 or more joints , arthritis of hand joint , symmetric arthritis , rheumatoid nodules , positive serum rheumatoid factor & radiographic changes (hand & wrist) . RA is defined by presence of 4 or more criteria & criteria 1 through 4 must be present for at least 6 weeks. The presented article concern with a brief idea about Rheumatoid Arthritis (RA)

***Keywords**: rheumatoid arthritis, ADL modification, rehabilitation program, bautonnier deformity, Osteoclastic*

1. INTRODUCTION

Rheumatoid arthritis (RA) is a long-term autoimmune disorder that primarily affects joints. 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, including skin, eyes, lungs, heart, nerves and blood. 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. This results in inflammation and thickening of the joint capsule .It also affects the underlying bone and cartilage.

RA affects about 24.5 million people as of 2015.This is between 0.5 and 1% of adults in the developed world with 5 and 50 per 100,000 people newly developing the condition each year. Onset is most frequent during middle age and women are affected 2.5 times as frequently as men. It resulted in 38,000 deaths in 2013, up from 28,000 deaths in 1990. The first recognized description of RA was made in 1800 by Dr. Augustin Jacob Landre - Beauvais (1772–1840) of Paris. The term rheumatoid arthritis is based on the Greek for watery and inflamed joints .



CHARACTERISTICS:

Rheumatoid arthritis is characterized by:

- Synovial inflammation and hyperplasia (“swelling”)
- Autoantibody production (rheumatoid factor and anti-citrullinated protein antibody [ACPA])
- Cartilage and bone destruction (“deformity”)

SIGN & SYMPTOMS:

Early stage symptoms: While RA can affect anyone , it most commonly present between the ages of 30 & 50 & more often in woman . The early stage symptoms of RA don’t always include swelling & redness in the joints , but there can be suitable sign that something is up . Some if the early stage symptoms include :

- Tenderness & pain in certain areas of your body .
- A noticeable increase in fatigue.
- Weakness in certain areas of your body that weren’t there before.

Later stage symptoms: Once RA inflammation has been active in your body for a period of weeks or months, you’ll being to notice more obvious signs that something is up.

- **Swelling, redness & warmth in joints**: Rheumatoid arthritis attacks the lining of your joints, and when this inflammation flares up, your joints may become red, and feel warm to the touch. They might also swell.

- **Fatigue**: Because it takes energy for your body to fight inflammation, you may notice a marked increase in fatigue and tiredness while doing the same activities you’ve always done. If this fatigue lasts more than a few weeks — even if you don’t notice any other symptoms — you could be dealing with an RA flare. Fatigue is sometimes accompanied by an overwhelming “I don’t feel good but don’t know why” sensation or even depression.

- **Morning sickness**: Morning stiffness is one of the main symptoms of many types of arthritis, including RA. If certain joints feel stiff when you first wake up and that stiffness lasts longer than 30 minutes, you could be dealing with an RA flare. It’s common for joints to feel more mobile after prolonged activity.

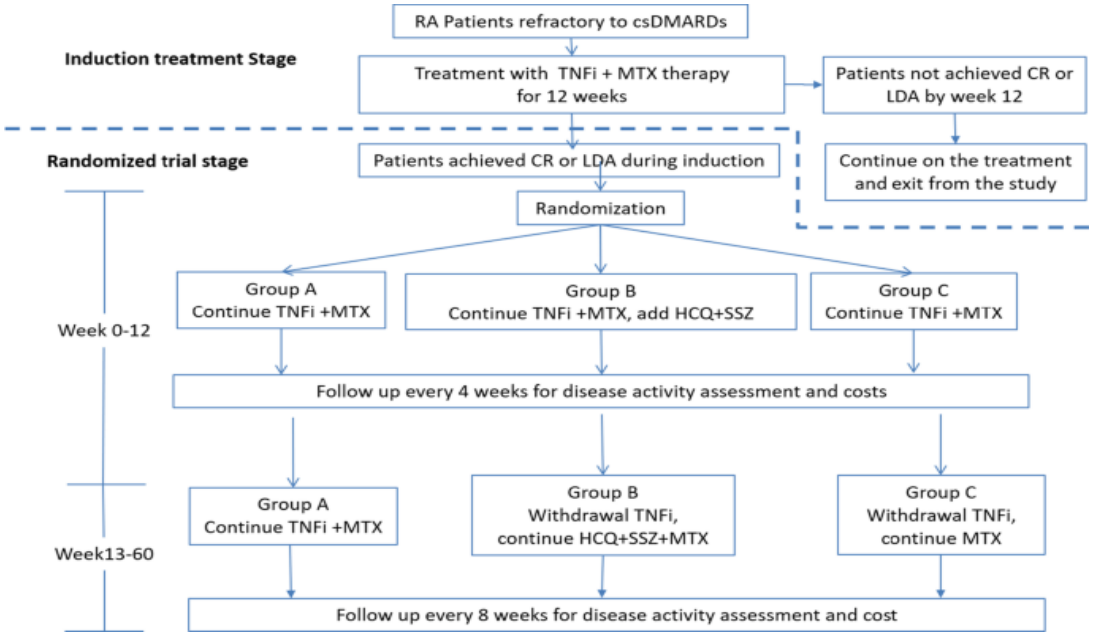
- **General joint pain & sickness**: In addition to morning joint stiffness, you may also experience general joint stiffness throughout the day, especially after a period of inactivity. Some of the first areas RA stiffness typically affects are the wrists and certain joints in the hands and feet, but it’s also possible to experience pain and stiffness in your knees or shoulders. Usually, both sides of your body will be affected.

Other symptoms of RA: There are a few other RA symptoms that affect more than just your joints. These include:

- loss of appetite
- dry eyes and mouth (caused by a related symptom, Sjogren’s syndrome)
- rheumatoid nodules, which are hard lumps that grow beneath the skin in places like the elbow and hands
- weight loss
- chest pain
- nerve or skin damage

Symptoms by body part: The most commonly affected areas during the onset of RA are the small joints in your hands and feet. This is where you may first feel stiffness and an ache. It’s also possible for RA inflammation to affect your knees and hips. Because the disease presents differently in different people, it can go on to affect almost any joint. Your organs are another area that can be disrupted by RA inflammation:

- Your heart muscle can become damaged.
- Your lungs can become scarred.
- Blood vessel damage can lead to subsequent skin and nerve issues.



MORPHOLOGY

Joints: RA causes a broad spectrum of morphological alteration. The more severe are manifested in the joints. Initially the synovium becomes grossly edematous thickened & hyperplastic transferring it's smooth contour to one covered by delicate & bulbous fronds. The characteristic histologic feature includes:

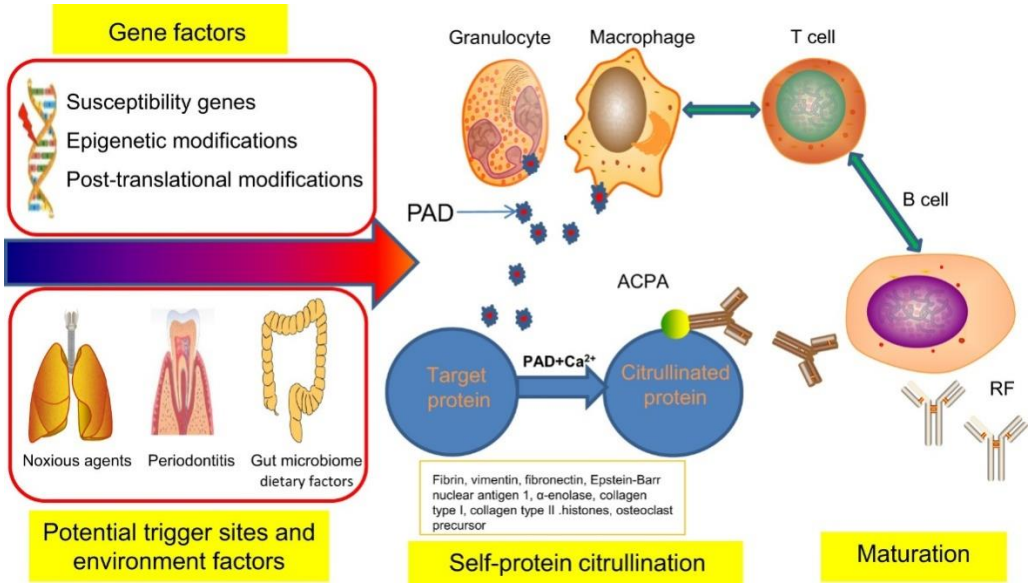
- Infiltration of synovial stroma by dense perivascular inflammatory cells consisting of B-cells, CD4 + T cell, plasma cells, macrophages .
- Increase vascularity owing to vasodilation & angiogenesis with superficial hemosiderin deposit.
- Aggregation of organizing fibrin covering portion of the synovium & floating in the joint space.
- Accumulation of neutrophils in the synovial fluid but not deep in the synovial stroma.
- Osteoclastic activity in underlying bone allowing the synovium to penetrate into the bone forming juxtra articular erosions, subchondral cysts & osteoporosis & pannus formation. Which growth over the articular cartilage causes it's erosion.

PATHOPHYSIOLOGY:

RA primarily starts as a state of persistent cellular activation leading to autoimmunity and immune complexes in joints and other organs where it manifests. The clinical manifestations of disease are primarily inflammation of the synovial membrane and joint damage, and the fibroblast-like synoviocytes play a key role in these pathogenic processes. Three phases of progression of RA are an initiation phase (due to non-specific inflammation), an amplification phase (due to T cell activation), and chronic inflammatory phase, with tissue injury resulting from the cytokines, IL–1, TNF-alpha, and IL–6 .

The synovitis, swelling, and joint damage that characterize active RA are the end results of complex autoimmune and inflammatory processes that involve components of both the innate and adaptive immune systems. In a susceptible individual, the interaction of environment and genes results in a loss of tolerance of self-proteins that contain a citrulline residue. These proteins are generated via post translational modification of arginine residues to citrulline residues by the enzyme peptidylarginine deiminase.[9] Patients with shared epitopes generate citrullinated peptides that are no longer recognized as "self" by the immune system, which consequently develops ACPAs against them. Comparison of magnetic resonance imaging (MRI) and synovial biopsy data from healthy individuals with MRI and biopsy data from patients positive for RF and/or ACPA demonstrate that systemic autoantibody production precedes inflammation and adhesion molecule formation in the synovium, indicating that perhaps some secondary event is required to initiate involvement of the synovium in RA. In a study of 79 patients with RA, the initial appearance of RF and ACPA preceded the development of clinical RA involving the synovium by a median of 4.5 years.

Immune activation and RA disease progression is a complex process that involves interactions between components of both the adaptive and innate immune pathways. The nature of these interactions is greatly affected by the local cytokine and chemokine environment of the synovium in which they take place. In established RA, the synovial membrane is populated by a variety of inflammatory cell types that work together to cause joint destruction.



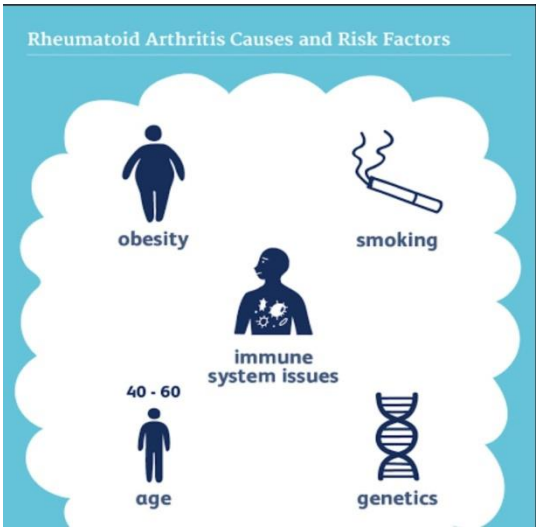
FACTOR ASSOCIATED FOR PATHOGENESIS OF RA

- Cigarette smoking.
- Tumor necrosis factor (TNF)-a activity.
- Abnormal and inappropriate B-lymphocyte activity, i.e. abnormal antibody production.
- Detection of circulating autoantibodies against IgFc, these autoantibodies have been termed ‘rheumatoid factor’, and they may be involved in the inappropriate presentation of antigens to T cells by B cells.
- Abnormal activity of certain signaling pathways in synovial tissue, e.g. the Wnt signaling pathway, which is involved in embryonic development and cell renewal. In patients with RA, it has been reported that the synovial cells have abnormally high activity of the Wnt gene, as well as a number of other genes for several of the cytokines, cell adhesion molecules and chemokine’s.

Diagnosis of rheumatoid arthritis can be done by detection of serum RF, morning stiffness for 1 hour or longer for 6 weeks or more, arthritis in three or more joints persisting for 6 weeks or more, persistence for 6 weeks or more of symmetrical arthritis , persistence for 6 weeks or more of arthritis of the hand joints , rheumatoid nodules, observation, using hand radiographs, of changes, erosion or unequivocal bony decalcification

RISK FACTOR:

Rheumatoid arthritis is an inflammatory condition that affects the joints and other parts of the body. The exact causes are unclear, but certain factors increase the risk of it developing. Several issues can increase a person’s chances of having rheumatoid arthritis (RA). Some are unavoidable, but



a person can take action to prevent others from leading to RA.

Changing the diet, quitting smoking, looking after the teeth and gums, and taking probiotics may reduce the risk of developing this condition. In this article, learn more about the risk factors for RA and which steps can help prevent it.

1. Genetic factors

Share on Pinteres t If a close family member has RA, a person ma have a higher risk of developing it. However, a range of environmental and genetic factors are likely to contribute. There is no single genetic change that causes RA in everyone who has it.

2. Hormones

According to the Centers for Disease Control and Prevention (CDC), women are two or three times more likely to develop RA than men. Hormones may play a role, and research into this is ongoing.

- **Estrogen**

  High levels of estrogen, a female sex hormone also present in males, may contribute to the development of the disease. Also, the CDC note, women who have never given birth may have a higher likelihood of developing RA.

- **Testosterone**

  Some research points to a link between low testosterone levels and RA. In 2018, researchers published the results of a study involving 59 participants with RA and 61 participants without the condition, matched for sex and age. Those with RA were more likely to have testosterone levels outside the normal range.

Some participants with RA then received serum testosterone therapy, and the activity of their RA reduced. The study's authors believe that hormone replacement therapy may help treat symptoms of RA.

- **Menopause**

  During and after menopause, some females with RA experience a decline in physical ability, according to results of a different 2018 study. This finding also suggests that hormones play a role in the progression of RA.

  Meanwhile, research in animals and humans suggests that receiving estrogen replacement therapy after menopause may increase the risk of developing RA.

3. Age

RA can develop at any age, but the risk increases as people get older. It is most likely to arise when a person is in their 60s, according to the CDC.

4. Smoking

Scientists have found links between smoking and an increased risk of developing RA, even among people with low-level, lifelong exposure to smoke. Also, heavy smokers may have more severe RA symptoms, the research suggests.

Smoking can cause oxidative stress and increase the frequency of the body's inflammatory response. It can also make some prescription RA medications less effective.

5. Stress

Some researchers believe that stress may play a role in RA. For example, the way the body reacts to stress may worsen symptoms. People with rheumatic conditions often report that their symptoms first appeared shortly after traumatic or stressful experiences, and many people find that stress causes RA symptoms to flare up.

6. Obesity

The CDC report that obesity increases the risk of developing RA. Also, researchers associate obesity with several health issues, such as metabolic syndrome, that can exacerbate RA symptoms. For example, inflammation is a common feature of both obesity and metabolic syndrome. Here, learn about 10 effective weight loss strategies.

7. Health inequity

Results of a 2018 study from Taiwan suggest that socioeconomic status may affect the risk of developing RA. The authors found that people had a higher chance of developing it if they lived in an area where a low monthly income was common.

This could be due to factors such as occupation, housing conditions, stress, and diet, but access to healthcare may also play a role, as the researchers note.

The authors of a 2014 study in the southeastern United States concluded that socioeconomic factors and racial prejudice may help shape the experiences of African Americans with RA. They called for more research into these effects on African American people in other regions of the country.

8. A previous infection

An infection's impact on the immune system may trigger RA. According to 2013 research, an infection may have this effect if:

- Part of the immune system loses its ability to handle certain microbes, such as bacteria or viruses.
- The infection triggers the production of new antigens, causing the immune system to become overactive.
- The immune system's response to the infection also attacks some of the body's functions, in a process called "bystander activation."

Which infections may contribute to RA?

Some people develop signs of some kinds of arthritis within 4 weeks of experiencing a genitourinary or gastrointestinal infection. Some research indicates that the following infections, in particular, may contribute to RA:

- a urinary tract infection with Proteus mirabilis bacteria
- an infection with the Epstein–Barr virus
- an infection with bacteria in the Mycoplasma genus
- some types of gum disease

Gum disease may be twice as common in people with RA than in those without the condition. This does not necessarily mean that having gum disease increases the risk of developing RA, however. Other factors may need to be present to trigger arthritis.

Other pathogens that might trigger arthritis or cause symptoms similar to those of RA include:

- HIV
- parvovirus
- hepatitis viruses B and C
  alphaviruses, such as chikungunya

9. Gut bacteria

A 2013 study found that 75% of participants with new-onset, untreated RA had Prevotella copri bacteria in their intestines. This was present in only 21% of participants in a control group and in only 12% of a group receiving treatment for chronic RA. The researchers proposed that P. copri may play a role in inflammation, which can help trigger RA. Authors of a 2016 study concluded that people with RA may have an abundance of certain microbes and that finding indications of these microbes in the gut may predict the development of the disease. Almost a year later, in an animal-based study, researchers found that altering the balance of microbes in the gut could prevent the onset of RA.

10. Diet

Dietary factors can affect the risk of many diseases, and some researchers have suggested that certain substances in foods can trigger the onset of RA. Authors of a 2018 study found that a type of bacteria in some milk and beef may trigger RA in people with genetic predispositions. A year earlier, other researchers had identified a number of foods that may help reduce inflammation in people with RA, possibly due to their antioxidant properties.

The researchers recommended, among other foods:

- raw or lightly cooked vegetables, especially legumes and green vegetables
- spices, such as turmeric and ginger
- seasonal fruits
- probiotic yogurts

They urged people to avoid animal-based products and foods that contain high amounts of salt and oil, including many processed products.
The research team did not suggest that dietary interventions could prevent RA but that consuming anti-inflammatory foods may help manage the symptoms.

TAKEAWAY:

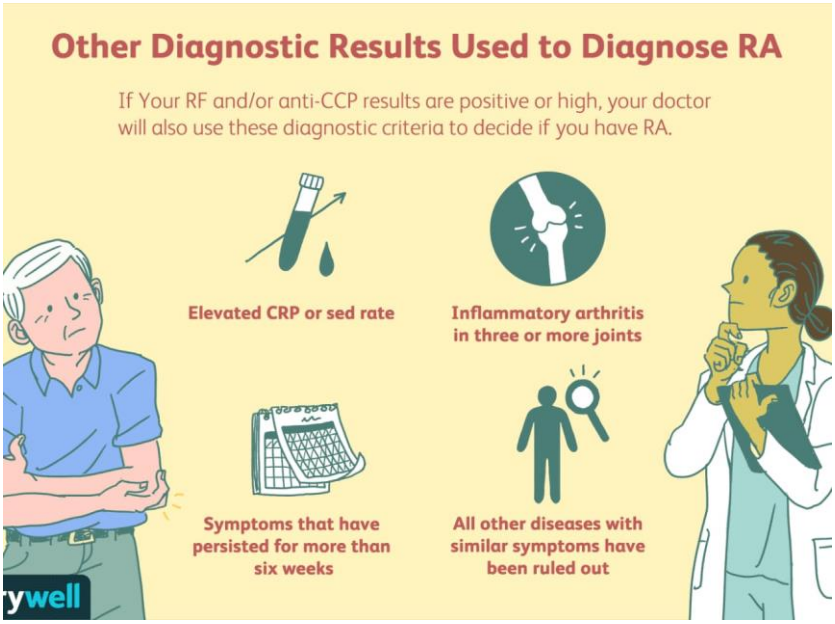
The exact causes of RA remain unclear, but experts have identified some factors that may increase the risk of developing it. Some of these, such as age, are unavoidable. However, some lifestyle choices, such as quitting smoking, can help prevent the condition

DIGNOSIS OF RA:

The diagnosis of RA is made clinically based primarily on physical examination findings. The classification criteria published in 1987 by the American College of Rheumatology (ACR), formerly the American Rheumatism Association, have been criticized for their focus on identifying patients with more-established RA disease (ie, those who have already developed chronic erosive disease). Consequently, the 1987 criteria failed to identify patients with early disease, who could gain the most benefit from available therapies.7 Recently, the ACR and European League Against Rheumatism (EULAR) created a joint working group with the primary goal of developing classification criteria to identify patients earlier in the disease process.As with the 1987 effort, the 2010 classification criteria are a means to identify patients for clinical trials, to differentiate patients with synovitis, and to determine the group at highest risk for developing persistent or erosive RA. However, the 2010 ACR/EULAR classification criteria also created a schematic for identifying definite RA.

- There are some important differences between the 1987 and 2010 classification criteria for RA . The 1987 criteria required a score of at least 4 from a tally of 7 domains, including: morning stiffness, the overall number of joints involved, hand involvement, presence of symmetry, rheumatoid nodules, positive rheumatoid factor (RF) test, and radiographic changes.7 In the 2010 criteria, patient assessment was recommended for those with clinical synovitis in at least 1 joint not explained by another disease. Assessment involves a scoring system from 0 to 5, based on the number and type of joint(s) involved. An involved joint was defined as joint swelling or tenderness on examination indicative of active synovitis. Large joints include the shoulders, elbows, hips, knees, and ankles. Small joints refer to the metacarpophalangeal (MCP), proximal interphalangeal (PIP), second through fifth metatarsophalangeal (MTP), thumb interphalangeal joints, and wrists. The distal interphalangeal, first carpometacarpal joints, and the first metatarsophalangeal joints are excluded from assessment due to their involvement in osteoarthritis. There was no specific requirement for hand arthritis, rheumatoid nodules, or symmetric arthritis in the 2010 criteria. The authors noted that symmetric involvement was not an independent feature of RA, although the likelihood of bilateral presentation was increased with greater joint involvement and more progressive disease.

- Similar to the 1987 criteria, the 2010 criteria utilize the presence or absence of RF (a high-affinity autoantibody directed against the Fc portion of immunoglobulin) as one of the domains. In addition, the 2010 criteria utilize the presence or absence of a marker that was identified more recently, the anticitrullinated protein antibody.



(ACPA). Values for RF and ACPA, markers of autoimmune dysfunction, are scored according to ranges of values, where normal is defined as less than the upper limit of normal (ULN) for the laboratory or assay, low-positive is between the ULN and less than 3 times the ULN, and high-positive is greater than 3 times the ULN. Markers of inflammation, the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level, are scored based on whether they are normal or abnormal according to reference laboratory standards. Unlike the 1987 criteria, the 2010 criteria considered duration of

therapy, but not the presence or absence of radiographic changes, to factor into the final score. In the 2010 RA classification criteria, a score of at least 6 out of 10 was considered to be indicative of RA, and hence a patient would be considered for treatment. The authors recommend that the 2010 ACR/EULAR criteria be used for assessment of existing and future patients to facilitate earlier use of treatments capable of altering disease progression.

- Present in periodontal disease and in patients who smoke cigarettes. Cigarette smoking appears to be associated with an increased risk of RA, and the development of a positive RF.

- Twin studies show concordance rates of 15% to 30% between monozygotic twins and 5% among dizygotic twins, suggesting that 50% to 60% of RA cases are due to genetic factors. Among the genetic factors linked to RA susceptibility are differences in human leukocyte antigen (HLA)-DRB1 alleles, especially in patients positive for RF and ACPA.[1] HLA-DRB1 genotypes appear to affect both disease susceptibility and disease severity.10 Gene-environment interactions have been observed; there is an increased incidence of RA in HLA-DRB1 individuals who smoke cigarettes. Chromosome 6, which contains the genes for HLA-DRB1, influences a number of immune processes, including production of tumor necrosis factor (TNF).

2. CONCLUSION

RA is debilitating, chronic, inflammatory disease, capable of caution joint damage as well as long term disability. Early diagnosis and intervention are essential for the prevention of serious damage and loss of essential bodily function. The treating physician should consider adhering to treat to target recommendation by first outlining the aims and them. Furthermore, early referral to a specialist can help to ensure better treatment outcomes. With advances in the field of molecular medicine, we have a better understanding of disease mechanism which can aid in the designing more effective treatment. Old treatment modalities have been optimized and new one have been produced. Gene array analysis is proving beneficial in finding out which patient will be more responsive to specific medications .this customized will allow for more rapid treatment as well as decrease the likelihood disease progression during experimental phase to seek an appropriate treatment to particular patient.it is foreseen that treatment method will face tremendous improvements in the management of RA.

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