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Review Article

DECODING DIFFERENCES: EXPLORING THE DIVERGENCE OF RHEUMATOID ARTHRITIS & ANKYLOSING SPONDYLITIS

Jessica Dhindsa[1]*, Dr. Rojin G Raj[2], Tarun Sharma[3]

[1,3]Department of Pharmacy Practice, ISF College of Pharmacy, Moga.
[2]Assistant Professor, Department of Pharmacy Practice, ISF College of Pharmacy, Moga.

Corresponding Author*: Jessica Dhindsa, Department of Pharmacy Practice, ISF College of Pharmacy, Moga.

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Abstract

Objective: This review article presents a comprehensive overview of the distinctions between two enduring autoimmune disorders: Rheumatoid arthritis (RA) and Ankyliosing spondylitis (AS), both of which affect the musculoskeletal system. The article highlights the differences in clinical manifestations, underlying mechanisms, and treatment approaches for these conditions. Methodology: This study is conducted by reviewing on google scholar using keywords such as RA and AS. Discussion: The article emphasizes that the key differences between these conditions lie in the affected body areas, genetic predisposition, and joint involvement. While RA mainly affects peripheral joints with inflammation of synovial tissues, AS primarily impacts the axial skeleton, leading to the fusion of spinal structures. RA has a strong autoimmune component, whereas AS is linked to HLA-B27. Treatment strategies differ, with RA benefiting from DMARDs and biologics, while AS relies on NSAIDs and TNF inhibitors. Understanding these distinctions is vital for accurate diagnosis and effective treatment planning. A patient's quality of life may be significantly impacted by either of disease, underscoring the importance of early intervention and a multidisciplinary approach. Tailoring management to individual patient needs, considering factors like disease severity, comorbidities, and patient preferences, is essential. Regular monitoring, physical therapy, and lifestyle adjustments play crucial roles in managing these chronic conditions.

Keywords: Rheumatoid Arthritis, Ankylosing Spondylitis, Autoimmune Disorder, Immunity, Joint Inflammation.

1. Background

Ankylosing spondylitis (AS) and rheumatoid arthritis (RA) are two prevalent, severe, long-term inflammatory skeletal diseases that have a significant impact on society. This is especially true given that many patients with both conditions are young and there is no known solution for them[1]. The hallmarks of rheumatoid arthritis include inflammatory changes that affect bone, cartilage, and synovial tissue in joints; extra-articular areas are less frequently affected. In order to conduct diagnosis, rheumatologists rely on their clinical knowledge[2]. The 1987 American Rheumatism Association criteria, which include symmetrical polyarthritis, involvement of the hand joints, rheumatoid nodules, radiographic erosions, and the existence of the rheumatoid factor, are the most often used categorization standards[3,4]. AS is a form of autoimmune inflammatory disorder influencing the axial skeletal structure and joints, especially

the joints of the sacroiliac spine, particularly in young adults[5]. Moreover, taking into account problems other than the joints such as psoriasis, and bowel-related disorders, the inflammation affects tendons, peripheral joints, entheseal structures, and cartilaginous tissue, and can last for years before irreversible damage occurs[6]. A diagnosis of definitive AS is made using the modified New York criteria which must be satisfied. These include having a pelvic X-ray with a grade of 2-4 for bilateral or unilateral sacroiliitis, as well as at least one of the following three criteria: restriction of the lumbar vertebrae's range of motion in the sagittal and frontal planes, less chest expansion than usual, and back pain due to inflammation[3,5].

2. Etiology

Inflammatory changes in bone, cartilage, and synovial joints, as well as, in areas other than joints, are the hallmarks of RA[7]. Autoantibodies are produced when cellular and humoral immune responses are abnormal. Post-translationally changed proteins, including those with acetylation, carbamylation, and citrullination, are the focus of these antibodies. Furthermore, they aid in T and B lymphocyte infiltration into the synovium. The affected tissue regions also experience a robust activation of the innate immune system, exhibiting highly triggered monocyte/macrophage system cells. Different phenomena lead to the histomorphological and clinical manifestations of RA. Inflammation is characterized by pain, swelling, and tenderness in the joints. It is thought that this is caused by arachidonic acid metabolites and different inflammatory cytokines, which in turn cause bone and cartilage degradation[7,8]. Even though they are present in healthy people and other medical situations, rheumatoid factors continue to be crucial humoral characteristics in rheumatoid arthritis[9]. IgM-RF is simple to find. In the test systems, it possesses free reaction partners as a result of its free arms. IgG rheumatoid factors promote the development of substantial immune complexes[10].

AS is an autoimmune disease that develops from complex interactions between environmental and genetic variables[11]. Despite significant advancements in recent decades, the etiology of AS remains poorly understood. Numerous factors, including bacterial infection, endocrine anomalies genetic makeup, and immune system response, have been linked to the emergence of ASHC adds 40–50% to the inherited vulnerability to this disease, while HLA B27 contributes just 20–30%[12]. Another gene that might be a component of the MHC is the TNF gene, however, it is doubtful that TNF polymorphisms play a significant influence in people with this condition[13,14].

3. Epidemiology

Numerous researches on the incidence and prevalence rates of RA were published during the last few decades, revealing a significant heterogeneity in the disease's occurrence among various groups. Most prevalence surveys conducted in North America and Northern Europe in regions place the incidence there between 0.5 and 1.1%[15,16]. Studies from southern European nations estimate the incidence to be between 0.3% and 0.7%. Studies from emerging nations also indicate that the condition is considerably less common (between 0.1% and 0.5%). Some Native Americans have been found to have a greater incidence of RA, whilst some rural areas of Africa have relatively low RA prevalence rates[17]. In North American and North European nations, the incidence rates of RA yearly range between 20 and 50 cases per 100,000 population[18].

Ankylosing spondylitis usually affects young people; symptoms usually start to show around age 26[19]. With a ratio of roughly 2 to 1, compared to women, men are more commonly impacted. Less than 5% of people over 45 show symptoms, while over 80% of patients initially experience symptoms before the age of thirty. A general link has been observed between the frequency and occurrence of this disease in a given community and HLA B27 prevalence[20]. With up to 50% of cases, the majority of northern nations and some tribes are home to HLA B27, with Eskimo and Haida Indian communities having the

highest prevalence. Between 0% and 14% of people have ankylosing spondylitis, with the majority of those suffering from it[13].

4. Lab Investigations

Serological indicators of RA, such as the IgM rheumatoid factor along with more specific anti-CCP antibodies, are frequently found in patient groups of RA at early stage; RF prevalence ranges from 50 to 66% and the anti-CCP prevalence ranges from 41-48%[21]. Current research on biomarkers associated with RA has uncovered the specificity of anticitrullinated peptide antibodies for RA[22]. Commercially available enzyme-linked immunosorbent assays are used to detect both cyclic citrullinated peptides and mutated citrullinated vimentin (anti-MCV)[23]. Despite significant disease activity in AS, laboratory testing for rheumatoid arthritis usually shows greater quantities of acute phase reactants, like ESR and CRP[24]. The anti-CCP and IgM rheumatoid elements are typically undetectable in AS. In clinically unclear instances, the HLA-B27 antigen has some applications in AS diagnosis, whereas it is frequently lacking in RA. For several reasons, the experts made the decision to exclude laboratory tests from the guidelines for monitoring patients with AS. This is due to the fact that only 30–40% of people with AS have abnormally high erythrocyte sedimentation rates (ESR) or serum CRP levels[25].

5. Pathophysiology

Dysregulation of the humoral and cell-mediated immune system components leads to RA and is briefly explained as follows: Due to genetic susceptibility and antigenic stimulation, $CD4^{+}T$ cells gets activated which further leads to activation of B cell and T cell activation as explained clearly in Fig.1. Their activation leads to antibody production which leads to the release of cytotoxins and hydroxyl radicals that promote cellular damage to synovium and bone that ultimately result into RA. $CD4^{+}T$ cells also causes activation of endothelial cells and macrophages. Whereas, activation of endothelial cells results into increased expression of adhesion molecules and accumulation of inflammatory cells. In case of macrophages, TNF-α, IL-1β, IL-NF-kB releases vasoactive substances and increased blood flow. This all leads to pannus formation and hence, lead to RA.

Whereas, in the case of AS due to HLAB27, environmental and genetic factors activation of $CD8^{+}T$ cells take place which leads to activation of the immune system involving TNFα and IL-1 as explained in Fig.2.This further leads to enthesitis and synovitis leading to AS.

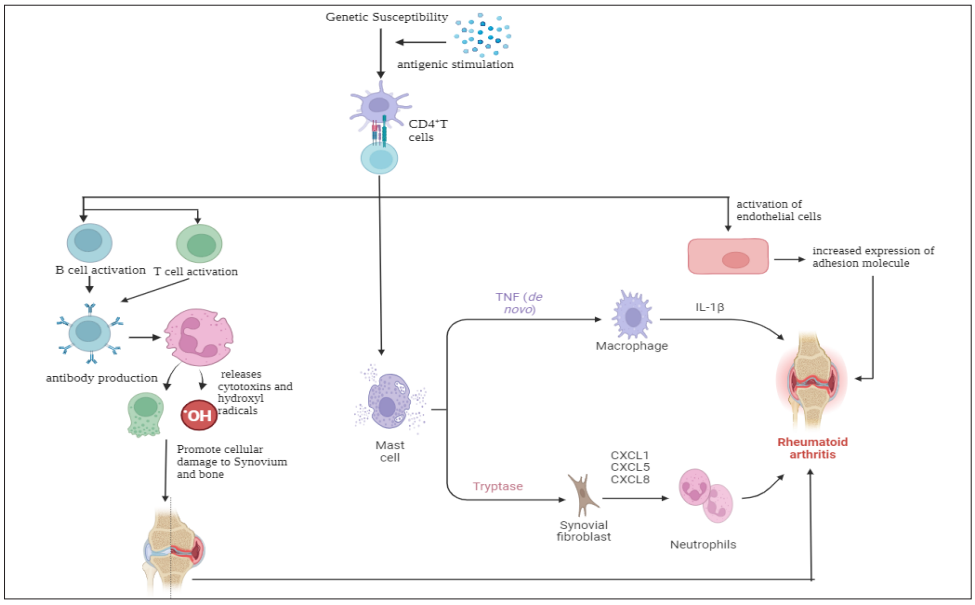

Figure 1: Pathophysiology of RA

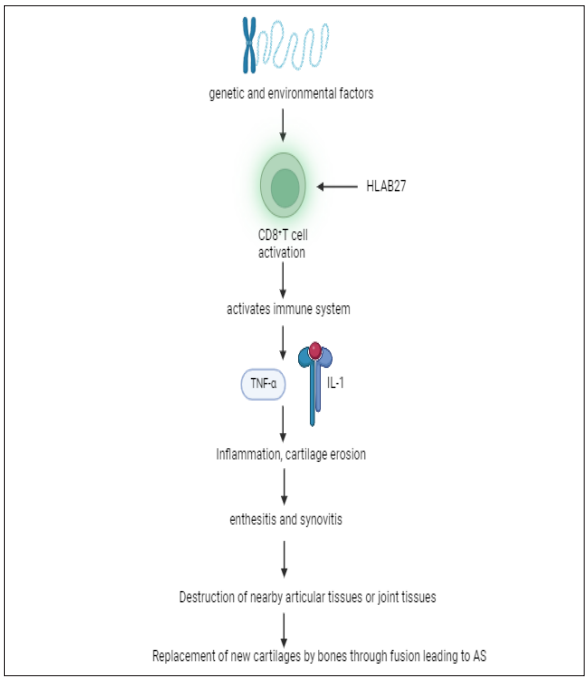

Figure 2: Pathophysiology of AS

6. Risk Factors

The causes of RA include genetic, environmental, and stochastic variables[26]. Scientific studies reported a 50% inherited risk for RA[27,28]. Rheumatoid factor (RF) and ACPA can be used to distinguish between seropositive and seronegative RA patients[29].

Smoking and drinking were two lifestyle behaviors that were frequently identified as risk factors for several diseases, although the degree of correlation varied. Smoking and RA have long been linked[30]. Another factor is the link between taking statins and a lower risk of developing an inflammatory condition[31]. Statin users are less likely to develop RA, according to studies. AS has been linked to gastrointestinal infections, which may indicate a connection between infections and the start of autoimmune illnesses[32]. Moreover, thyroid disease acts as a risk factor for RA. While AS does not have any such risk factor[33]. Pregnancy appears to have a positive outcome in both delaying the beginning of the disease and reducing disease activity while pregnant[34]. However, only 30% of patients with AS showed improvement in disease activity during pregnancy, and pregnancy was shown to be a triggering factor for AS[35].

7. Clinical Features

In RA, there is symmetrical discomfort and swelling in the proximal interphalangeal, metacarpal, and metatarsal feet and hand joints[36]. Arthritis can appear in a number of joints, including the shoulders, knees, hips, elbows, ankles, and wrists. The disease might begin with a mono- or oligoarticular pattern at the initiation, but it frequently evolves to a polyarticular form[37]. Exhaustion, stiffness that lasts more than one hour in the morning, and joint discomfort and swelling are examples of clinical signs. Peripheral arthritis, which typically affects the knees, hips, and shoulders and has an uneven pattern, affects about one-third of AS patients[38]. Hip involvement is typically bilateral and can result in destruction, necessitating total replacement of joint at early years of age. Other peripheral joints, like the wrists, elbows, hands, and feet, might develop arthritis. In contrast to RA, dactylitis, a sausage-like enlargement of a finger or toe, is more common in AS[39]. Olecranon bursitis, subacromial subdeltoid bursitis, and trochanteric bursitis are just a few locations where bursitis can form. Sarcopenia is a frequent ailment characterized by muscle deconditioning brought on by pain, corticosteroid use, and neuropathy. In severe RA, atrophy of the

hand's intrinsic muscles can be clearly seen[40]. 30- 40% of AS patients experience acute anterior uveitis, which presents with abrupt discomfort, visual loss, and one eye's redness that goes away on its own within a few weeks[41]. Whereas keratoconjunctivitis sicca is more typical in RA. Chronic inflammatory stiffness in the morning and pain in the back region are reported as a result of spinal involvement in AS[42]. Sacroiliac (SI) joint and spinal column inflammation is the root cause of low back discomfort. The cervical and costovertebral joints may be involved in thoracic spine pain, especially when the chest is expanded[43]. Ankylosing spondylitis (AS) patients should have a thorough physical examination that includes two main parts: assessing the spine, which includes measuring mobility in the lumbar, thoracic, and cervical spine, evaluating overall height, looking for inappropriate curves, examining spinal alignment, and checking for abnormal curvatures; and looking at the peripheral joints and entheses[44].

8. Diagnosis

8.1 For Rheumatoid Arthritis

The American College of Rheumatology(ACR) (formerly the American Rheumatism Association) 1987 revised criteria for the classification of rheumatoid arthritis:

1. Morning stiffness of at least 1 hour before maximal improvement
2. Arthritis of three joint areas or more
3. Arthritis of hand joints
4. Symmetric arthritis
5. Rheumatoid nodules
6. Rheumatoid factor positivity
7. Radiographic changes on hand and wrist radiographs

For classification purposes, a patient shall be said to have rheumatoid arthritis if he/she has satisfied at least four of these seven criteria. Criteria 1–4 must have been present for at least 6 weeks.

8.2 For Ankylosing Spondylitis

The most popular classification standards for ankylosing spondylitis according to New York clinical criteria were created in 1966 and revised in 1984[45].

1. Low back pain of at least three months duration with inflammatory characteristics (improved by exercise, not relieved by rest)
2. Limitation of lumbar spine motion in sagittal and frontal planes
3. Decreased chest expansion (relative to normal values for age and sex)
4. Bilateral sacroiliitis grade 2 or higher
5. Unilateral sacroiliitis grade 3 or higher

When any clinical criteria are met for the fourth or fifth criterion, definitive ankylosing spondylitis is considered to be present[46]. Imaging using Conventional X-rays and Magnetic Resonance Imaging along with histological techniques is also used for the Diagnosis of Rheumatoid arthritis and Ankylosing spondylitis[47].

9. Management

Significant advancements in pharmaceutical methodologies and tactics for drug design have resulted in substantial progress in the realm of pharmacology, bringing us closer to discovering potential cures for these diseases.

The current approach to managing RA, as per the recommendations of ACR and EULAR, involves addressing the condition through two main avenues: symptomatic relief and disease-modifying strategies[48,49]. For relief of symptoms rheumatoid arthritis predominantly relies on Non-steroidal anti-inflammatory drugs (NSAIDs) and Glucocorticoids (GCs). In certain cases, weak opioid analgesics could be considered as temporary pain relievers, following a thorough evaluation of the potential benefits and risks[50,51].

NSAIDs, such as naproxen, ibuprofen, and coxibs,

are used to lower inflammation and alleviate pain during the acute phase response. These drugs achieve their pharmacological impact by inhibiting the activity of cyclooxygenase (COX), particularly COX[50,52].

GCs such as prednisone exhibit greater potency and effectiveness compared to NSAIDs[53]. This is due to the intricate mechanisms through which they show their immunosuppressive and anti-inflammatory properties. However, it's worth noting that NSAIDs have a slightly better safety profile. Long-term usage of GCs can lead to various side effects like weight gain, fluid retention, muscle weakness, diabetes, and osteoporosis[54]. Therefore, GCs are typically intended for short-term use and can be administered through oral, intravenous, intramuscular, or intra-articular routes[53,55].

Disease-modifying antirheumatic Drugs (DMARDs) are pharmacological therapies that decrease autoimmune reactions in an effort to halt or stop joint deterioration and facilitate remission.[56]. DMARDs are categorized into three categories: conventional synthetic DMARDs (csDMARDs), biologic DMARDs (bDMARDs), and targeted synthetic DMARDs (tsDMARDs)[57]. csDMARDs represent a diverse group of medications, which involves methotrexate (MTX), hydroxychloroquine (HCQ), leflunomide (LEF), and sulfasalazine (SSZ) [58]. These medications are more often used than others that have less favorable safety and efficacious profiles, like minocycline, d-penicillamine, azathioprine, cyclosporine, and cyclophosphamide. They function by suppressing the hyperactive immune system in a non-specific manner[59,60]. The latest FDA and EMA-approved treatment approach for rheumatoid arthritis (RA) revolves around the utilization of JAK inhibitors (JAKi)[61]. These molecules fall into two classes according to how selective they are. The first category consists of weakly selective inhibitors that can obstruct a variety of cytokines' signaling pathways[62]. In contrast, the second generation of JAK inhibitors possesses the ability to selectively inhibit specific signaling processes[63]. Individuals suffering from rheumatic diseases frequently opt for diverse treatment choices, which may include methods falling under the umbrella of complementary and alternative medicine (CAM[64,65]. CAM is described as a diverse array of health practices that exist outside of the mainstream healthcare system. This includes Pilates, Massage, Balenotherapy, Yoga, Tai Chi, Acupuncture, and Hypnotherapy along with nutritional therapy[65].

Physical therapy and education are two components of the complementing nonpharmacological and pharmacological therapies that are necessary for the effective management of AS. The administration of anti-TNF therapy should align with the guidelines outlined by AS[66]. In individuals exhibiting advanced hip damage evident in radiographic images and experiencing persistent, unmanageable pain and disability, joint replacement must be contemplated. In the case of specific individuals experiencing symptoms and impairment stemming from a debilitating posture or an unstable spine, spinal surgery can be beneficial[67].

For people with ankylosing spondylitis, the traditional method of treating spinal problems has been to employ NSAIDs and regimented exercise programs[68,69]. The results of using disease-modifying antirheumatic medications to treat axial involvement in spondyloarthritides have been a little disappointing[67,70].

The development of TNF blockers was of great importance in the management of spondyloarthritides, including AS[71]. As of right now, three such medications are approved that can be used in the management of AS: Every other week, a 40 mg dosage of adalimumab—a fully-humanized monoclonal antibody—is subcutaneously delivered. The 75 kD TNF receptor fusion protein etanercept is administered subcutaneously once a week at a dose of 50 mg or twice a week at a dose of 25 mg. The recommended protocol for intravenous administration of infliximab, a monoclonal

chimeric antibody, is 5 mg/kg every 6-8 weeks. The recommended dose for this medication is 3-5 mg per kilogram. Anti-TNF treatment is likely useful in treating spondyloarthritis, and this family of drugs probably shares this trait[72,73].

12. Conclusion

In summary, RA and AS are both enduring autoimmune disorders impacting the musculoskeletal system. Nevertheless, they exhibit notable distinctions in their clinical manifestations, underlying mechanisms, and therapeutic methods. Comprehending these distinctions is crucial for precise diagnosis and therapy strategizing. It is noteworthy to emphasize that the individual's standard of existence can be greatly impacted by both illnesses, and early intervention and a multidisciplinary approach are crucial in managing the symptoms and preventing long-term complications. In both instances, care should be individualized for each patient, taking into account goals, preferences, comorbidities, and the severity of the illness. Regular monitoring, physical therapy, and lifestyle modifications play crucial roles in the management and treatment of these conditions. While RA and AS exchange some commonalities as autoimmune conditions affecting the musculoskeletal system, their differences are substantial. Understanding the unique characteristics of each disease is essential for healthcare professionals to make accurate diagnoses and provide effective treatment strategies. Patients living with these conditions must also be well-informed about their condition and actively participate in their care to achieve the best results. Ongoing research and advancements in the field of rheumatology continue to improve our understanding and management of these complex diseases, offering hope for better outcomes and improved quality of life for those affected by rheumatoid arthritis and ankylosing spondylitis.

13. List of Abbreviations

RA- Rheumatoid Arthritis

AS- Ankylosing Spondylitis

DMARDs- Disease Modifying Anti-Rheumatic Drugs

NSAIDs- Non Steroidal Anti Inflammatory Drugs

TNF- Tumor Necrosis Factor

MHC- Major Histocompatibility Complex

RF- Rheumatoid Factor

ESR- Erythrocyte Sedimentation Rate

CCP- Cyclic Citrullinated Peptide

CRP- C-RSeactive Protein

EULAR- European Alliance of Associations for Rheumatology

Table 1: General differences between rheumatoid arthritis and ankylosing spondylitis

Characteristics	Rheumatoid Arthritis	Ankylosing Spondylitis
Genetic Association	HLA-DR4 and DR1	HLA-B27
Age of Incidence	40-70 Years	20-45 Years
Rheumatoid factor	Present in 60-70% cases	Absent
Predominant Localization	Hands and feet: MCP, PIP, MTP joints	Sacroiliac joints: hips, shoulder and knees
Increased ESR or CRP	Majority in active disease	Only 50-60% in active disease
Radiographic Signs	Bone resorption, Sacroiliitis absent	Bone formation, Sacroiliitis present

Conflict of Interest: None

References

1. Bevan, S., Economic impact of musculoskeletal disorders (MSDs) on work in Europe. Best Practice & Research Clinical Rheumatology, 2015. 29(3): p. 356-373.
2. Littlejohn, E.A. and S.U. Monrad, Early diagnosis and treatment of rheumatoid arthritis. Primary Care: Clinics in Office Practice, 2018. 45(2): p. 237-255.
3. Van der Horst-Bruinsma, I., W. Lems, and B. Dijkmans, A systematic comparison of rheumatoid arthritis and ankylosing spondylitis. Clinical & Experimental Rheumatology, 2009. 27(4): p. S43.
4. Kay, J. and K.S. Upchurch, ACR/EULAR 2010 rheumatoid arthritis classification criteria. Rheumatology, 2012. 51(suppl_6): p. vi5-vi9.
5. Weiss, P.F. and J. Roth, Juvenile-versus adult-onset spondyloarthritis: similar, but different. Rheumatic Disease Clinics, 2020. 46(2): p. 241-257.
6. Fotoh, D.S., et al., miRNA-451a and miRNA-125a expression levels in ankylosing spondylitis: impact on disease diagnosis, prognosis, and outcomes. Journal of Immunology Research, 2020. 2020.
7. Ioannidou, S., Case Study of Physiotherapy Treatment of a Patient with Rheumatoid Arthritis. 2021.
8. Williams, J., et al., Rheumatoid inflammation and joint destruction: cause and effect or parallel phenomena? Agents and Actions, 1986. 18: p. 538-543.
9. Westwood, O.M., P.N. Nelson, and F.C. Hay, Rheumatoid factors: what's new? Rheumatology, 2006. 45(4): p. 379-385.
10. Scherer, H.U., T. Häupl, and G.R. Burmester, The etiology of rheumatoid arthritis. Journal of autoimmunity, 2020. 110: p. 102400.
11. Ellis, J.A., A.S. Kemp, and A.-L. Ponsonby, Gene–environment interaction in autoimmune disease. Expert Reviews in Molecular Medicine, 2014. 16: p. e4.
12. Khan, M., Epidemiology of HLA-B27 and arthritis. Clinical rheumatology, 1996. 15: p. 10-12.
13. Braun, J. and J. Sieper, Ankylosing spondylitis. The Lancet, 2007. 369(9570): p. 1379-1390.
14. Feldtkeller, E., et al., Age at disease onset and diagnosis delay in HLA-B27 negative vs. positive patients with ankylosing spondylitis. Rheumatology international, 2003. 23: p. 61-66.
15. Gabriel, S.E. and K. Michaud, Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis research & therapy, 2009. 11: p. 1-16.
16. Tobón, G.J., P. Youinou, and A. Saraux, The environment, geo-epidemiology, and autoimmune disease: Rheumatoid arthritis. Autoimmunity reviews, 2010. 9(5): p. A288-A292.
17. Shapira, Y., N. Agmon-Levin, and Y. Shoenfeld, Geoepidemiology of autoimmune rheumatic diseases. Nature Reviews Rheumatology, 2010. 6(8): p. 468-476.
18. Alamanos, Y. and A.A. Drosos, Epidemiology of adult rheumatoid arthritis. Autoimmunity reviews, 2005. 4(3): p. 130-136.
19. Vander Cruyssen, B., et al., The epidemiology of ankylosing spondylitis and the commencement of anti-TNF therapy in daily rheumatology practice. Annals of the rheumatic diseases, 2007. 66(8): p. 1072-1077.
20. Exarchou, S., et al., The prevalence of clinically diagnosed ankylosing spondylitis and its clinical manifestations: a nationwide register study. Arthritis research & therapy, 2015. 17(1): p. 1-9.
21. Nielen, M.M., et al., Specific autoantibodies precede the symptoms of rheumatoid arthritis: a study of serial measurements in blood donors. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 2004. 50(2): p. 380-386.
22. Farng, E. and J.B. Friedrich, Laboratory diagnosis of rheumatoid arthritis. Journal of Hand Surgery, 2011. 36(5): p. 926-927.

23. Bayliss, C., et al., Laboratory diagnosis of rheumatoid arthritis. Prospective study of 85 patients. Annals of the Rheumatic Diseases, 1975. 34(5): p. 395-402.
24. Spoorenberg, A., et al., Relative value of erythrocyte sedimentation rate and C-reactive protein in assessment of disease activity in ankylosing spondylitis. Outcome and disease activity in ankylosing spondylitis: an international study, 2003.
25. Laurent, M. and G. Panayi, Acute-phase proteins and serum immunoglobulins in ankylosing spondylitis. Annals of the rheumatic diseases, 1983. 42(5): p. 524-528.
26. Roberts-Thomson, P.J., et al., Stochastic processes in the causation of rheumatic disease. The Journal of Rheumatology, 2002. 29(12): p. 2628-2634.
27. Petrovská, N., et al., The pre-clinical phase of rheumatoid arthritis: from risk factors to prevention of arthritis. Autoimmunity Reviews, 2021. 20(5): p. 102797.
28. MacGregor, A.J., et al., Characterizing the quantitative genetic contribution to rheumatoid arthritis using data from twins. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 2000. 43(1): p. 30-37.
29. Van der Helm-van Mil, A.H., et al., The HLA–DRB1 shared epitope alleles are primarily a risk factor for anti–cyclic citrullinated peptide antibodies and are not an independent risk factor for development of rheumatoid arthritis. Arthritis & Rheumatism, 2006. 54(4): p. 1117-1121.
30. Baka, Z., E. Buzás, and G. Nagy, Rheumatoid arthritis and smoking: putting the pieces together. Arthritis research & therapy, 2009. 11: p. 1-13.
31. Jick, S.S., et al., Hyperlipidaemia, statin use and the risk of developing rheumatoid arthritis. Annals of the rheumatic diseases, 2009. 68(4): p. 546-551.
32. Bach, J.-F., Infections and autoimmune diseases. Journal of autoimmunity, 2005. 25: p. 74-80.
33. Meer, E., et al., Risk factors for diagnosis of psoriatic arthritis, psoriasis, rheumatoid arthritis, and ankylosing spondylitis: a set of parallel case-control studies. The Journal of Rheumatology, 2022. 49(1): p. 53-59.
34. De Man, Y.A., et al., Disease activity of rheumatoid arthritis during pregnancy: results from a nationwide prospective study. Arthritis Care & Research: Official Journal of the American College of Rheumatology, 2008. 59(9): p. 1241-1248.
35. OSTENSEN, M., The effect of pregnancy on ankylosing spondylitis, psoriatic arthritis, and juvenile rheumatoid arthritis. American journal of reproductive immunology, 1992. 28(3-4): p. 235-237.
36. Khanna, M., 6 Rheumatoid Arthritis: Etiopathogenesis, Clinical Features, and Management. Textbook of Orthopedic Rheumatology, 2021: p. 26.
37. Armas, J.B., A.R. Couto, and B.F. Bettencourt, Spondyloarthritis, diffuse idiopathic skeletal hyperostosis (DISH) and chondrocalcinosis. Molecular Mechanisms of Spondyloarthropathies, 2009: p. 37-56.
38. Williams, R. and B. Ansell, Radiological findings in seropositive juvenile chronic arthritis (juvenile rheumatoid arthritis) with particular reference to progression. Annals of the rheumatic diseases, 1985. 44(10): p. 685-693.
39. Burgos-Vargas, R. and J.V. Zquez-Mellado, The early clinical recognition of juvenile-onset ankylosing spondylitis and its differentiation from juvenile rheumatoid arthritis. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 1995. 38(6): p. 835-844.
40. Gulati, M., Z. Farah, and M. Mouyis, Clinical features of rheumatoid arthritis. Medicine, 2018. 46(4): p. 211-215.
41. Mythili, T., A Clinical Study on Visual Outcome following Uveitis. 2016, Thanjavur Medical College, Thanjavur.
42. Rudwaleit, M., et al., Inflammatory back pain in ankylosing spondylitis: a reassessment of the clinical history for application as classification

and diagnostic criteria. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 2006. 54(2): p. 569-578.
43. Van der Horst-Bruinsma, I.E., Clinical aspects of ankylosing spondylitis. Ankylosing Spondylitis. Diagnosis and Management. Van Royen BJ, Dijkmans BAC, editors. New York, London: Taylor and Francis, 2006: p. 45-70.
44. Dernis, E., et al., Clinical and laboratory follow-up for treating and monitoring patients with ankylosing spondylitis: development of recommendations for clinical practice based on published evidence and expert opinion. Joint Bone Spine, 2007. 74(4): p. 330-337.
45. Moll, J. and V. Wright, New York clinical criteria for ankylosing spondylitis. A statistical evaluation. Annals of the rheumatic diseases, 1973. 32(4): p. 354.
46. McVeigh, C.M. and A.P. Cairns, Diagnosis and management of ankylosing spondylitis. Bmj, 2006. 333(7568): p. 581-585.
47. Østergaard, M., S.J. Pedersen, and U.M. Døhn, Imaging in rheumatoid arthritis–status and recent advances for magnetic resonance imaging, ultrasonography, computed tomography and conventional radiography. Best practice & research Clinical rheumatology, 2008. 22(6): p. 1019-1044.
48. Singh, J.A., et al., 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis & rheumatology, 2016. 68(1): p. 1-26.
49. Sun, J., et al., Investigating the safety and compliance of using csDMARDs in rheumatoid arthritis treatment through face-to-face interviews: a cross-sectional study in China. Clinical Rheumatology, 2021. 40: p. 1789-1798.
50. Moura, M.D.G., et al., Use of steroid and nonsteroidal anti-inflammatories in the treatment of rheumatoid arthritis: Systematic review protocol. Medicine, 2018. 97(41).
51. Whittle, S.L., et al., Multinational evidence-based recommendations for pain management by pharmacotherapy in inflammatory arthritis: integrating systematic literature research and expert opinion of a broad panel of rheumatologists in the 3e Initiative. Rheumatology, 2012. 51(8): p. 1416-1425.
52. Crofford, L.J., Use of NSAIDs in treating patients with arthritis. Arthritis research & therapy, 2013. 15: p. 1-10.
53. Bullock, J., et al., Rheumatoid arthritis: a brief overview of the treatment. Medical Principles and Practice, 2019. 27(6): p. 501-507.
54. Liu, D., et al., A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. Allergy, asthma & clinical immunology, 2013. 9: p. 1-25.
55. Hua, C., F. Buttgereit, and B. Combe, Glucocorticoids in rheumatoid arthritis: current status and future studies. RMD open, 2020. 6(1): p. e000536.
56. Buckley, C., EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Annals of the Rheumatic Diseases, 2017.
57. Smolen, J.S., et al., Proposal for a new nomenclature of disease-modifying antirheumatic drugs. Annals of the rheumatic diseases, 2014. 73(1): p. 3-5.
58. Curtis, J.R., et al., Real-world outcomes associated with methotrexate, sulfasalazine, and hydroxychloroquine triple therapy versus tumor necrosis factor inhibitor/methotrexate combination therapy in patients with rheumatoid arthritis. Arthritis Care & Research, 2021. 73(8): p. 1114-1124.
59. Monti, S., et al., Factors influencing the choice of first-and second-line biologic therapy for the treatment of rheumatoid arthritis: real-life data from the Italian LORHEN Registry. Clinical Rheumatology, 2017. 36: p. 753-761.
60. Bywall, K.S., et al., Patient preferences on rheumatoid arthritis second-line treatment: a discrete choice experiment of Swedish patients. Arthritis Research & Therapy, 2020. 22(1): p. 1-10.

61. Smolen, J.S., et al., EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Annals of the rheumatic diseases, 2017: p. annrheumdis-2016-210715.
62. Yamaoka, K., Janus kinase inhibitors for rheumatoid arthritis. Current opinion in chemical biology, 2016. 32: p. 29-33.
63. Radu, A.-F. and S.G. Bungau, Management of rheumatoid arthritis: an overview. Cells, 2021. 10(11): p. 2857.
64. Sangha, O., Epidemiology of rheumatic diseases. Rheumatology, 2000. 39(suppl_2): p. 3-12.
65. James, P.B., et al., Traditional, complementary and alternative medicine use in Sub-Saharan Africa: a systematic review. BMJ global health, 2018. 3(5): p. e000895.
66. Baraliakos, X., et al., Progression of radiographic damage in patients with ankylosing spondylitis: defining the central role of syndesmophytes. Annals of the rheumatic diseases, 2007. 66(7): p. 910-915.
67. Zochling, J., et al., ASAS/EULAR recommendations for the management of ankylosing spondylitis. Annals of the rheumatic diseases, 2006. 65(4): p. 442-452.
68. Dougados, M., et al., Conventional treatments for ankylosing spondylitis. Annals of the rheumatic diseases, 2002. 61(suppl 3): p. iii40-iii50.
69. Kraag, G., et al., The effects of comprehensive home physiotherapy and supervision on patients with ankylosing spondylitis--a randomized controlled trial. The Journal of rheumatology, 1990. 17(2): p. 228-233.
70. Braun, J., et al., Major reduction in spinal inflammation in patients with ankylosing spondylitis after treatment with infliximab: results of a multicenter, randomized, double-blind, placebo-controlled magnetic resonance imaging study. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 2006. 54(5): p. 1646-1652.
71. Braun, J. and D. van der Heijde, Novel approaches in the treatment of ankylosing spondylitis and other spondyloarthritides. Expert Opinion on Investigational Drugs, 2003. 12(7): p. 1097-1109.
72. Heiberg, M.S., et al., The comparative effectiveness of tumor necrosis factor–blocking agents in patients with rheumatoid arthritis and patients with ankylosing spondylitis: a six-month, longitudinal, observational, multicenter study. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 2005. 52(8): p. 2506-2512.
73. Braun, J. and J. Sieper, Therapy of ankylosing spondylitis and other spondyloarthritides: established medical treatment, anti-TNF-α therapy and other novel approaches. Arthritis Research & Therapy, 2002. 4(5): p. 1-15.

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