A Brief Review Of Pathophysiology And Management Of Different Types Of Arthritis

Shadab Ali[1]*, Sayad Ahad Ali[1], Pydiraju Kondrapu[2], Nidhi Tripathi[3], Pramod Bhaskar Kumar[4], Dr P. Dharani Prasad[5], Manisha Madhukar Tonape[6], Mr. Pratik P. Terse[7], Muhammed Ameen MP[8], Sunil Kumar[9], Abhisek Saha[10]

[1,2] Assistant Professor, Department of Pharmacy, IIMT College of Medical Sciences, IIMT University, 'O' Pocket, Ganganagar, Meerut, U.P., 250001, India

[2] Assistant Professor, Aditya Pharmacy College

[3] Assistant Professor, Anuragh Memorial College, Katari Hill Road, Gaya 823001

[4] Associate Professor, Shree Devi College of Pharmacy. Airport Road. Kenjar. Mangalore, DK Karnataka 574142

[5] Professor, MB University erstwhile (Sree Vidyaniketan College of Pharmacy) Tirupati 517102

[6] Head of the Department and Associate Professor, Physiotherapy Department, School of Allied Health Science, The Assam Kaziranga University, Koraikowa, Jorhat, Assam 785006

[7] Research Scholar, Madhav University Rajasthan, Pin: 307026

[8] Assistant Professor, Department of Pharmacology, Yenepoya Pharmacy College & Research Centre, Yenepoya (Deemed to be University), Mangaluru-575018

[9] Associate professor, Faculty of pharmacy, P.K.University, Village - Thanra, Teshsil- Karera, Dist: Shivpuri, M.P.- 473665

[10] Associate Professor in Chemistry, Tufanganj College, West Bengal, Pin code 736160

Corresponding Author

Shadab Ali,

Assistant Professor, Department of Pharmacy, IIMT College of Medical Sciences, IIMT University, 'O' Pocket, Ganganagar, Meerut, U.P., 250001, India

shadabali12341234@gmail.com, ahadali75405@gmail.com

Article History: Received: 10/5/2023 Revised: 12/6/2023 Accepted: 14/7/2023

Abstract

Arthritis is derived from the Greek term "disease of the joints." It is defined as an acute or chronic joint inflammation that often co-exists with pain and structural damage. Hereditary and acquired autoinflammatory illnesses have a direct correlation with several inflammasomes. Numerous autoimmune illnesses, including systemic lupus erythematosus (SLE), type 1 and type 2 diabetes, neurological disorders, and cancer, have been linked to excessive inflammasome activation. A frequent kind of systemic autoimmune illness that mostly affects synovial joints is rheumatoid arthritis (RA). Osteoarthritis (OA) is the most common form of arthritis that simultaneously affects the lives of elderly people as well as young individuals suffering post-traumatic injuries. Any articular joint in the body may be affected by this chronic inflammatory

disease, but knees, hands, feet, and fingers are most frequently affected. Compared to RA, OA synovitis is more localized; in the knee, the suprapatellar pouch is the most prevalent location. While synovitis may only play a small part in the development of OA in some people, it plays a significant role in the destruction of joints in RA. Psoriasis is a multisystem, chronic inflammatory skin illness that most frequently affects the extensor surfaces of the elbows and knees. Blood and serological markers hold advantages over articular chemokines and radiology. Since the autoantibodies can be identified in pre articular phase in blood. Rheumatoid arthritis is allied with different autoantibodies including Rheumatoid factor (RF), Anti cyclic citrullinated peptide antibody (ACPA), Anti keratin antibody (AKA), Anti perinuclear factor (APF) and Anti-filaggrin antibody. Conventional radiography (CR) is currently regarded as the gold standard approach for evaluating structural damage. Radiography emphasizes the importance of cortical bone, which is visible on standard X-rays due to its calcium concentration. Ultrasound is an important tool in medical diagnostics. It is non-invasive and simple to perform, does not involve radiation, and requires extremely portable equipment. PET is used in conjunction with a structural imaging modality (most commonly CT) to generate detailed cross-sectional anatomical pictures on which functional information can be placed. Several studies have already demonstrated that PET can predict the onset of RA in patients without arthritis. Joint scintigraphy is a non-invasive technique for detecting and measuring joint inflammation. Skeletal scintigraphy is a more selective tool for detecting joint inflammation than radiography and is more sensitive than clinical examination.

Keywords: Rheumatoid Arthritis, Rheumatoid Factor, Conventional radiography, Osteoarthritis

DOI:10.48047/ecb/2023.12.si12.016

1. INTRODUCTION

Arthritis is derived from the Greek term “disease of the joints.” It is defined as an acute or chronic joint inflammation that often co-exists with pain and structural damage(Singh and Vogelgesang 2017). Arthritis is not the same as arthralgia, which is a term for pain that is restricted to a joint, independent of its cause (which may or may not be a result of joint inflammation). More than 100 different forms of arthritis have been identified, with osteoarthritis—a non-inflammatory form of arthritis—being the most prevalent. Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, etc.), crystal deposition-induced inflammation (gout, pseudogout, basic calcium phosphate disease), or infections (septic arthritis, Lyme's arthritis) can all result in inflammation-related arthritis(Heras and Gahunia 2020). Along with other autoimmune connective tissue illnesses such systemic lupus erythematosus, Sjogren syndrome, scleroderma, myositis, inflammatory bowel disease, celiac disease, etc., inflammatory arthritis can also occur with these conditions(Mohana-Borges, Chung, and Resnick 2004). Clinical features that are present in all types of arthritis include monocyte infiltration, inflammation, synovial edoema, synovial tissue proliferation, stiffness in the joints, and articular cartilage degradation. Anti-inflammatory drugs are widely prescribed for the treatment of arthritis, but they may also have harmful side effects, such as gastrointestinal bleeding, an

increased risk of heart attacks, and other cardiovascular problems. Novel therapy approaches and additional prognostic markers are desperately needed for these patients(Tang 2019).

The cytoplasm of innate immune cells contains molecules termed inflammasomes. After activation, these signalling systems have a proteolytic activity that initiates inflammatory processes such the production of the pro-inflammatory cytokine interleukin 1 (IL-1), among others. Inflammasomes can detect two insults: pathogens and tissue damage. Numerous inflammasomes are directly correlated with hereditary and acquired autoinflammatory diseases. Excessive inflammasome activation has been shown to induce autoimmune diseases such systemic lupus erythematosus (SLE), type 1 and type 2 diabetes, neurological disorders, and cancer(Spel and Martinon 2020).

1.1. Rheumatoid Arthritis (RA)

Rheumatoid arthritis (RA) is a common systemic autoimmune disease principally affecting synovial joints. Immune cell infiltration in the joint is a hallmark of RA. It affects 0.5–1% of the world's population. Incidence of RA rises with age and is more common in women than in males. Although any joint might be damaged, the condition primarily affects the hands, feet, and knees. Pain, stiffness and swelling of the joints, as well as possible cartilage and bone degeneration that may cause loss of joint function, are the primary signs and symptoms of RA (van Delft and Huizinga 2020). Rheumatoid arthritis (RA) is defined as a systemic autoimmune pathology associated with a chronic inflammatory process, which can damage both joints and extra-articular organs, including the heart, kidney, lungs, digestive system, eye, skin, and nervous system(Radu and Bungau 2021).

With a prevalence ranging from 0.4% to 1.3% of the population depending on both sex (women are affected two to three times more often than men), age (frequency of new RA diagnoses peaks in the sixth decade of life), and studied patient collective (RA frequency increases from south to north and is higher in urban than rural areas), RA is one of the most prevalent chronic inflammatory diseases(Kavanaugh 1999). Non-hematopoietic, tissue-resident fibroblasts, contributes to the pathogenesis of many diseases and are known to develop epigenetically imprinted, site, and disease-specific phenotypes. Rheumatoid arthritis (RA) is a prototypic IMID in which synovial fibroblasts (SFs) contribute to both joint damage and inflammation(Croft et al. 2019).

Proinflammatory pathways result in localized joint and systemic inflammation, with cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-a (TNF-a), IL-1b, as well as downstream signaling pathways, e.g., the Janus kinase (JAK)/signal transducers and activators of transcription pathway, playing important roles. One function of IL-6 is to drive the production of the acute-phase reactant C-reactive protein (CRP) following an inflammatory event(Pope and Choy 2021). As a clinical entity, RA is a disease of the 6th decade of life. As an immunological entity, RA begins years to decades earlier. Genetic polymorphisms contribute 30–60% of the risk. HLA-class II alleles confer the strongest risk; specifically, HLA-DRB1 alleles containing a sequence stretch from position 71–74 of the β-chain(Sivanand 2019). Studies investigating the correlation between variations in human genome sequences and RA case–control phenotypes

have identified many genetic variants associated with RA susceptibility. Here, we briefly review the history of RA genetics research (table 1) (Okada et al. 2019).

Won et al. most recently revised the algorithm for determining RA using claims, which had previously been validated in Korea. We chose people having claims data for RA (ICD-10 codes M05 or M06) who were under the age of 19 in agreement with Won et al. If a prescription for disease-modifying antirheumatic medication was written within a year of the RA code being assigned, RA was considered to have been confirmed. A one-year window period (during which no RA codes or prescriptions may be written) and three years of treatment are required for incident RA, also known as new RA cases(Joo et al. 2019). Congestive heart failure (CHF) and ischemic heart disease are the two most prevalent clinical symptoms of CVD in RA. Mantel et al. found that patients with RA have worse outcomes after attacks and more severe acute coronary syndromes than the general population (HR= 1.50 [95% CI 1.19-1.90]), which can only be partially accounted for by the severity of the event. They compared 1135 RA patients with 3184 controls in 2015(河合 and 草野 1969). According to a recent cross-sectional epidemiological study, Spain has a prevalence of RA of 1.07% [95% confidence interval (CI): 0.70-1.44], which is comparable to that of Western nations. Osteoporosis (OP) is a common systemic skeletal condition marked by decreased bone mass and microarchitecture bone tissue degeneration, which causes bone fragility and fracture susceptibility. Fragility fracture is characterized as a spontaneous fracture that develops from little to no discernible trauma and indicates OP(Llorente et al. 2020).

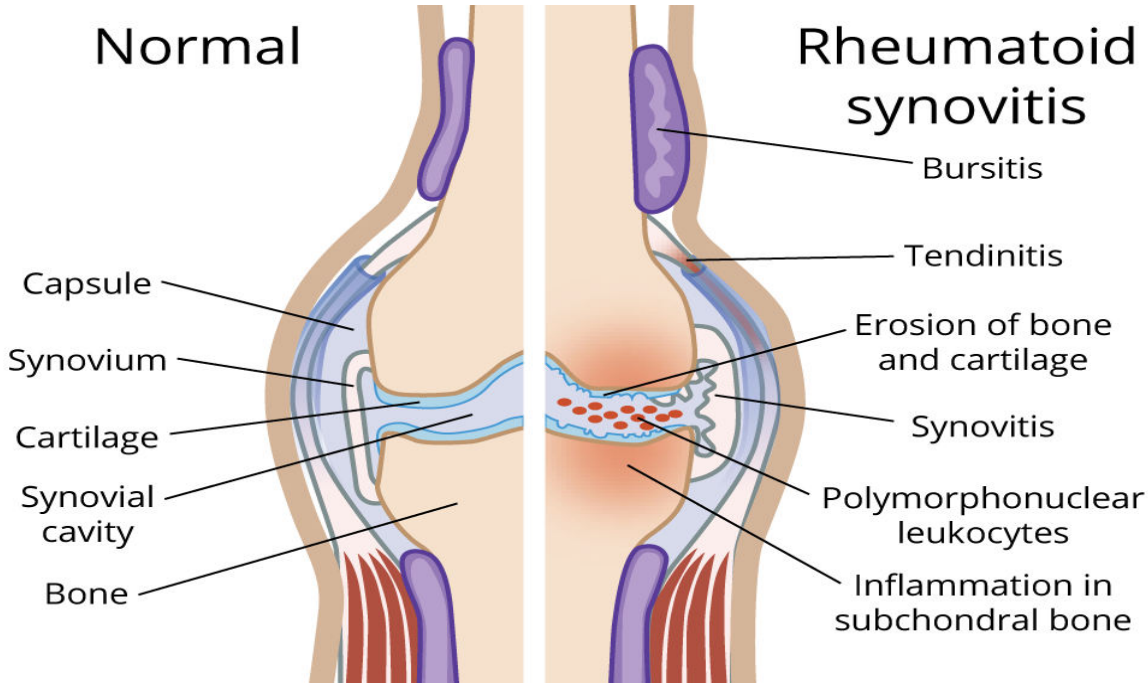
Periodontitis and tooth loss are more prevalent in rheumatoid arthritis patients. De Pablo et al. examined data from the third US National Health and Nutrition Examination Survey on 103 rheumatoid arthritis patients older than 60 years. After correcting for age, gender, ethnicity, and smoking, researchers discovered that people with rheumatoid arthritis had a higher chance of developing periodontitis (odds ratio 4.1, 95% confidence range 1.3-13.1)(González-Febles and Sanz 2021);(Ali, Pathak, and Mandal 2023). Even though correct assessment and diagnosis vary between research, mental health issues have long been acknowledged as significant rheumatoid arthritis co-morbidities(Nerurkar et al. 2019).

1.1.1. Sign and Symptoms:

The initial sign of RA is pain in the joints, particularly in the hands and feet, as well as morning stiffness that lasts longer than 30 minutes. As the disease progresses, RA-affected joints swell and become stiff. The rise and fall of the pain and swelling frequently include flares—abrupt increases in inflammation—followed by stretches of relative recovery. When the condition flares up, patients may also experience flu-like symptoms like fatigue and aches and pains(Aletaha and Smolen 2018). RA, which is characterized by discomfort and swelling, most frequently affects the tiny joints. This chronic, progressive joint degeneration reduces physical function, working capacity, and quality of life(Rein and Mueller 2017),(Alpizar-Rodriguez et al. 2019).

Some signs and symptoms are mentioned below:

Pain or aching in more than one joint, Stiffness in more than one joint, Tenderness and swelling in more than one joint, The same symptoms on both sides of the body (such as in both hands or both knees), Weight loss, Fever, Fatigue or tiredness, Weakness.



1.1.2. Pathophysiology of Rheumatoid Arthritis

The pathophysiology of RA is heavily influenced by monocytes and macrophages, which secrete pro-inflammatory cytokines such as TNF, IL-1, and IL-6. In RA, the CD14+ population of synovial macrophages and peripheral monocytes expressed more of the chemokine receptor CCR9, which is crucial for leukocyte migration to and retention in RA joints. Both RA patients and controls have macrophages colocalized with CCL25 (a CCR9 ligand) in the synovium. In comparison to controls, treatment with CCL25 in vitro often caused RA monocytes to differentiate more strongly from monocyte to macrophage(Cooles and Isaacs 2011). According to numerous studies, adiponectin can play a significant pro-inflammatory role in the development of RA, particularly in the joints, by activating synovial fibroblasts that express adiponectin receptors and causing them to secrete inflammatory mediators(Szumilas et al. 2020).

- **Rheumatoid arthritis synovial fibroblasts**

In RA synovium, particularly in FLSs and macrophage-like synoviocytes, Angptl2 and its mRNA are abundantly expressed. In addition, in vitro, Angptl2 enhances the chemotaxis of CD14+CD16- monocytes, hence boosting chronic inflammation.

- **ACPA Stimulate Macrophages to Produce TNF**

TNF- precursor molecules are initially created as transmembrane proteins (memTNF), which are then cleaved by metalloproteinases like TNF- converting enzyme (TACE), releasing soluble TNF (sTNF)(Kondo, Kuroda, and Kobayashi 2021).

- **Multidirectional Function of TNF in RA Pathogenesis**

TNF signaling has numerous roles in the etiology of RA. It recruits proinflammatory cells including synovial fibroblasts and macrophages, which release proinflammatory cytokines like IL-6, IL-1, and TNF. It also activates endothelial cells. Along with producing antibodies and regulating osteoclast differentiation, it also regulates T helper (Th)1 and Th17 T cell development.

- **Coordinated Interaction of TNF, IL-17, and IL-6 in RA Pathogenesis**

Numerous triggers, including Toll-like receptor (TLR) ligands, IL-1, and TNF, can trigger the transcription of IL-6. One of the characteristics of RA is the sustained production of IL-6 in synovial fibroblasts following stimulation with TNF. RA is characterized by an increase in IgM and IgG rheumatoid factors as well as antibodies to citrullinated peptides(Srirangan and Choy 2010).

- **Multidirectional Function of IL-6 in RA Pathogenesis**

The differentiation of Treg, Th17, and Tfh cells is controlled by IL-6. Th17 cell growth depends on the IL-6-STAT3 pathway, and increased IL-6-STAT3 signaling leads to IL-17A-dependent mouse autoimmune arthritis(Kondo, Kuroda, and Kobayashi 2021).

1.2. Osteoarthritis (OA)

Osteoarthritis (OA) is the most common form of arthritis that simultaneously affects the lives of elderly people as well as young individuals suffering post-traumatic injuries(Allen, Thoma, and Golightly 2022). Any articular joint in the body may be affected by this chronic inflammatory disease, but knees, hands, feet, and fingers are most frequently affected. Subchondral sclerosis, synovial membrane inflammation, and enzymatic extracellular matrix (ECM) degradation all simultaneously play a crucial part in the complicated illness known as OA that affects the entire joint(Di Francesco et al. 2022). Osteoarthritis (OA) is a condition that alters the anatomy and physiology of joint tissues, causing osteophyte production, cartilage degeneration, and bone remodeling. These changes result in pain, stiffness, swelling, and limitations on joint function.(Allen, Thoma, and Golightly 2022). OA is a heterogeneous and complex illness that affects several joints, including the knee, hip, lumbar facet joint, and temporomandibular joint (TMJ). The risk factors for knee and hip OA include heredity, aging, sex (female), race, occupation (physical labour), obesity, hypertension, aberrant joint strength lines, weak muscle strength, high-intensity exercise, and a history of joint damage. Around 61.2 million adults in China and 303 million adults worldwide were estimated to have OA in 2017(Tong et al. 2022).

According to data from the Global Burden of Disease (GBD), the age-standardized incidence rate (ASIR) of OA increased globally every year by 0.32% (95% CI 0.28, 0.36) or by almost 9% during a 28-year period. Without accounting for age, it is crucial to keep in mind that the aging world population is causing a significantly higher rise in the number of new cases of OA(Quicke et al. 2022). While T cells are more prevalent in the synovitis of rheumatoid arthritis (RA) than macrophages are in osteoarthritis (OA)(Katz, Arant, and Loeser 2021). This shows that the innate immune system is being activated in OA joints, perhaps as a result of joint tissue

destruction that creates an environment similar to a chronic wound(Orlowsky and Kraus 2015). The primary feature of low-grade synovitis is activation of innate immune effector cells, with macrophages emerging as a significant dysregulation cell type(van den Bosch 2021). Even though it has previously been demonstrated that T cells exist in the synovium, OA is typically not regarded as an autoimmune condition(Klein-Wieringa et al. 2016). Compared to RA, OA synovitis is more localized; in the knee, the suprapatellar pouch is the most prevalent location. While synovitis may only play a small part in the development of OA in some people, it plays a significant role in the destruction of joints in RA(Scanzello and Goldring 2012). Immune cells infiltrate the inflamed synovium of OA patients, and these cells can generate a variety of inflammatory mediators that may be responsible for the relationship between inflammation and pain/structural damage(de Lange-Brokaar et al. 2012).

1.2.1. Sign and Symptoms:

Pain around the joint is the most typical sign of OA. Pain can be dull, acute, ongoing, or sporadic. Mild to excruciating pain can exist. The range of motion may be reduced. Muscle weakness and grinding or popping noises could be heard by the practitioner. Problematic knee symptoms include swelling, locking, and giving way(Lespasio et al. 2017). These impairments, which are primarily pain-related, frequently appear as difficulty in walking, climbing stairs, performing domestic tasks, and sitting erect. They also have a detrimental psychological impact, which can all contribute to a lower quality of life(Mahir et al. 2016). Patients with early OA often report periodic diffuse joint pain that worsens after prolonged stress (such as physical activity), light crepitation, and/or discomfort that is depending on the angle at which the load is applied(Madry et al. 2016). Rest and some sports, such as low-resistance cycling, might ease the pain(JW, F, and FP. 2011). One of the initial symptoms is frequent pain when climbing stairs. Activities involving kneeling or squatting are linked to higher pain perception and repetitive loading during or after sports activity(Nóra 2014).

As with other types of pain, OA pain is exacerbated by joint use and is lessened by rest. The three stages it can go through are the most common and occur frequently(Hawker et al. 2008):

Stage1: Predictable, acute pain that is typically caused by a mechanical injury and that eventually limits high-impact activities with just a minimal impact on function.

Stage2: Pain intensifies and begins to interfere with regular activities. Unpredictable stiffness bouts could occur.

Stage3: Persistent dull/aching pain interspersed with periods of extreme, exhausting agony that are frequently unanticipated and cause substantial functional limits

Here are some signs that you should be on the lookout for:

Pain-affected joints might hurt during or after movement, Stiffness. Joint stiffness might be most noticeable upon awakening or after being inactive, such as Tenderness, Loss of flexibility, Grating sensation, Bone spurs, and Swelling.

The morphology of the osseous joint components, cortical bone integrity, and subcortical bone destruction/production can be viewed with higher sensitivity(Cömert Kiliç, Kiliç, and Sümbüllü 2015).

1.2.2. **Pathophysiology of Osteoarthritis**

- **The Role of Immune Cells in Osteoarthritis**

Activated immune cells like neutrophils and macrophages can release cytokines like IL-6 and IL-1, which intensify osteoarthritis' inflammatory process. Osteoarthritis is characterized by an increased infiltration of leukocytes (neutrophils, macrophages, T-lymphocytes, and B lymphocytes), notably in the subintimal layer of the synovium. According to Shan et al., peripheral blood from osteoarthritis patients had higher levels of PD1+CXCR5+ CD4+ T cells, ICOS+CXCR5+ CD4+ T cells, and IL 21+ CXCR5+ CD4+ T cells(Chow and Chin 2020).

- **The Role of Cytokines in Osteoarthritis**

Any inflammatory condition, including osteoarthritis, is primarily driven by cytokines secreted by immune cells. Among the mediators released in early osteoarthritis are proinflammatory cytokines including IL-1 and TNF-. They are made by synoviocytes, mononuclear cells, and activated chondrocytes. In chondrocyte and synoviocyte cultures, inflammation has been induced using TNF- and IL-1. The cells emit IL-6, IL-8, IL-10, IL-1, and TNF after activation.

- **The Role of Chemokines in Osteoarthritis**

T helper cell type 1, T helper cell type 17, and T helper cell type 22 are drawn to the injured joint as a result of these chemokines. Proinflammatory cytokines such as IL-1, IL-17, and IL-22 will consequently be released in the joint, starting the inflammation process.

- **The Role of Matrix Metalloproteinases(MMPs) in Osteoarthritis**

Animals with osteoarthritis were found to have higher levels of MMP-3, MMP-9, and MMP-13. Biological processes including cartilage, bone, synovium, ligaments, periarticular fat, meniscus, and muscle are involved in the development of OA. On radiographs, the hallmark signs of OA are a narrowing of the joint space brought on by the loss of meniscus and articular cartilage, as well as bony abnormalities including osteophytes and subchondral bone sclerosis. In the synovial fluid of people with OA, cytokines such as IL-6, MCP-1, VEGF, IP-10, and MIG are relatively abundant. The pro-inflammatory substances trigger matrix-degrading enzymes, such as the matrix metalloproteinases, causing the joint to gradually deteriorate and reorganize(Etc and Das C, Lucia MS 2019).

1.3. Psoriatic Arthritis (PsA)

Psoriasis is a multisystem, chronic inflammatory skin illness that most frequently affects the extensor surfaces of the elbows and knees. It can also occasionally affect the intergluteal and umbilical region, as well as other regions of the body. In Western adults, it affects 2-4% of the population, and 20–30% of people with psoriasis go on to develop psoriatic arthritis (PsA). In a prospective trial, 51 of 464 psoriasis patients who did not have inflammatory arthritis at the time of clinic presentation and were followed for 8 years acquired PsA, yielding an annual incidence of 2.7%(Ocampo and Gladman 2019).

Psoriatic arthritis (PsA) is a musculoskeletal condition that is persistent, inflammatory, and linked to psoriasis. PsA can occur in up to 30% of psoriasis sufferers throughout their lives. Peripheral arthritis, spondylitis, dactylitis (inflammation of the entire digit), and enthesitis (inflammation where a tendon, ligament, or joint capsule inserts onto the bone) are musculoskeletal symptoms of PsA(Ogdie, Coates, and Gladman 2021). Depending on the study and the nation, data on the prevalence of PsA in adults range from 0.01 to 0.19% of the general population and from 6 to 41% of psoriasis patients. Similarly to this, the annual incidence in the general population ranges from 0.1 to 23.1 cases per 100000 people. There are many different therapeutic choices. Several drugs, such as TNF inhibitors (etanercept, infliximab, adalimumab, certolizumab pegol, golimumab), an IL-12/23 inhibitor (ustekizumab), an IL-17 inhibitor (secukinumab), or targeted synthetic DMARDs (apremilast, tofacitinib), are advised(Pina Vegas et al. 2021). Inflammatory bowel disease (IBD), obesity, metabolic syndrome, cardiovascular disease, and depression are among the comorbidities linked to psoriasis(Carvalho and Hedrich 2021). The most frequent severe illness assumed to be the root of dactylitis is psoriatic arthritis (PsA). Experimental PsA-like disease models in animals, as well as improvements in imaging technology and other clinical investigations, have all contributed to our understanding of the etiology of PsA-related dactylitis(Items et al. 2019).

Other types of spondyloarthritis are grouped with these diseases because psoriatic arthritis has genetic and clinical characteristics in common with them(STEPHEN 1957). Psoriatic arthritis, reactive arthritis, arthritis linked to inflammatory bowel disease, a subgroup of juvenile idiopathic arthritis, and ankylosing spondylitis—the prototypical form of spondyloarthritis—are the disorders together referred to as spondyloarthritis(Dougados and Baeten 2011). Ankylosing spondylitis, also known as radiographic axial spondyloarthritis, is a condition in which the spine or sacroiliac joints have already experienced structural damage. Non-radiographic axial spondyloarthritis refers to patients who do not have this structural damage(Galloway and Machado 2022).

Psoriatic arthritis (PsA) was first described as a distinct illness in 1964 and is currently regarded as a subtype of spondyloarthropathy. Moll and Wright's original definition of PsA was " inflammatory arthritis in the presence of psoriasis with a typical absence of rheumatoid factor(Laura C. Coates and Helliwell 2017). PsA was once believed to be a relatively benign ailment, however, registry data have demonstrated the damaging and progressive nature of the condition(Gladman et al. 1987); it affects the quality of life and functional capacity similarly to rheumatoid arthritis(Sokoll and Helliwell 2001). PsA is a diverse disorder that can affect the musculoskeletal system and cause arthritis, enthesitis, dactylitis, and axial involvement as well as possible skin and nail conditions. PsA involvement can resemble other inflammatory arthritides in different ways(Wilson et al. 2009).

1.3.1. Sign and Symptoms:

The symptoms could appear alone or in combination. PsA affects both men and women equally, and most patients experience its onset between the ages of 30 and 50(A. Gottlieb et al. 2008).

Similar to psoriasis, PsA is linked to many co-morbid conditions, such as anxiety, depression, uveitis, metabolic syndrome, obesity, and diabetes(Ogdie, Schwartzman, and Husni 2015). Within two years of the initial evaluation, 50% of patients have structural damage and functional impairment(Kane et al. 2003); Along with the disease's progression, many patients suffer from permanent joint damage and disability. Symptoms of inflammation in the back include pain that gets better with movement but becomes worse with rest, and morning stiffness that lasts all day(A. B. Gottlieb and Merola 2021).

Here are some signs that you should be on the lookout for:
Moving around in the morning is challenging, your fingertips resemble burnt sausages, you're experiencing lower back pain, your nails are ridged and contain grooves, your eyesight is problematic, always exhausted.

Joint pain, stiffness, and edema are the main signs and symptoms of psoriatic arthritis. Any part of the body, including your fingertips and spine, can be affected, and they can range in severity from minor to severe. Both psoriasis and psoriatic arthritis may have disease flare-ups and remissions. However, dactylitis is not only related to SpA and can also affect those with gout, syphilis, TB, infections of the flexor sheath, sickle cell disease, and sarcoidosis(Kaeley et al. 2018).

1.3.2. Pathophysiology of Psoriatic Arthritis

The scientific community is currently debating and concentrating on two main hypotheses about the pathophysiology of PsA.

- **Classical autoimmune disease**

Investigating a traditional autoimmune mechanism wherein inflammatory CD8+ T cell clones cause reactivity. When a self-peptide is presented by MHC class I susceptibility molecules, autoreactive CD8+ T cells become activated, leading to the persistence of the disease and CD4+ T cell depletion in HIV-positive patients with PsA. Furthermore, PsA's status as an MHC class I-associated and CD8+ T cell-mediated autoimmune disease is supported by the absence of autoantibodies and the predominance of CD8+ T cells in synovial tissue and joint fluid (Kerschbaumer et al., 2016). A crucial transcriptional regulator of CD8 T-cell development is RUNX3(Veale 2013).

- **Enthesitis as the primary site of inflammation**

According to the concept, entheseal inflammation in spondylarthropathies may cause synovitis, which develops as an epiphenomenon of proinflammatory cytokines and growth factors from the enthesitis. Synovitis in spondylarthropathies may be secondary to entheseal inflammation, arising as an epiphenomenon of proinflammatory cytokines and growth factors from the enthesitis, according to the 1998 McGonagle et al. theory (Kerschbaumer et al., 2016). Entheses

are often inserted outside of the joint, which means that they are contacting the periosteal surface outside of the joint capsule(Araujo and Schett 2020).

- **Human leukocyte antigen (HLA) associations**

Candidate gene and linkage studies corroborated this association in PsA following the identification of the Psoriasis susceptibility (PSORS1) gene on 6p21.3 as the primary genetic driver of psoriasis(Emmungil, İlgen, and Direskeneli 2021).

2. DIAGNOSIS

2.1. Diagnosis of Rheumatoid Arthritis

Early diagnosis can stop the progression of the illness in many individuals, preventing or significantly reducing joint damage that cannot be repaired and disability that affects up to 90% of RA patients. This highlights the critical relevance of timely and accurate diagnosis in the treatment of RA(Aletaha and Smolen 2018). Symptoms of the patient, examination findings, risk factor evaluation, family history, joint evaluation by ultrasound sonography, and evaluation of laboratory markers like elevated CRP and ESR levels in the serum and the detection of RA-specific autoantibodies are typically combined to determine the presence of RA(Burmester and Pope 2017). In order to diagnose and track the progression of the disease in RA patients, both MRI and ultrasonography have been suggested. Inflamed joints can be imaged using ultrasound analyses, such as high-resolution musculoskeletal ultrasonography, to image synovial proliferation in grayscale and both current inflammation and neoangiogenesis in power Doppler(do Prado et al. 2018). Additionally, ultrasound can detect bone erosions(Zayat et al. 2015), additionally, subclinical synovitis, which even when a patient appears to be in apparent clinical remission, may lead to radiographic disease progression(Iwamoto et al. 2014). Due to these capabilities, ultrasonography is frequently utilized for the diagnosis of RA and the monitoring of disease states in clinical practice as well as in clinical trials(Lin, Anzaghe, and Schülke 2020).

One or a few joints may be affected by RA in its early stages. Tendon inflammation (tenosynovitis) appears concurrently or even earlier. Imaging with colour Doppler sonography or gadolinium-enhanced magnetic resonance imaging, which show expansion of intra-articular soft tissue or hypervascularization of the synovial membrane, can detect the presence of tenosynovitis, for example at the flexor carpi ulnaris tendon, and subclinical synovial inflammation(Aletaha and Smolen 2018). There are no diagnostic standards for RA. However, despite being primarily created for the identification of homogenous patient populations in clinical studies of RA, the 2010 classification criteria may assist medical professionals in making a diagnosis(Radner et al. 2014); In a recent report, the distinctions between classification and diagnosis were listed(Aggarwal et al. 2015). At least one clinically swollen joint must be present, and a scoring system must yield at least 6 out of 10 points for the condition to be classified as RA(Aletaha et al. 2010).

2.2. Diagnosis of Osteoarthritis

With or without radiographic data, a comprehensive medical history and physical examination findings serve as the main foundation for the diagnosis of OA. The most typical symptom, even if some people may initially show no symptoms, is pain. The weight-bearing joints, such as the knees, hips, and spine, are typically affected first by primary OA, which is typically symmetrical(Taruc-Uy and Lynch 2013).

When a person is 45 years old, has activity-related joint pain, morning stiffness lasting 30 min, crepitus on active motion, bony enlargement, and no palpable warmth, a clinical diagnosis of typical OA can be made without the need for further examination(R. Altman et al. 1990). Deformity, instability, periarticular or joint-line soreness, and pain on patellofemoral compression are other characteristics that may exist(Zhang et al. 2010). Hip OA may be confidently diagnosed by the physician using examination findings such as a loss in internal rotation and hip pain, which is typically felt in the groyne or deep buttock(R. D. Altman 1991). In clinical practice, laboratory testing (such as RF, ESR, and CRP) would be required in patients with suspicious OA symptoms or signs to confirm or rule out coexisting inflammatory illness. However, a diagnosis can be made without these laboratory examinations of the blood, urine, or SF(Wang, Oo, and Linklater 2018).

Osteoarthritis (OA) is a disease affecting the entire joint that is characterized by degenerative changes in the bones, cartilage, menisci, ligaments, and synovial tissue. Recent advancements in soft tissue depiction in other imaging techniques, including magnetic resonance imaging (MRI), ultrasound, and optical coherence tomography (OCT), have improved the diagnosis and treatment of OA(Braun and Gold 2012).

Erythrocyte sedimentation rate and rheumatoid factor tests may be part of clinically appropriate laboratory investigations. Analyses of synovial fluid can be done to help rule out alternative conditions. The white blood cell count in osteoarthritis is often fewer than 500 cells per mm^2 (0.5 × 109 per L) and is primarily made up of mononuclear cells. White blood cell counts in inflammatory aspirates are often more than 2,000 cells per mm^2 (2.0 × 109 per L), and neutrophils are typically the most prevalent cell type(Hinton et al. 2002).

A narrowing of the joint space, the development of osteophytes, the presence of pseudocysts in the subchondral bone, and an increase in subchondral bone density are all osteoarthritis-confirming findings(Kraus 1997). To be sure, osteoarthritis can still be diagnosed even in the absence of radiographic abnormalities(Buckwalter and Lane 1997). The existence of radiographic abnormalities in the absence of symptoms should not result in the diagnosis of osteoarthritis, as many patients with radiographic changes compatible with osteoarthritis are asymptomatic or do not display any disability(Spector et al. 1996).

2.3. Diagnosis of Psoriatic Arthritis

The history, physical examination, typical lack of RF, and radiographic findings are the main factors used to make the diagnosis. The physical examination includes determining the number, distribution, and locations of the affected joints as well as the existence of psoriatic skin lesions(Barth 1997). Most people with psoriatic arthritis are seronegative for RF, although 5% to 9% of patients do have RF identified(Alonso et al. 1991). Since the RF test has a high rate of

false-positive results, a diagnosis must be made using the results in conjunction with additional physical findings(Gardner and Kadel 2003). Elevated erythrocyte sedimentation rate (ESR) and other acute-phase reactants, especially C-reactive protein, are the most typical laboratory abnormalities in psoriatic arthritis patients(Rahman et al. 2001).

Imaging methods for the diagnosis of PsA include radiography, ultrasonography, MRI, computed tomography (CT), and bone scintigraphy(Sankowski et al. 2013). MRI and ultrasonography are now frequently used to evaluate PsA, providing more details about the pathophysiology of the condition. Bone destruction and proliferation are the radiological findings that are most typical with PsA(Möller et al. 2009). In order to investigate subclinical Achilles tendon enthesopathy and confirm a diagnosis in symptomatic patients, ultrasonography is a reliable approach(De Simone et al. 2003). This technique can be utilized to detect retrocalcaneal or preAchilles bursitis, rupture, peritendinitis, and acute or degenerative tendinitis(De Simone et al. 2003). In order to distinguish PsA from rheumatoid arthritis, extra synovial involvement is typically secondary to synovial inflammation, which has been discovered by MRI examination to be a more accurate method of diagnosis for PsA(Schwenzer et al. 2010). Another helpful method for identifying PsA is CT. A limited role for CT played in the diagnosis of peripheral joints, although it may help evaluate spine illness(Laura C. Coates et al. 2012). Multiple psoriasis-affected sites, including the skin, joints, tendons, entheses, and nails, can be thoroughly analyzed using radiography for morpho-structural and blood flow changes(Gutierrez et al. 2010).

3. TREATMENT

3.1. Pharmacological treatment of Arthritis

The intervention was defined as any disease modifying antirheumatic drug (DMARD), either biological (bDMARD) or synthetic (sDMARD), the latter in turn including conventional (csDMARD) and targeted (tsDMARD) sDMARDs;(Smolen et al. 2014) systemic glucocorticoids; non-steroidal anti-inflammatory drugs (NSAIDs) or any combination of them. The following bDMARDs were included: anakinra, infliximab, etanercept, adalimumab, rituximab, abatacept, tocilizumab, golimumab, certolizumab pegol, ustekinumab (UST), secukinumab (SEC), brodalumab, ixekizumab, in all formulations, and duration, as well as biosimilars if data were available. Similarly, all sDMARDs were considered, including csDMARDs previously analysed in PsA: methotrexate (MTX), leflunomide, hydroxychloroquine, sulfasalazine, gold/auranofin, azathioprine, chlorambucil, chloroquine, ciclosporine, cyclophosphamide, mycophenolate, minocycline or penicillamine, but also the tsDMARDs apremilast (APR) and tofacitinib. The comparator was any bDMARD, sDMARD, glucocorticoid, NSAID, combination of any of these or placebo (PBO)(L. C. Coates, Fransen, and Helliwell 2010).

Sr. No.	Drug	Brand Name	Dose	Mechanism of Action	References
1.	Acetaminophen (paracetamol)	Panadol	4 g/day, orally	Inhibits prostaglandin synthesis by	(Towheed et al. 2006)

				reducing the active form of COX-1 and COX-2 enzymes	(Iversen, Bjertnæs, and Skudal 2014)
2.	Ibuprofen	Motrin	(400 - 600 mg thrice daily) with the maximum of 3200 mg/day	Inhibits prostaglandin synthesis by reducing the active form of COX-1 and COX-2 enzymes	(Chou et al. 2011)
3.	Diclofenac	Zorvolex	50 mg - 75 mg twice daily with a maximum of 200 mg/day	Inhibition of prostaglandin synthesis by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) with relative equipotency.	(Ghione et al. 2018)
4.	Codeine	Panadeine	15-60 mg PO q4-6hr PRN	changing the way the brain and nervous system respond to pain	(Sehgal, Colson, and Smith 2013)
5.	Glucocorticoids	Aristocort	7.5 mg/d, Oral or Parenteral route	inhibition of the HPA axis via repression of CRH and ACTH expression	(Pelletier et al. 1987) (DeLay et al. 2009)
6.	Hydroxychloroquine	Plaquenil	200 mg po bid	Modulates cytokine secretion, lysosomal enzymes, and macrophage function	(Case 2001a) (Jessop et al. 1998)
7.	Cyclosporin	Gengraf	2.5 mg/kg/day-4.5 mg/kg/day	Inhibits production of	(Case 2001b)

			po in bid dosing	IL-2 and other T-cell cytokines	
8.	Azathioprine	Imuran	1.5–2.5 mg/kg/day po qd	Inhibits purine metabolism, thereby inhibiting DNA synthesis and cellular proliferation	(Stolk et al. 1998) (Woodland et al. 1981)
9.	Sulphasalazine	Azulfidine	2–3 g/day in po in bid dosing	Modulates B-cell response and angiogenesis	(Plosker and Croom 2005)
10	Methotrexate (MTX)	Folitrax	2.5 milligrams (mg) 2 to 4 times a week	Methotrexate inhibits activation of nuclear factor-κB (NF-κB) by increasing both adenosine release and activation of adenosine receptor A_{2a} and by inhibiting the reduction of BH2 to BH4	(Cronstein and Aune 2020)
11.	Leflunomide	Arava	20 mg once daily	Inhibit the mitochondrial enzyme dihydroorotate dehydrogenase (DHODH)	(Fox et al. 1999)
12.	Certolizumab pegol	Cimzia	400 mg or 200 mg every 2 weeks	Inhibit TNF-α biologic activity, TNFi reduce IL-23 production from inflammatory dendritic cells as well as Th17 cell	(Esposito et al. 2020)

13.	Adalimumab	Amgevita	40 mg every other week	It inhibits TNF-α interaction with p55 (TNFR1) and p75 (TNFR2) cell surface TNF receptors	(Brankov and Jacob 2016)
14.	Infliximab	Remicade	5 mg/kg/ I.V./ regimen at 0, 2, and 6 weeks	Infliximab is a rDNA-derived chimeric IgG monoclonal antibody protein, contains both murine and human components that inhibit (TNF-α), This inhibition of TNF-α stops inflammatory reaction	(Urbánek 2017)
15.	Etanercept	Enbrel	50 mg subcutaneously once a week	Etanercept (TNF) inhibitor; the drug binds TNF-α and TNF-β.TNF is a cytokine that can bind to (TNFR1) or (TNFR2) and is involved in inflammation and the immune response.	(Azevedo et al. 2015) (Zhao, Mysler, and Moots 2018)
16.	Ustekinumab	Stelara	45 mg subcutaneously initially and 4 weeks later	Ustekinumab mediates the body's T-cell response by acting as an	(Cingoz 2009)

				antagonist against interleukin-12 (IL12) and interleukin-23 (IL23)	

3.2. Non Pharmacological Treatment for Arthritis

Importantly, patients with high levels of self-efficacy in their treatment of their arthritis report less pain, exhaustion, physical impairment, and emotional anguish(Liu, Xu, and Wang 2017). Self-efficacy and coping skills appear to be strongly associated, and in arthritis sufferers, this may prevent anxiety brought on by pain(Strahl, Kleinknecht, and Dinnel 2000). Several non-pharmacologic therapy modalities, such as self-management with a focus on exercise, mindfulness based interventions (MBIs), and cognitive behavioural treatments (CBTs), have been popular in recent years.

Sr. No.	Treatment options	General Description	Programs	Result	References
1.	Self-Management	Group or online programmes that support disease understanding, emphasize the individual's involvement in controlling symptoms, emotions, and medicines, and encourage good lifestyle habits including food and exercise.	Arthritis Self-Management Program	Self-management techniques may operate as a moderator in the relationship between self-efficacy and physical activity.	(K. R. Lorig et al. 2001) (Kate R. Lorig et al. 2004) (Ndosi et al. 2016)
2.	Mindfulness Based Interventions	Group-based therapies that often last 8 weeks or longer and are intended to teach people how to practice mindfulness by being mindful in the moment and not	Internal family systems, mindfulness attention and awareness training, mindfulness-based	Through emotion control and positive reevaluation mindfulness may increase self-efficacy.	(Kabat-Zinn 1982) (DiRenzo et al. 2018) (Smith and Zautra 2008)

		passing judgment. Traditional sitting meditations, whole-body scans, moderate yoga, and diverse activities to deal with pain, physical sensations, and emotions are frequently included in programmes.	cognitive therapy (office), and vitality training programme.		
3.	Cognitive Behavioral Therapy	The link between thoughts, physical symptoms, and behaviors is the subject of individualized psychotherapy, which can be conducted in person or online.	(Traditional) Cognitive Behavioral Therapy, Pain Coping Skills Training	Through reorganizing unhealthy attitudes and behaviors with an emphasis on symptom management and symptom prediction, CBT may increase self-efficacy.	(Ólason et al. 2018) (Turner et al. 2016) (Bennell et al. 2018)
4.	Exercises	Physical exercises and sports can be recommended to patients with early RA; muscle strength exercises are advisable	Participate in exercise programmes, Aerobic exercise	Dynamic exercises, occupational therapy, and hydrotherapy can be applied as treatment adjunct to pharmaceutical interventions in patients with early arthritis	(Caspersen, Powell, and Christenson 2013) (Lineker et al. 2001) (Brodin et al. 2008)
5.	Massage	Massage reduces the pain of smooth muscles.	A form of manual therapy,	Systematic manipulation of soft tissues of the body for	(Ernst 2004) (Ernst 2003)

				pain reduction or other therapeutic purposes	
6.	Diet	Dietary measures may be appropriate in patients with early RA to correct nutritional deficiencies	Lifestyle advice should be given to all RA patients to encourage smoking cessation, dietary modification, weight control and exercise.	Dietary therapy is an area of self-help which RA patients frequently want to explore, typically in the early stages of disease, Studies of dietary interventions in the management of musculoskeletal conditions have recently been reviewed	(Rayman and Pattison 2008) (Westhoff, Rau, and Zink 2007) (Van Der Helm-van Mil et al. 2008) (García-Poma et al. 2007)

4. FUTURE DIRECTIONS

Despite significant progress in the pharmacotherapy of arthritis, some patients continue to suffer from progressive and disabling arthritis. In an attempt to understand developing potentially curative therapy, multiple avenues of research are currently underway.

Current experience with biological agents has confirmed the effectiveness of TNF-α blockade in the treatment of RA. Key signalling molecules, such as p38 mitogenactivated protein kinase, nuclear factor-kappa B and c-Jun N-terminal kinase, are involved in modulating the gene transcription and mRNA translation of multiple inflammatory cytokines, including TNF-α. Studies assessing inhibitors of these key signalling molecules are in progress.

There is a large body of evidence which suggests that T cells serve a key role orchestrating the immune-driven inflammatory response in RA. Productive immune responses require T-cell activation. Currently, the most interest in taking advantage of such an approach has been in altering the function of the CD80-CD86/CD28-CTLA-4 (cytotoxic T-lymphocyte-associated antigen) co-stimulatory complex. CD28 and CTLA-4 are present on T cells and bind to CD80 and CD86 molecules present on antigen-presenting cells. CD28 potently stimulates T cells, whereas CTLA-4 serves an inhibitory role. CTLA-4-Ig, a soluble fusion protein of human CTLA-4 combined with the Fc portion of human IgG, has been developed in an attempt to down

regulate T-cell responses(Moreland et al. 2002)(Abrams et al. 1999)(Webb, Walmsley, and Feldmann 1996).

Rituximab is a chimeric monoclonal antibody against CD20, which is present only on the surface of resting and activated mature B cells. It has been used successfully in B-cell-mediated diseases such as non-Hodgkin's lymphoma, idiopathic thrombocytopenia, and autoimmune haemolytic anaemia. In preliminary controlled studies, rituximab has been shown to be efficacious in refractory RA. Further trials are currently ongoing to validate these earlier findings and to define the optimal treatment paradigms(Reduction et al. 2021).

There are various other potential strategies for modulating the immune system in an effort to improve disease outcome. For example, clinical trials assessing the use of agents that modulate the function of adhesion molecules, chemokines and other cytokines are underway. Given the success of the biological therapies brought to the clinic to date, there has been a great deal of interest in identifying subsets of patient who may be the most appropriate candidates for specific therapies. A greater understanding of genomics and proteomics may allow the refinement of therapeutic strategies for individual patients with RA, thereby optimizing efficacy while minimizing toxicity(De Vita et al. 2002)(Leandro, Edwards, and Cambridge 2002)(Zaja et al. 2002) (Köhler et al. 2019).

5. CONCLUSION

This review has provided a thorough summary of the information on the many forms of arthritis, including Rheumatoid Arthritis (RA), Osteoarthritis (OA), and Psoriatic Arthritis (PsA), as well as possible diagnostic techniques (serological and radiographic).Before further conclusive findings were produced, a viable strategy required the development of anti-CD20 treatments. Prof. Smolen's contributions to the subject of autoantibodies cannot be adequately summed up in a review article's brief section, therefore for readers who are interested; we direct them to a lovely review that was published in the Journal of Experimental Medicine(Tan and Smolen 2016). The ultimate objective of RA care is to begin an intensive pharmacological regimen in order to achieve full remission, or at the very least, a marked improvement in symptoms and clinical indicators. The outcomes of the studies were used to create novel therapy strategies and to better understand the pathophysiological pathways, making RA a more manageable disease.

Abbreviations: R.A –Rheumatoid Arthritis, RF- Rheumatoid Factor, CR- Conventional radiography, OA-Osteoarthritis, PET- positron emission tomography

REFERENCES

Abrams, Judith R., Mark G. Lebwohl, Cynthia A. Guzzo, Brian V. Jegasothy, Michael T. Goldfarb, Bernard S. Goffe, Alan Menter, et al. 1999. "CTLA4Ig-Mediated Blockade of T-Cell Costimulation in Patients with Psoriasis Vulgaris." *Journal of Clinical Investigation*. https://doi.org/10.1172/JCI5857.

Aggarwal, Rohit, Sarah Ringold, Dinesh Khanna, Tuhina Neogi, Sindhu R. Johnson, Amy Miller, Hermine I. Brunner, et al. 2015. "Distinctions between Diagnostic and Classification Criteria?" *Arthritis Care and Research*. https://doi.org/10.1002/acr.22583.

Aletaha, Daniel, Tuhina Neogi, Alan J. Silman, Julia Funovits, David T. Felson, Clifton O.

Bingham, Neal S. Birnbaum, et al. 2010. "2010 Rheumatoid Arthritis Classification Criteria: An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative." *Arthritis and Rheumatism*. https://doi.org/10.1002/art.27584.

Aletaha, Daniel, and Josef S. Smolen. 2018. "Diagnosis and Management of Rheumatoid Arthritis: A Review." *JAMA - Journal of the American Medical Association* 320 (13): 1360–72. https://doi.org/10.1001/jama.2018.13103.

Ali, Sayad Ahad, Divya Pathak, and Suraj Mandal. 2023. "INTERNATIONAL JOURNAL OF COVID-19 AND THEIR RELATIONSHIP WITH ENVIRONMENT" 14 (1): 1–5.

Allen, K. D., L. M. Thoma, and Y. M. Golightly. 2022. "Epidemiology of Osteoarthritis." *Osteoarthritis and Cartilage* 30 (2): 184–95. https://doi.org/10.1016/j.joca.2021.04.020.

Alonso, J. C.Torre, A. Rodriguez Perez, J. M.Arribas Castrillo, J. Ballina Garcia, J. L.Riestra Noriega, and C. Lopez Larrea. 1991. "Psoriatic Arthritis (PA): A Clinical, Immunological and Radiological Study of 180 Patients." *Rheumatology*. https://doi.org/10.1093/rheumatology/30.4.245.

Alpizar-Rodriguez, Deshire, Till Robin Lesker, Achim Gronow, Benoît Gilbert, Elena Raemy, Celine Lamacchia, Cem Gabay, Axel Finckh, and Till Strowig. 2019. "Prevotella Copri in Individuals at Risk for Rheumatoid Arthritis." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/annrheumdis-2018-214514.

Altman, R., G. Alarcon, D. Appelrouth, D. Bloch, D. Borenstein, K. Brandt, C. Brown, et al. 1990. "The American College of Rheumatology Criteria for the Classification and Reporting of Osteoarthritis of the Hand." *Arthritis & Rheumatism*. https://doi.org/10.1002/art.1780331101.

Altman, Roy D. 1991. "Classification of Disease: Osteoarthritis." *Seminars in Arthritis and Rheumatism*. https://doi.org/10.1016/0049-0172(91)90026-V.

Araujo, Elizabeth G., and Georg Schett. 2020. "Enthesitis in Psoriatic Arthritis (Part 1): Pathophysiology." *Rheumatology (United Kingdom)* 59 (Part 1): I10–14. https://doi.org/10.1093/RHEUMATOLOGY/KEAA039.

Azevedo, Valderilio F., Nathalia Galli, Alais Kleinfelder, Julia D'Ippolito, and Paulo C.M. Urbano. 2015. "Etanercept Biosimilars." *Rheumatology International*. https://doi.org/10.1007/s00296-014-3080-5.

Barth, Werner F. 1997. "Office Evaluation of the Patient with Musculoskeletal Complaints." In *American Journal of Medicine*. https://doi.org/10.1016/S0002-9343(97)00410-5.

Bennell, Kim L., Rachel K. Nelligan, Christine Rini, Francis J. Keefe, Jessica Kasza, Simon Frencha, Andrew Forbes, et al. 2018. "Effects of Internet-Based Pain Coping Skills Training before Home Exercise for Individuals with Hip Osteoarthritis (HOPE Trial): A Randomised Controlled Trial." *Pain*. https://doi.org/10.1097/j.pain.0000000000001281.

Bosch, M. H.J. van den. 2021. "Osteoarthritis Year in Review 2020: Biology." *Osteoarthritis and Cartilage*. https://doi.org/10.1016/j.joca.2020.10.006.

Brankov, Nikoleta, and Sharon E. Jacob. 2016. "Adalimumab." *Journal of the Dermatology Nurses' Association*. https://doi.org/10.1097/JDN.0000000000000229.

Braun, Hillary J., and Garry E. Gold. 2012. "Diagnosis of Osteoarthritis: Imaging." *Bone*. https://doi.org/10.1016/j.bone.2011.11.019.

Brodin, Nina, Eva Eurenius, Irene Jensen, Ralph Nisell, Christina H. Opava, Marita Algebrandt, Ingrid Almin, et al. 2008. "Coaching Patients with Early Rheumatoid Arthritis to Healthy Physical Activity: A Multicenter, Randomized, Controlled Study." *Arthritis Care and Research*. https://doi.org/10.1002/art.23327.

Buckwalter, Joseph A., and Nancy E. Lane. 1997. "Athletics and Osteoarthritis." *American Journal of Sports Medicine*. https://doi.org/10.1177/036354659702500624.

Burmester, Gerd R., and Janet E. Pope. 2017. "Novel Treatment Strategies in Rheumatoid Arthritis." *The Lancet*. https://doi.org/10.1016/S0140-6736(17)31491-5.

Carvalho, Ana L., and Christian M. Hedrich. 2021. "The Molecular Pathophysiology of Psoriatic Arthritis—The Complex Interplay Between Genetic Predisposition, Epigenetics Factors, and the Microbiome." *Frontiers in Molecular Biosciences* 8 (April): 1–20. https://doi.org/10.3389/fmolb.2021.662047.

Case, John P. 2001a. "Old and New Drugs Used in Rheumatoid Arthritis: A Historical Perspective Part 1: The Older Drugs." *American Journal of Therapeutics*. https://doi.org/10.1097/00045391-200103000-00007.

———. 2001b. "Old and New Drugs Used in Rheumatoid Arthritis: A Historical Perspective Part 2: The Newer Drugs and Drug Strategies." *American Journal of Therapeutics*. https://doi.org/10.1097/00045391-200105000-00005.

Caspersen, Carl J, Kenneth E Powell, and Gregory M Christenson. 2013. "Physical Activity , Exercise , and Physical Fitness : Definitions and Distinctions for Health- Related Research Reviewed Work." *Public Health Reports*.

Chou, R, Ms McDonagh, E Nakamoto, and J Griffin. 2011. "Analgesics for Osteoarthritis: An Update of the 2006 Comparative Effectiveness Review." *Agency Fo Healthcare Research and Quality*.

Chow, Yoke Yue, and Kok Yong Chin. 2020. "The Role of Inflammation in the Pathogenesis of Osteoarthritis." *Mediators of Inflammation* 2020. https://doi.org/10.1155/2020/8293921.

Cingoz, Oya. 2009. "Ustekinumab." *MAbs*. https://doi.org/10.4161/mabs.1.3.8593.

Coates, L. C., J. Fransen, and P. S. Helliwell. 2010. "Defining Minimal Disease Activity in Psoriatic Arthritis: A Proposed Objective Target for Treatment." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/ard.2008.102053.

Coates, Laura C., and Philip S. Helliwell. 2017. "Psoriatic Arthritis: State of the Art Review." *Clinical Medicine, Journal of the Royal College of Physicians of London*. https://doi.org/10.7861/clinmedicine.17-1-65.

Coates, Laura C., Richard Hodgson, Philip G. Conaghan, and Jane E. Freeston. 2012. "MRI and Ultrasonography for Diagnosis and Monitoring of Psoriatic Arthritis." *Best Practice and Research: Clinical Rheumatology*. https://doi.org/10.1016/j.berh.2012.09.004.

Cömert Kiliç, S., N. Kiliç, and M. A. Sümbüllü. 2015. "Temporomandibular Joint Osteoarthritis: Cone Beam Computed Tomography Findings, Clinical Features, and Correlations."

International Journal of Oral and Maxillofacial Surgery. https://doi.org/10.1016/j.ijom.2015.06.023.

Cooles, Faye A.H., and John D. Isaacs. 2011. "Pathophysiology of Rheumatoid Arthritis." *Current Opinion in Rheumatology* 23 (3): 233–40. https://doi.org/10.1097/BOR.0b013e32834518a3.

Croft, Adam P., Joana Campos, Kathrin Jansen, Jason D. Turner, Jennifer Marshall, Moustafa Attar, Loriane Savary, et al. 2019. "Distinct Fibroblast Subsets Drive Inflammation and Damage in Arthritis." *Nature* 570 (7760): 246–51. https://doi.org/10.1038/s41586-019-1263-7.

Cronstein, Bruce N., and Thomas M. Aune. 2020. "Methotrexate and Its Mechanisms of Action in Inflammatory Arthritis." *Nature Reviews Rheumatology*. https://doi.org/10.1038/s41584-020-0373-9.

DeLay, Monica L., Matthew J. Turner, Erin I. Klenk, Judith A. Smith, Dawn P. Sowders, and Robert A. Colbert. 2009. "HLA-B27 Misfolding and the Unfolded Protein Response Augment Interleukin-23 Production and Are Associated with Th17 Activation in Transgenic Rats." *Arthritis and Rheumatism*. https://doi.org/10.1002/art.24763.

Delft, Myrthe A.M. van, and Tom W.J. Huizinga. 2020. "An Overview of Autoantibodies in Rheumatoid Arthritis." *Journal of Autoimmunity* 110 (December). https://doi.org/10.1016/j.jaut.2019.102392.

DiRenzo, Dana, Monica Crespo-Bosque, Neda Gould, Patrick Finan, Julie Nanavati, and Clifton O. Bingham. 2018. "Systematic Review and Meta-Analysis: Mindfulness-Based Interventions for Rheumatoid Arthritis." *Current Rheumatology Reports*. https://doi.org/10.1007/s11926-018-0787-4.

Dougados, Maxime, and Dominique Baeten. 2011. "Spondyloarthritis." *The Lancet* 377 (9783): 2127–37. https://doi.org/10.1016/S0140-6736(11)60071-8.

Emmungil, Hakan, Ufuk İlgen, and Rafi Haner Direskeneli. 2021. "Autoimmunity in Psoriatic Arthritis: Pathophysiological and Clinical Aspects." *Turkish Journal of Medical Sciences* 51 (4): 1601–14. https://doi.org/10.3906/sag-2011-235.

Ernst, Edzard. 2003. "The Safety of Massage Therapy." *Rheumatology*. https://doi.org/10.1093/rheumatology/keg306.

———. 2004. "Musculoskeletal Conditions and Complementary/Alternative Medicine." *Best Practice and Research: Clinical Rheumatology*. https://doi.org/10.1016/j.berh.2004.03.005.

Esposito, Maria, Francesco Carubbi, Alessandro Giunta, Alessia Alunno, Roberto Giacomelli, and Maria Concetta Fargnoli. 2020. "Certolizumab Pegol for the Treatment of Psoriatic Arthritis and Plaque Psoriasis." *Expert Review of Clinical Immunology*. https://doi.org/10.1080/1744666X.2020.1713754.

Etc, Monica C. Serra, and Hansen KC and Tyler JK Das C, Lucia MS. 2019. "乳鼠心肌提取 HHS Public Access." *Physiology & Behavior* 176 (3): 139–48. https://doi.org/10.1001/jama.2020.22171.Diagnosis.

Fox, Robert I., Matthias L. Herrmann, Costakis G. Frangou, Geoffrey M. Wahl, Randall E.

Morris, Vibeke Strand, and Bernhard J. Kirschbaum. 1999. "Mechanism of Action for Leflunomide in Rheumatoid Arthritis." *Clinical Immunology*. https://doi.org/10.1006/clim.1999.4777.

Francesco, Martina Di, Agnese Fragassi, Martina Pannuzzo, Miguel Ferreira, Sayanti Brahmachari, and Paolo Decuzzi. 2022. "Management of Osteoarthritis: From Drug Molecules to Nano/Micromedicines." *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology* 14 (3): 1–22. https://doi.org/10.1002/wnan.1780.

Galloway, Megan, and Pedro M. Machado. 2022. "Axial Spondyloarthritis." *Medicine (United Kingdom)*. https://doi.org/10.1016/j.mpmed.2021.12.005.

García-Poma, Augusto, Maria I. Segami, Claudia S. Mora, Manuel F. Ugarte, Henry N. Terrazas, Eduardo A. Rhor, Elmer García, et al. 2007. "Obesity Is Independently Associated with Impaired Quality of Life in Patients with Rheumatoid Arthritis." *Clinical Rheumatology*. https://doi.org/10.1007/s10067-007-0583-4.

Gardner, Gregory C., and Nancy J. Kadel. 2003. "Ordering and Interpreting Rheumatologic Laboratory Tests." *The Journal of the American Academy of Orthopaedic Surgeons*. https://doi.org/10.5435/00124635-200301000-00008.

Ghione, Silvia, Hélène Sarter, Mathurin Fumery, Laura Armengol-Debeir, Guillaume Savoye, Delphine Ley, Claire Spyckerelle, et al. 2018. "Dramatic Increase in Incidence of Ulcerative Colitis and Crohn's Disease (1988-2011): A Population-Based Study of French Adolescents." *American Journal of Gastroenterology*. https://doi.org/10.1038/ajg.2017.228.

Gladman, D. D., R. Shuckett, M. L. Russell, J. C. Thorne, and R. K. Schachter. 1987. "Psoriatic Arthritis (PSA) - an Analysis of 220 Patients." *Quarterly Journal of Medicine*. https://doi.org/10.1093/oxfordjournals.qjmed.a068085.

González-Febles, Jerián, and Mariano Sanz. 2021. "Periodontitis and Rheumatoid Arthritis: What Have We Learned about Their Connection and Their Treatment?" *Periodontology 2000* 87 (1): 181–203. https://doi.org/10.1111/prd.12385.

Gottlieb, Alice B., and Joseph F. Merola. 2021. "Axial Psoriatic Arthritis: An Update for Dermatologists." *Journal of the American Academy of Dermatology*. https://doi.org/10.1016/j.jaad.2020.05.089.

Gottlieb, Alice, Neil J. Korman, Kenneth B. Gordon, Steven R. Feldman, Mark Lebwohl, John Y.M. Koo, Abby S. Van Voorhees, et al. 2008. "Guidelines of Care for the Management of Psoriasis and Psoriatic Arthritis. Section 2. Psoriatic Arthritis: Overview and Guidelines of Care for Treatment with an Emphasis on the Biologics." *Journal of the American Academy of Dermatology*. https://doi.org/10.1016/j.jaad.2008.02.040.

Gutierrez, Marwin, Emilio Filippucci, Rossella De Angelis, Giorgio Filosa, David Kane, and Walter Grassi. 2010. "A Sonographic Spectrum of Psoriatic Arthritis: 'The Five Targets.'" *Clinical Rheumatology*. https://doi.org/10.1007/s10067-009-1292-y.

Hawker, G. A., L. Stewart, M. R. French, J. Cibere, J. M. Jordan, L. March, M. Suarez-Almazor, and R. Gooberman-Hill. 2008. "Understanding the Pain Experience in Hip and Knee Osteoarthritis - an OARSI/OMERACT Initiative." *Osteoarthritis and Cartilage*.

https://doi.org/10.1016/j.joca.2007.12.017.

Helm-van Mil, A. H.M. Van Der, S. M. Van Der Kooij, C. F. Allaart, R. E.M. Toes, and T. W.J. Huizinga. 2008. "A High Body Mass Index Has a Protective Effect on the Amount of Joint Destruction in Small Joints in Early Rheumatoid Arthritis." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/ard.2007.078832.

Heras, Facundo Las, and Harpal K. Gahunia. 2020. "Growth and Development of Articular Cartilage." In *Articular Cartilage of the Knee: Health, Disease and Therapy*. https://doi.org/10.1007/978-1-4939-7587-7_2.

Hinton, Ralph, Ron L. Moody, Alan W. Davis, and Sean F. Thomas. 2002. "Osteoarthritis: Diagnosis and Therapeutic Considerations." *American Family Physician*.

Items, Reuse, White Rose, White Rose, Takedown If, and White Rose. 2019. "This Is a Repository Copy of Pathophysiology , Assessment and Treatment of Psoriatic White Rose Research Online URL for This Paper : Version : Accepted Version Article : McGonagle , D , Tan , AL , Watad , A et Al . (1 More Author) (2019) Pathophysiolo."

Iversen, Hilde Hestad, Øyvind Andresen Bjertnæs, and Kjersti Eeg Skudal. 2014. "Patient Evaluation of Hospital Outcomes: An Analysis of Open-Ended Comments from Extreme Clusters in a National Survey." *BMJ Open*. https://doi.org/10.1136/bmjopen-2014-004848.

Iwamoto, Taro, Kei Ikeda, Junichi Hosokawa, Mieko Yamagata, Shigeru Tanaka, Ayako Norimoto, Yoshie Sanayama, et al. 2014. "Prediction of Relapse after Discontinuation of Biologic Agents by Ultrasonographic Assessment in Patients with Rheumatoid Arthritis in Clinical Remission: High Predictive Values of Total Gray-Scale and Power Doppler Scores That Represent Residual Synovial." *Arthritis Care and Research*. https://doi.org/10.1002/acr.22303.

Jessop, J D, M M O Sullivan, P A Lewis, L A Williams, J P Camilleri, M J Plant, and E C Coles. 1998. "A LONG-TERM FIVE-YEAR RANDOMIZED CONTROLLED TRIAL OF HYDROXYCHLOROQUINE , SODIUM AUROTHIOMALATE , AURANOFIN AND PENICILLAMINE IN THE TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS," 992–1002.

Joo, Young Bin, Youn Hee Lim, Ki Jo Kim, Kyung Su Park, and Yune Jung Park. 2019. "Respiratory Viral Infections and the Risk of Rheumatoid Arthritis." *Arthritis Research and Therapy* 21 (1): 1–8. https://doi.org/10.1186/s13075-019-1977-9.

JW, Bijlsma, Berenbaum F, and Lafeber FP. 2011. "Osteoarthritis: An Update with Relevance for Clinical Practice." *The Lancet*.

Kabat-Zinn, Jon. 1982. "An Outpatient Program in Behavioral Medicine for Chronic Pain Patients Based on the Practice of Mindfulness Meditation: Theoretical Considerations and Preliminary Results." *General Hospital Psychiatry*. https://doi.org/10.1016/0163-8343(82)90026-3.

Kaeley, Gurjit S., Lihi Eder, Sibel Z. Aydin, Marwin Gutierrez, and Catherine Bakewell. 2018. "Dactylitis: A Hallmark of Psoriatic Arthritis." *Seminars in Arthritis and Rheumatism*. https://doi.org/10.1016/j.semarthrit.2018.02.002.

Kane, David, L. Stafford, B. Bresniham, and O. FitzGerard. 2003. "A Prospective, Clinical and Radiological Study of Early Psoriatic Arthritis: An Early Synovitis Clinic Experience." *Rheumatology*. https://doi.org/10.1093/rheumatology/keg384.

Katz, Jeffrey N., Kaetlyn R. Arant, and Richard F. Loeser. 2021. "Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review." *JAMA - Journal of the American Medical Association*. https://doi.org/10.1001/jama.2020.22171.

Kavanaugh, Arthur F. 1999. "Treatment Options for Rheumatoid Arthritis." *American Journal of Managed Care* 5 (14 SUPPL.).

Klein-Wieringa, Inge R., Badelog J.E. De Lange-Brokaar, Erlangga Yusuf, Stefan N. Andersen, Joanneke C. Kwekkeboom, Herman M. Kroon, Gerjo J.V.M. Van Osch, et al. 2016. "Inflammatory Cells in Patients with Endstage Knee Osteoarthritis: A Comparison between the Synovium and the Infrapatellar Fat Pad." *Journal of Rheumatology*. https://doi.org/10.3899/jrheum.151068.

Köhler, Birgit M., Janine Günther, Dorothee Kaudewitz, and Hanns Martin Lorenz. 2019. "Current Therapeutic Options in the Treatment of Rheumatoid Arthritis." *Journal of Clinical Medicine* 8 (7): 1–15. https://doi.org/10.3390/jcm8070938.

Kondo, Naoki, Takeshi Kuroda, and Daisuke Kobayashi. 2021. "Cytokine Networks in the Pathogenesis of Rheumatoid Arthritis." *International Journal of Molecular Sciences* 22 (20). https://doi.org/10.3390/ijms222010922.

Kraus, V. B. 1997. "Pathogenesis and Treatment of Osteoarthritis." *Medical Clinics of North America*. https://doi.org/10.1016/S0025-7125(05)70506-X.

Lange-Brokaar, B. J.E. de, A. Ioan-Facsinay, G. J.V.M. van Osch, A. M. Zuurmond, J. Schoones, R. E.M. Toes, T. W.J. Huizinga, and M. Kloppenburg. 2012. "Synovial Inflammation, Immune Cells and Their Cytokines in Osteoarthritis: A Review." *Osteoarthritis and Cartilage*. https://doi.org/10.1016/j.joca.2012.08.027.

Leandro, M. J., Jo C.W. Edwards, and G. Cambridge. 2002. "Clinical Outcome in 22 Patients with Rheumatoid Arthritis Treated with B Lymphocyte Depletion." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/ard.61.10.883.

Lespasio, Michelle J., Nicolas S. Piuzzi, M. Elaine Husni, George F. Muschler, Aj Guarino, and Michael A. Mont. 2017. "Knee Osteoarthritis: A Primer." *The Permanente Journal*. https://doi.org/10.7812/TPP/16-183.

Lin, Yen Ju, Martina Anzaghe, and Stefan Schülke. 2020. "Update on the Pathomechanism, Diagnosis, and Treatment Options for Rheumatoid Arthritis." *Cells*. https://doi.org/10.3390/cells9040880.

Lineker, S. C., M. J. Bell, A. L. Wilkins, and E. M. Badley. 2001. "Improvements Following Short Term Home Based Physical Therapy Are Maintained at One Year in People with Moderate to Severe Rheumatoid Arthritis." *Journal of Rheumatology*.

Liu, Li, Neili Xu, and Lie Wang. 2017. "Moderating Role of Self-Efficacy on the Associations of Social Support with Depressive and Anxiety Symptoms in Chinese Patients with Rheumatoid Arthritis." *Neuropsychiatric Disease and Treatment*.

https://doi.org/10.2147/NDT.S137233.

Llorente, Irene, Noelia García-Castañeda, Cristina Valero, Isidoro González-Álvaro, and Santos Castañeda. 2020. "Osteoporosis in Rheumatoid Arthritis: Dangerous Liaisons." *Frontiers in Medicine* 7 (November): 1–11. https://doi.org/10.3389/fmed.2020.601618.

Lorig, K. R., D. S. Sobel, P. L. Ritter, D. Laurent, and M. Hobbs. 2001. "Effect of a Self-Management Program on Patients with Chronic Disease." *Effective Clinical Practice : ECP*.

Lorig, Kate R., Philip L. Ritter, Diana D. Laurent, and James F. Fries. 2004. "Long-Term Randomized Controlled Trials of Tailored-Print and Small-Group Arthritis Self-Management Interventions." *Medical Care*. https://doi.org/10.1097/01.mlr.0000118709.74348.65.

Madry, Henning, Elizaveta Kon, Vincenzo Condello, Giuseppe M. Peretti, Matthias Steinwachs, Romain Seil, Massimo Berruto, Lars Engebretsen, Giuseppe Filardo, and Peter Angele. 2016. "Early Osteoarthritis of the Knee." *Knee Surgery, Sports Traumatology, Arthroscopy*. https://doi.org/10.1007/s00167-016-4068-3.

Mahir, Laila, Karima Belhaj, Siham Zahi, Herman Azanmasso, Fatima Lmidmani, and Abdellatif El Fatimi. 2016. "Impact of Knee Osteoarthritis on the Quality of Life." *Annals of Physical and Rehabilitation Medicine*. https://doi.org/10.1016/j.rehab.2016.07.355.

Mohana-Borges, Aurea V.R., Christine B. Chung, and Donald Resnick. 2004. "Monoarticular Arthritis." *Radiologic Clinics of North America*. https://doi.org/10.1016/S0033-8389(03)00168-4.

Möller, Burkhard, Harald Bonel, Marianne Rotzetter, Peter M. Villiger, and Hans Rudolf Ziswiler. 2009. "Measuring Finger Joint Cartilage by Ultrasound as a Promising Alternative to Conventional Radiograph Imaging." *Arthritis Care and Research*. https://doi.org/10.1002/art.24424.

Moreland, Larry W., Rieke Alten, Filip Van Den Bosch, Thierry Appelboom, Marc Leon, Paul Emery, Stanley Cohen, et al. 2002. "Costimulatory Blockade in Patients with Rheumatoid Arthritis: A Pilot, Dose-Finding, Double-Blind, Placebo-Controlled Clinical Trial Evaluating CTLA-4Ig and LEA29Y Eighty-Five Days after the First Infusion." *Arthritis and Rheumatism*. https://doi.org/10.1002/art.10294.

Ndosi, M., D. Johnson, T. Young, B. Hardware, J. Hill, C. Hale, J. Maxwell, E. Roussou, and A. Adebajo. 2016. "Effects of Needs-Based Patient Education on Self-Efficacy and Health Outcomes in People with Rheumatoid Arthritis: A Multicentre, Single Blind, Randomised Controlled Trial." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/annrheumdis-2014-207171.

Nerurkar, Louis, Stefan Siebert, Iain B. McInnes, and Jonathan Cavanagh. 2019. "Rheumatoid Arthritis and Depression: An Inflammatory Perspective." *The Lancet Psychiatry* 6 (2): 164–73. https://doi.org/10.1016/S2215-0366(18)30255-4.

Nóra, Román. 2014. "* 于长虹 1,2， **王运武** 1， 马 **武** 2" 9860: 7–12.

Ocampo, Vanessa D., and Dafna Gladman. 2019. "Psoriatic Arthritis [Version 1; Peer Review: 2 Approved]." *F1000Research* 8: 1–16. https://doi.org/10.12688/f1000research.19144.1.

Ogdie, Alexis, Laura C. Coates, and Dafna D. Gladman. 2021. "Treatment Guidelines in Psoriatic Arthritis." *Rheumatology (United Kingdom)* 59: I37–46. https://doi.org/10.1093/RHEUMATOLOGY/KEZ383.

Ogdie, Alexis, Sergio Schwartzman, and M. Elaine Husni. 2015. "Recognizing and Managing Comorbidities in Psoriatic Arthritis." *Current Opinion in Rheumatology*. https://doi.org/10.1097/BOR.0000000000000152.

Okada, Yukinori, Stephen Eyre, Akari Suzuki, Yuta Kochi, and Kazuhiko Yamamoto. 2019. "Genetics of Rheumatoid Arthritis: 2018 Status." *Annals of the Rheumatic Diseases* 78 (4): 446–53. https://doi.org/10.1136/annrheumdis-2018-213678.

Ólason, Magnús, Rúnar H. Andrason, Inga H. Jónsdóttir, Hlín Kristbergsdóttir, and Mark P. Jensen. 2018. "Cognitive Behavioral Therapy for Depression and Anxiety in an Interdisciplinary Rehabilitation Program for Chronic Pain: A Randomized Controlled Trial with a 3-Year Follow-Up." *International Journal of Behavioral Medicine*. https://doi.org/10.1007/s12529-017-9690-z.

Orlowsky, Eric W., and Virginia Byers Kraus. 2015. "The Role of Innate Immunity in Osteoarthritis: When Our First Line of Defense Goes on the Offensive." *Journal of Rheumatology*. https://doi.org/10.3899/jrheum.140382.

Pelletier, J. P., J. Martel-Pelletier, J. M. Cloutier, and J. F. Woessner. 1987. "Proteoglycan-degrading Acid Metalloprotease Activity in Human Osteoarthritic Cartilage, and the Effect of Intraarticular Steroid Injections." *Arthritis & Rheumatism*. https://doi.org/10.1002/art.1780300508.

Pina Vegas, Laura, Emilie Sbidian, Laetitia Penso, and Pascal Claudepierre. 2021. "Epidemiologic Study of Patients with Psoriatic Arthritis in a Real-World Analysis: A Cohort Study of the French Health Insurance Database." *Rheumatology (United Kingdom)* 60 (3): 1243–51. https://doi.org/10.1093/rheumatology/keaa448.

Plosker, Greg L., and Katherine F. Croom. 2005. "Sulfasalazine: A Review of Its Use in the Management of Rheumatoid Arthritis." *Drugs*. https://doi.org/10.2165/00003495-200565130-00008.

Pope, Janet E., and Ernest H. Choy. 2021. "C-Reactive Protein and Implications in Rheumatoid Arthritis and Associated Comorbidities." *Seminars in Arthritis and Rheumatism* 51 (1): 219–29. https://doi.org/10.1016/j.semarthrit.2020.11.005.

Prado, Aline Defaveri do, Henrique Luiz Staub, Melissa Cláudia Bisi, Inês Guimarães da Silveira, José Alexandre Mendonça, Joaquim Polido-Pereira, and João Eurico Fonseca. 2018. "Ultrasound and Its Clinical Use in Rheumatoid Arthritis: Where Do We Stand?" *Advances in Rheumatology (London, England)*. https://doi.org/10.1186/s42358-018-0023-y.

Quicke, J. G., P. G. Conaghan, N. Corp, and G. Peat. 2022. "Osteoarthritis Year in Review 2021: Epidemiology & Therapy." *Osteoarthritis and Cartilage* 30 (2): 196–206. https://doi.org/10.1016/j.joca.2021.10.003.

Radner, Helga, Tuhina Neogi, Josef S. Smolen, and Daniel Aletaha. 2014. "Performance of the 2010 ACR/EULAR Classification Criteria for Rheumatoid Arthritis: A Systematic

Literature Review." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/annrheumdis-2013-203284.

Radu, Andrei Flavius, and Simona Gabriela Bungau. 2021. "Management of Rheumatoid Arthritis: An Overview." *Cells* 10 (11): 1–33. https://doi.org/10.3390/cells10112857.

Rahman, P., E. Nguyen, C. Cheung, C. T. Schentag, and D. D. Gladman. 2001. "Comparison of Radiological Severity in Psoriatic Arthritis and Rheumatoid Arthritis." *Journal of Rheumatology*.

Rayman, Margaret P., and Dorothy J. Pattison. 2008. "Dietary Manipulation in Musculoskeletal Conditions." *Best Practice and Research: Clinical Rheumatology*. https://doi.org/10.1016/j.berh.2007.12.010.

Reduction, Drudgery, Acceptability Of, Drudgery Reducing, Tool In, and O F Dairy Animals. 2021. "Plant Archives" 21 (table 1): 2184–85.

Rein, Philipp, and Ruediger B. Mueller. 2017. "Treatment with Biologicals in Rheumatoid Arthritis: An Overview." *Rheumatology and Therapy*. https://doi.org/10.1007/s40744-017-0073-3.

Sankowski, Artur Jacek, Urszula Maria Łebkowska, Jarosław Ćwikła, Irena Walecka, and Jerzy Walecki. 2013. "The Comparison of Efficacy of Different Imaging Techniques (Conventional Radiography, Ultrasonography, Magnetic Resonance) in Assessment of Wrist Joints and Metacarpophalangeal Joints in Patients with Psoriatic Arthritis Se." *Polish Journal of Radiology*. https://doi.org/10.12659/PJR.883764.

Scanzello, Carla R., and Steven R. Goldring. 2012. "The Role of Synovitis in Osteoarthritis Pathogenesis." *Bone*. https://doi.org/10.1016/j.bone.2012.02.012.

Schwenzer, Nina F., Ina Kötter, Jörg C. Henes, Christina Schraml, Jan Fritz, Claus D. Claussen, and Marius Horger. 2010. "The Role of Dynamic Contrast-Enhanced MRI in the Differential Diagnosis of Psoriatic and Rheumatoid Arthritis." *American Journal of Roentgenology*. https://doi.org/10.2214/AJR.09.2671.

Sehgal, Nalini, James Colson, and Howard S. Smith. 2013. "Chronic Pain Treatment with Opioid Analgesics: Benefits versus Harms of Long-Term Therapy." *Expert Review of Neurotherapeutics*. https://doi.org/10.1586/14737175.2013.846517.

Simone, Clara De, Cristina Guerriero, Anna Rita Giampietruzzi, Melania Costantini, Flavio Di Gregorio, and Pierluigi Amerio. 2003. "Achilles Tendinitis in Psoriasis: Clinical and Sonographic Findings." *Journal of the American Academy of Dermatology*. https://doi.org/10.1067/S0190-9622(03)00904-6.

Singh, Namrata, and Scott A. Vogelgesang. 2017. "Monoarticular Arthritis." *Medical Clinics of North America*. https://doi.org/10.1016/j.mcna.2016.12.004.

Sivanand. 2019. "乳鼠心肌提取 HHS Public Access." *Physiology & Behavior* 176 (3): 139–48. https://doi.org/10.1038/s41590-020-00816-x.The.

Smith, Bruce W., and Alex J. Zautra. 2008. "The Effects of Anxiety and Depression on Weekly Pain in Women with Arthritis." *Pain*. https://doi.org/10.1016/j.pain.2008.01.008.

Smolen, Josef S., Désirée Van Der Heijde, Klaus P. MacHold, Daniel Aletaha, and Robert

Landewé. 2014. "Proposal for a New Nomenclature of Disease-Modifying Antirheumatic Drugs." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/annrheumdis-2013-204317.

Sokoll, K. B., and P. S. Helliwell. 2001. "Comparison of Disability and Quality of Life in Rheumatoid and Psoriatic Arthritis." *Journal of Rheumatology*.

Spector, Tim D., Pat A. Harris, Deborah J. Hart, Flavia M. Cicuttini, Dalbir Nandra, John Etherington, Roger L. Wolman, and David V. Doyle. 1996. "Risk of Osteoarthritis Associated with Long-Term Weight-Bearing Sports: A Radiologic Survey of the Hips and Knees in Female Ex-Athletes and Population Controls." *Arthritis and Rheumatism*. https://doi.org/10.1002/art.1780390616.

Spel, Lotte, and Fabio Martinon. 2020. "Inflammasomes Contributing to Inflammation in Arthritis." *Immunological Reviews* 294 (1): 48–62. https://doi.org/10.1111/imr.12839.

Srirangan, Srinivasan, and Ernest H. Choy. 2010. "The Role of Interleukin 6 in the Pathophysiology of Rheumatoid Arthritis." *Therapeutic Advances in Musculoskeletal Disease* 2 (5): 247–56. https://doi.org/10.1177/1759720X10378372.

STEPHEN, D. D. 1957. "Psoriatic Arthritis." *Australasian Radiology* 1 (2): 80–82. https://doi.org/10.1111/j.1440-1673.1957.tb00848.x.

Stolk, Jan N., Agnes M.T. Boerbooms, Ronney A. De Abreu, Diana G.M. De Koning, Henk J. Van Beusekom, Wim Hissink Muller, and Leo B.A. Van De Putte. 1998. "Reduced Thiopurine Methyltransferase Activity and Development of Side Effects of Azathioprine Treatment in Patients with Rheumatoid Arthritis." *Arthritis and Rheumatism*. https://doi.org/10.1002/1529-0131(199810)41:10<1858::AID-ART19>3.0.CO;2-8.

Strahl, Carolyn, Ronald A. Kleinknecht, and Dale L. Dinnel. 2000. "The Role of Pain Anxiety, Coping, and Pain Self-Efficacy in Rheumatoid Arthritis Patient Functioning." *Behaviour Research and Therapy*. https://doi.org/10.1016/S0005-7967(99)00102-3.

Szumilas, Kamila, Paweł Szumilas, Sylwia Słuczanowska-Głąbowska, Katarzyna Zgutka, and Andrzej Pawlik. 2020. "Role of Adiponectin in the Pathogenesis of Rheumatoid Arthritis." *International Journal of Molecular Sciences* 21 (21): 1–14. https://doi.org/10.3390/ijms21218265.

Tan, Eng M., and Josef S. Smolen. 2016. "Historical Observations Contributing Insights on Etiopathogenesis of Rheumatoid Arthritis and Role of Rheumatoid Factor." *Journal of Experimental Medicine*. https://doi.org/10.1084/jem.20160792.

Tang, Chih Hsin. 2019. "Research of Pathogenesis and Novel Therapeutics in Arthritis." *International Journal of Molecular Sciences* 20 (7): 10–13. https://doi.org/10.3390/ijms20071646.

Taruc-Uy, Rafaelani L., and Scott A. Lynch. 2013. "Diagnosis and Treatment of Osteoarthritis." *Primary Care - Clinics in Office Practice* 40 (4): 821–36. https://doi.org/10.1016/j.pop.2013.08.003.

Tong, Liping, Huan Yu, Xingyun Huang, Jie Shen, Guozhi Xiao, Lin Chen, Huaiyu Wang, Lianping Xing, and Di Chen. 2022. "Current Understanding of Osteoarthritis Pathogenesis

and Relevant New Approaches." *Bone Research* 10 (1): 1–17. https://doi.org/10.1038/s41413-022-00226-9.

Towheed, Tanveer, Lara Maxwell, Maria Judd, Michelle Catton, Marc C. Hochberg, and George A. Wells. 2006. "Acetaminophen for Osteoarthritis." *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD004257.pub2.

Turner, Judith A., Melissa L. Anderson, Benjamin H. Balderson, Andrea J. Cook, Karen J. Sherman, and Daniel C. Cherkin. 2016. "Mindfulness-Based Stress Reduction and Cognitive Behavioral Therapy for Chronic Low Back Pain: Similar Effects on Mindfulness, Catastrophizing, Self-Efficacy, and Acceptance in a Randomized Controlled Trial." *Pain*. https://doi.org/10.1097/j.pain.0000000000000635.

Urbánek, Karel. 2017. "Infliximab." *Interni Medicina pro Praxi*. https://doi.org/10.4274/turkderm.galenos.2022.54782.

Veale, Douglas J. 2013. "Psoriatic Arthritis: Recent Progress in Pathophysiology and Drug Development." *Arthritis Research and Therapy* 15 (6). https://doi.org/10.1186/ar4414.

Vita, Salvatore De, Francesco Zaja, Stefania Sacco, Alessandro De Candia, Renato Fanin, and Gianfranco Ferraccioli. 2002. "Efficacy of Selective B Cell Blockade in the Treatment of Rheumatoid Arthritis: Evidence for a Pathogenetic Role of B Cells." *Arthritis and Rheumatism*. https://doi.org/10.1002/art.10467.

Wang, Xia, Win Min Oo, and James M. Linklater. 2018. "What Is the Role of Imaging in the Clinical Diagnosis of Osteoarthritis and Disease Management?" *Rheumatology (United Kingdom)*. https://doi.org/10.1093/rheumatology/kex501.

Webb, Louise M.C., Marita J. Walmsley, and Marc Feldmann. 1996. "Prevention and Amelioration of Collagen-Induced Arthritis by Blockade of the CD28 Co-Stimulatory Pathway: Requirement for Both B7-1 and B7-2." *European Journal of Immunology*. https://doi.org/10.1002/eji.1830261008.

Westhoff, Gisela, Rolf Rau, and Angela Zink. 2007. "Radiographic Joint Damage in Early Rheumatoid Arthritis Is Highly Dependent on Body Mass Index." *Arthritis and Rheumatism* 56 (11): 3575–82. https://doi.org/10.1002/art.23033.

Wilson, Floranne C., Murat Icen, Cynthia S. Crowson, Marian T. McEvoy, Sherine E. Gabriel, and Hilal Maradit Kremers. 2009. "Incidence and Clinical Predictors of Psoriatic Arthritis in Patients with Psoriasis: A Population-Based Study." *Arthritis Care and Research*. https://doi.org/10.1002/art.24172.

Woodland, J., D. M. Chaput De Saintonge, S. J.W. Evans, V. L. Sharman, and H. L. Currey. 1981. "Azathioprine in Rheumatoid Arthritis: Double-Blind Study of Full versus Half Doses versus Placebo." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/ard.40.4.355.

Zaja, Francesco, Isabella Iacona, Paola Masolini, Domenico Russo, Alessandra Sperotto, Simonetta Prosdocimo, Francesca Patriarca, et al. 2002. "B-Cell Depletion with Rituximab as Treatment for Immune Hemolytic Anemia and Chronic Thrombocytopenia." *Haematologica*.

Zayat, Ahmed S., Karen Ellegaard, Philip G. Conaghan, Lene Terslev, Elizabeth M.A. Hensor, Jane E. Freeston, Paul Emery, Richard J. Wakefield, and Tore K. Kvien. 2015. "The Specificity of Ultrasound-Detected Bone Erosions for Rheumatoid Arthritis." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/annrheumdis-2013-204864.

Zhang, Weiya, M. Doherty, G. Peat, S. M.A. Bierma-Zeinstra, N. K. Arden, B. Bresnihan, G. Herrero-Beaumont, et al. 2010. "EULAR Evidence-Based Recommendations for the Diagnosis of Knee Osteoarthritis." *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/ard.2009.113100.

Zhao, Sizheng, Eduardo Mysler, and Robert J. Moots. 2018. "Etanercept for the Treatment of Rheumatoid Arthritis." *Immunotherapy*. https://doi.org/10.2217/imt-2017-0155.

河合孝, and 草野忠治. 1969. "モンシロチョウの蛹体色の発現に関与する環境因子 : 第 1 報 2, 3 の緑葉および揮発性物質の効果." 昆蟲 37 (2): 172–78. https://ci.nii.ac.jp/naid/110003378770/.