Workplace Safety and Insurance
Appeals Tribunal

Tribunal d'appel de la sécurité professionnelle
et de l'assurance contre les accidents du travail

Trauma and Inflammatory Arthritis

Discussion paper prepared for

The Workplace Safety and Insurance Appeals Tribunal

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Prepared by:

Dr. Dafna D. Gladman MD, FRCPC

Professor of Medicine, University of TorontoSenior Scientist, Toronto Western Research InstituteDeputy Director, Centre for Prognosis Studies in the Rheumatic DiseaseUniversity Health NetworkDirector, Psoriatic Arthritis Program, University Health Network

Dr. Dafna D. Gladman graduated from the University of Toronto in 1971. She did post-graduate training in internal medicine from 1972 to 1975 and in rheumatology from 1975 to 1977 at the University of Toronto. She was granted her fellowship in internal medicine and in rheumatology in 1976. She joined the the University of Toronto faculty in 1977 and holds the rank of Professor of Medicine in the Department of Medicine. Her clinical and research interests have been in Psoriatic Arthritis clinical features and genetics. She has published widely in that area. She serves as Consultant or Active Staff at Mount Sinai Hospital, University Health Network, at Sunnybrook Health Sciences Centre and at Women's College Hospital.

WSIAT literature search reviewed by Dr. A. Weinberg in 2013, who is of the opinion that this paper still provides a balanced overview of the medical knowledge in this area.

This medical discussion paper will be useful to those seeking general information about the medical issue involved. It is intended to provide a broad and general overview of a medical topic that is frequently considered in Tribunal appeals.

Each medical discussion paper is written by a recognized expert in the field, who has been recommended by the Tribunal's medical counsellors. Each author is asked to present a balanced view of the current medical knowledge on the topic. Discussion papers are not peer reviewed. They are written to be understood by lay individuals.

Discussion papers do not necessarily represent the views of the Tribunal. A vice-chair or panel may consider and rely on the medical information provided in the discussion paper, but the

Tribunal is not bound by an opinion expressed in a discussion paper in any particular case. Every Tribunal decision must be based on the facts of the particular appeal. Tribunal adjudicators recognize that It is always open to the parties to an appeal to rely on or to distinguish a medical discussion paper, and to challenge it with alternative evidence: see *Kamara v. Ontario (Workplace Safety and Insurance Appeals Tribunal)* [2009] O.J. No. 2080 (Ont Div Court).

What is inflammatory arthritis?

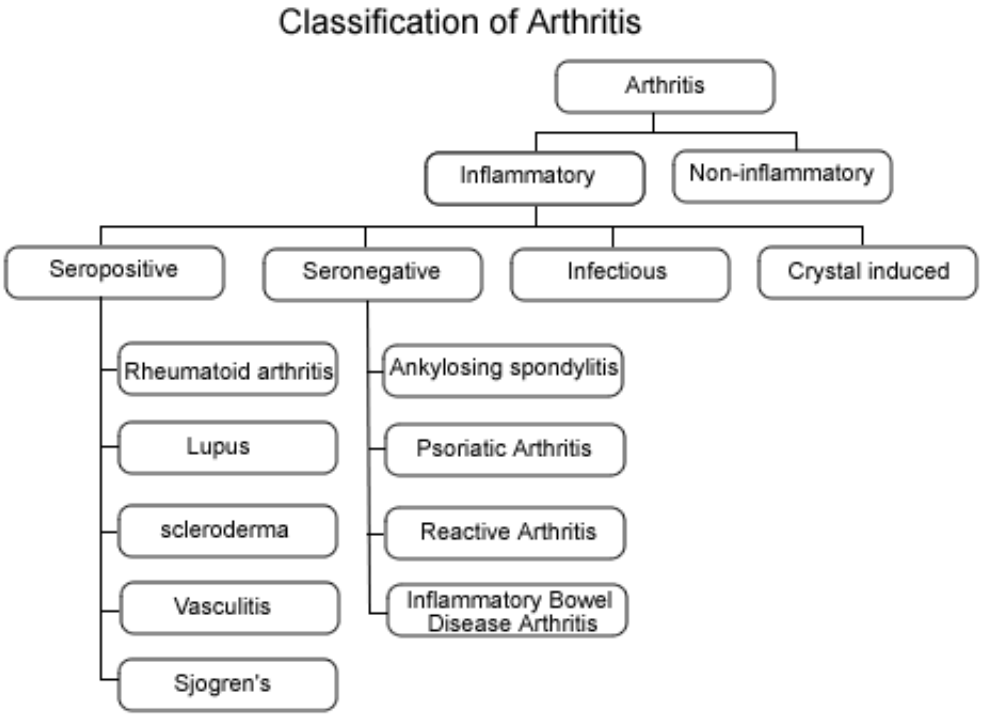
Inflammatory arthritis refers to those forms of arthritis in which the primary process thought to be inflammation in the synovium, the lining tissue of the joint. Inflammatory arthritis is characterized clinically by the presence of inflammatory type pain, that is pain which is made worse with rest and improves with activity, is associated with prolonged morning stiffness, and is associated with other signs of inflammation including swelling of the joint, redness over the joint and limitation of joint movement. Inflammatory arthritis can thus be differentiated from non-inflammatory or mechanical forms of arthritis by the nature of the joint pain. In inflammatory arthritis the pain is associated with inactivity, whereas in non-inflammatory arthritis the pain usually results from physical activity. Inflammatory pain is associated with prolonged morning stiffness of at least 30-45 minutes duration whereas in non-inflammatory arthritis morning stiffness is not a feature, and if it occurs, it is usually short-lived. Both forms of arthritis may lead to limitation of joint movement and disability, although in mechanical forms that tends to be persistent whereas in inflammatory forms the limitation of movement may resolve with control of inflammation. Although there are no definitive figures for the prevalence of inflammatory arthritis, it is thought that between 3 and 5% of the population suffer from some form of inflammatory arthritis.

Classification of inflammatory arthritis

Inflammatory arthritis is generally classified into seropositive and seronegative groups. These are based on the presence of rheumatoid factor, an immunoglobulin which reacts with gamma globulin, in the blood of the majority of patients with seropositive disease and in a small minority of patients with seronegative disease. The prototype seropositive form of arthritis is rheumatoid arthritis. Other members include the group of conditions labelled collagen vascular diseases, such as systemic lupus erythematosus, scleroderma, vasculitis, Sjogren's syndrome. Only rheumatoid arthritis will be considered in this paper.

Among the seronegative inflammatory joint diseases is a group labelled spondyloarthritis. This condition is characterized by inflammatory disease of the joints of the back, both the sacroiliac joints and the apophyseal joints of the spine. Members of this group include ankylosing spondylitis, psoriatic arthritis, reactive arthritis, and arthritis of inflammatory bowel disease. While the prototype for this group is ankylosing spondylitis, psoriatic arthritis will also be discussed.

In addition to the presence of rheumatoid factor, there are extra-articular features which distinguish the seropositive from the seronegative forms of inflammatory arthritis.



Rheumatoid arthritis

General Features: Rheumatoid arthritis is an inflammatory arthritis affecting both small and large joints in a symmetric distribution. The disease affects women more than men and usually begins in the 4th decade although may occur at any age. It presents with pain and swelling in the affected joints, associated with prolonged morning stiffness and quickly leads to limitation of daily activities. In addition to the peripheral arthritis, rheumatoid arthritis may affect internal organs such as the heart, lungs, skin, and peripheral nerves. When systemic manifestations are present the condition is often referred to as rheumatoid disease.

Etiology and Pathogenesis: The cause of rheumatoid arthritis is unknown. However, factors considered important in its development include genetic, immunological and environmental factors.

Genetic factors: It is well recognized now that genes at the major histocompatibility complex (MHC) are associated with rheumatoid arthritis. In humans, the MHC is located on the short arm of chromosome 6 and is termed HLA (Hunan Leukocyte Antigens). HLA-DRB*0401 has been identified as a risk factor for the development of rheumatoid arthritis. It has further been demonstrated that there is a conserved amino acid sequence which maps to the third hypervariable region of HLA-DR beta chains containing amino acids 70-74, known as the “shared epitope”. The shared epitope occurs in a number of HLA alleles which have been associated with rheumatoid arthritis is various ethnic

groups. Whether this shared epitope plays a direct role in the immune response leading to rheumatoid arthritis, or whether it is related to the production of autoantibodies directed against cyclic citrulinated peptide (CCP) is still being debated. Polyomorphisms in several other genes may also contribute to the development of rheumatoid arthritis.

Other Risk Factors: Non genetic risk factors include female sex, as women are 2-3 times more likely to develop rheumatoid arthritis than males, Hormonal factors such as estrogen and progesterone may potentially explain the gender effect. While estrogen isassociated with an effect on the immune response its role in the development of rheumatoid arthritis remains controversial.

Several environmental factors have been implicated in the etiology of rheumatoid arthritis. Exposure to tobacco is the best characterized. It turns out that smoking enhances the risk of developing anti-CCP antibodies which occur commonly among patients with rheumatoid arthritis, and have been detected long before the diagnosis of the disease. It is hypothesized that inhaled smoke generates anti-CCP antibodies which in turn lead to inflammation and activation of innate immunity eventually leading to rheumatoid arthritis. Infectious agents have also been implicated in the development of rheumatoid arthritis, although no specific agent has yet been identified. Stress, either physical or psychological has been proposed as a mechanism for the development ofautoimmune diseases such as rheumatoid arthritis, as stress leads to immune dysregulation in a similar way that occurs in rheumatoid arthritis. While patients with rheumatoid arthritis may provide a history of stress prior the onset of the disease, there are no studies that identify a particular for of trauma as associated with the disease.

Immune pathogenesis: Whatever the cause of RA, the disease is associated with a number of immunologic alterations. It is thought that through genetic and environmental factors there is activation of innate immunity and antigen loading onto macrophages. This leads to inflammatory cell recruitment, including polymoprhonucelar cells, T cells Bcells and osteoclasts. Through activation of T cells there is production of cytokines, activation of B cells and autoantibody production, immune complex formation and deposition within the synovium. Once it starts, the process seems self-perpertuating leading to synovial cell proliferation and cartilage and bone destruction.

Clinical features of Rheumatoid Arthritis: Rheumatoid arthritis affects primarily small and medium sized joints in a symmetric distribution. The joints are painful and swollen and the morning stiffness is usually prolonged. It usually spares the distal interphalangeal joints of the hands and feet, and usually does not affect the joints of the spine. The most common extra articular feature of rheumatoid arthritis is the rheumatoid nodule, which occurs most commonly on the extensor surfaces of the forearm near the elbow, but can occur at any site of pressure. The nodule is usually soft, non painful. The rheumatoid nodules can develop in the lungs and other internal sites, including the spinal canal in which case they may lead to spinal symptoms.

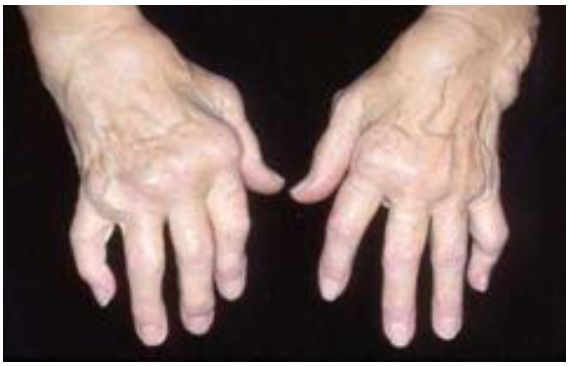


Figure 1 - Rheumatoid hands showing the swollen joints and some deformities.

In addition to the joint inflammation, internal organs may be affected by the rheumatoid process. The eye is commonly affected with dry eyes, conjunctivitis, and inflammation indifferent parts of the eye including episcleritis, and scleritis. In the lungs, rheumatoid nodules can occur which can be confused with cancer. Interstitial lung disease may develop in patients with rheumatoid arthritis, particularly smokers, and may lead to severe shortness of breath. Inflammation of the lining of the lung, pleurisy may also occur leading to chest pain and shortness of breath. In the heart rheumatoid nodules may occur and may interfere with the conduction system leading to irregular heart beat. Alternatively, inflammation of the heart muscle, myocarditis may occur, or inflammation in the lining of the heart, pericarditis may develop, both leading to chest pain and possibly shortness of breath. The peripheral nervous system is affected by compression neuropathies such as carpal tunnel syndrome. Occasionally patients with rheumatoid arthritis present with an inflammatory neuropathy which may lead to paraesthesias ornumbness and sometimes dysfunction. In addition cervical myelopathy may occur secondary to vertebral subluxation in the neck. This may present with headaches, numbness, loss of balance or in severe cases frank paralysis. In addition to the subcutaneous nodules the skin may demonstrate vasculitis which may present with redness around the nail bed as well as hemorrhages in the fingers, or with large ulcers particularly on the medial aspect of the lower extremities as is seen in patients with Felty's syndrome, in which the arthritis is coupled with a large spleen, low platelet countand skin ulcers.

Natural history: If left untreated rheumatoid arthritis leads to deformities, joint destruction and premature death. Patients with rheumatoid arthritis are at an increased risk of death, as well as cardiovascular disease, including myocardial infarction and strokes.

Diagnosis: The diagnosis of RA is made on the basis of the history of inflammatory joint disease, physical examination demonstrating evidence of arthritis usually in a symmetric distribution, laboratory confirmation with a positive rheumatoid factor test, and x-rays confirming erosive disease in the appropriate distribution. The American

College of Rheumatology has developed classification criteria which include the presence of morning stiffness, arthritis in 3 or more joint areas, arthritis of the hand joints, symmetric arthritis, rheumatoid nodules, positive rheumatoid factor and radiographic changes. The radiographic changes include erosions which are mostcommon in the wrists, metacaropophalangeal joints of the hands, and the metatarsophalangeal joints of the feet. The presence of 4 or more of these items classifies a patient as having rheumatoid arthritis..

Role of trauma: As noted above, stress may aggravate the immune response leading to changes similar to those occurring in rheumatoid arthritis thus stress may lead to exacerbations of the disease. However, a specific role for trauma in the development ofrheumatoid arthritis has not bee proven. On the other hand, since compression neuropathies may occur, repetitive movement may aggravate some aspects of rheumatoid arthritis. Unfortunately there is no evidence in the literature to help understand the role of trauma in either the development or perpetuation of rheumatoid arthritis.

Seronegative disease

Ankylosing spondylitis

General features: Ankylosing spondylitis is an inflammatory arthritis of the sacroiliac joints and the spine. It occurs in men more commonly than women, and usually begins in the late teens or early twenties, although there is often a delay in diagnosis. Over thepast few decades it has become clear that the gender difference is not as high as previously thought as the original studies were reported from veteran affairs hospitals thus were biased towards a male predilection. The current male to female ratio is quoted as 2:1.

Etiology and pathogenesis: Although the etiology of ankylosing spondylitis remains unclear a strong genetic component is evident both from the familial distribution of the disease and the strong association with the HLA-B*27 allele. Several other genes have been demonstrated to be associated with ankylosing spondylitis. Infective mechanisms have also been proposed but none has been proven to date, although in reactive arthritis, infective organisms clearly play a role. A role for trauma has been proposed although not proven. In some patients the diagnosis is only made after trauma has occurred and a back problem which initially is thought to be related to the trauma is eventually diagnosed as ankylosing spondylitis.

Clinical features of ankylosing spondylitis: The principal features of ankylosing spondylitis result from enthesitis, inflammation at the insertion of tendons into bone, and synovitis. The usual presenting symptom is inflammatory back pain. Inflammatory back pain worsens with rest and improves with activity or exercise, and is associated with prolonged morning stiffness. The pain is often nocturnal, waking the patient up between 2 and 5 o’clock in the morning. Many patients recognize the benefit of getting out of bed and either walking around or taking a shower to improve the pain and stiffness. The location

of the pain depends on the site involved. Sacroiliac pain is most often felt in thebuttocks, and often alternates from one side to the other. Spinal discomfort typically ascends from the thoraco-lumbar junction towards the neck. The most common initial finding is loss of lumbar lordosis. Other clinical findings on examination include limitation of chest expansion, reduced neck movement and limited forward and lateral flexion of the lumbar spine. Although the clinical examination of the sacroiliac joints is not uniformly reliable, some patients may demonstrate acute inflammation in these joints.

In addition to the spinal features, patients with ankylosing spondylitis may present with inflammatory peripheral arthritis. The arthritis is usually oligoarticular, affecting 4 or less joints, affects the large joints, and is often asymmetric in distribution. The shoulder joints and the hip joints, often referred to as axial joints, are commonly affected in ankylosing spondylitis. Enthesitis is a common feature with Achilles, plantar fascia, as well as sites around the pelvis being most common. The presence of enthesitis is thought to result in the syndesmophytes that are detected in the spine of patients with ankylosing spondylitis. These in turn lead to markedly restricted spinal mobility. The pain and inflammation usually result first in loss of lumbar lordosis followed by a thoracic kyphosis, then hyperextension of the neck. Then in order to maintain upright posture the patients usually bend their knees and hips with resultant flexion contractures. Eventually patients may lose balance and require either aids for walking or surgical intervention (see figure 2).

Extra-articular features seen among patients with ankylosing spondylitis include iritis, orinflammation of the anterior part of the eye, which occurs in 40% of the patients and presents with a painful eye with blurred vision and sensitivity to light. Patients with ankylosing spondylitis can present with urethritis, inflammation of the urethra, with burning pain on passing urine and a discharge. Inflammatory bowel disease, either Crohn's disease or ulcerative colitis may complicate ankylosing spondylitis. However, some patients with ankylosing spondylitis develop episodes of diarrhea even in the absence of a documented inflammatory bowel disease. Psoriasis occurs in about 10% of patients with ankylosing spondylitis. Patients with ankylosing spondylitis may develop inflammation at the base of the aorta which may present with chest pain or abnormal heart rhythm. There may also be respiratory problems related to fibrosis of the upper part of the lung which may be related to the restricted chest mobility because of the spondylitic process.

Natural history: Left untreated ankylosing spondlylitis leads to severe spinal deformities, with resultant disability. Indeed, the typical picture of a patients with ankylosing spondylitis 50 years ago would be of a person bent over with contracted knees and hips, hyperextended neck using a cane for balance. Fortunately with the use of non steroidal anti-inflammatory drugs and exercise program the natural history has been modified and this picture is no longer dominant among patients with ankylosing spondylitis. The advent of biologic therapy actually has made an even more remarkable difference in the lives of patients with ankylosing spondylitis.

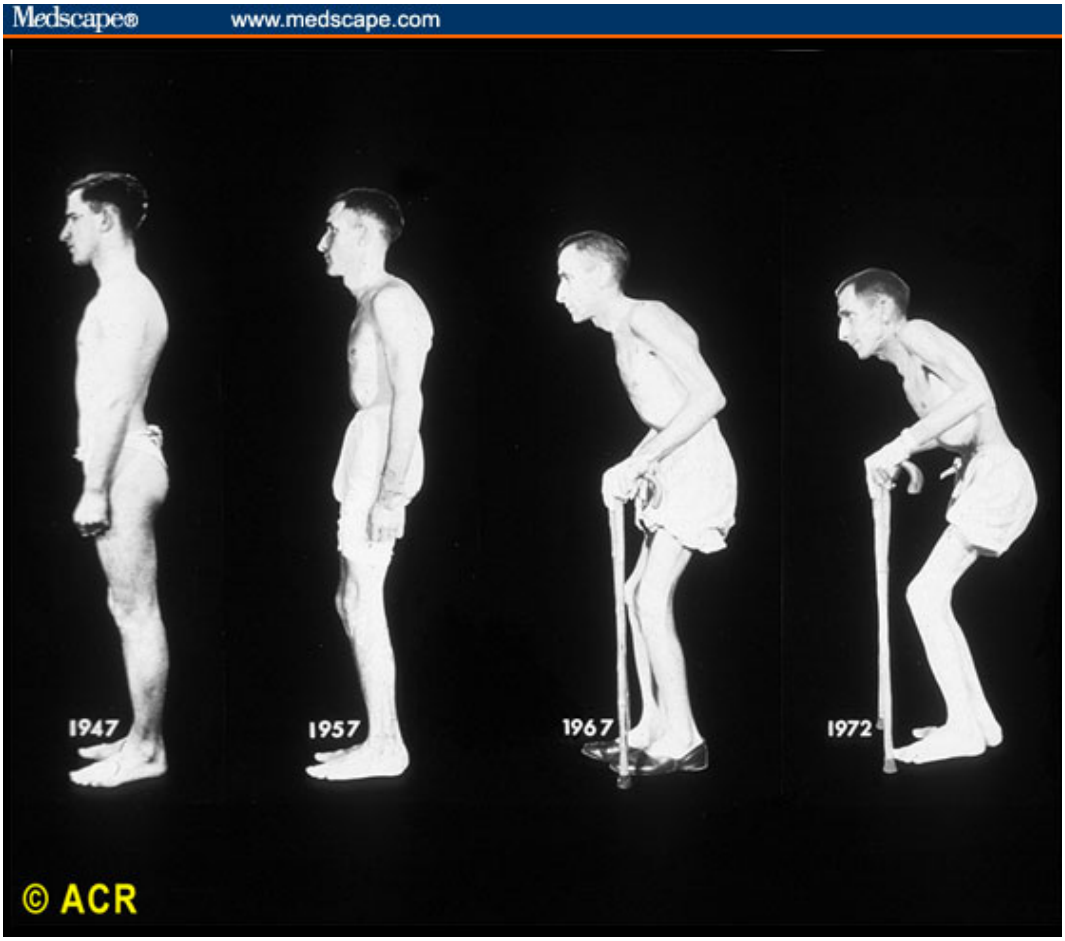


Figure 2 - Progression of changes in the spine in ankylosing spondylitis.

Diagnosis: The diagnosis of ankylosing spondylitis is facilitated by the New York Criteria which include inflammatory back pain, restricted chest expansion, reduced lumbar flexion, and evidence of either bilateral grade 2 sacroiliitis or unilateral grade 3 or 4 sacroiliitis. X-rays commonly identify the sacroiliitis and the syndesmophytes. However, it should be noted that when all these features are present the disease is quite advanced. There is currently an attempt to develop criteria to identify ankylosing spondylitis early so that proper treatment may be provided and the natural history may be altered to improve outcome among patients with ankylosing spondylitis.

Role of Trauma in ankylosing spondylitis: The role of trauma in relation to the development and exacerbation of ankylosing spondylitis has been controversial. Since immunologic mechanisms do play a role the same concern about the stress related immunological change discussed earlier for rheumatoid arthritis applies. In addition, trauma may aggravate ankylosing spondylitis in that patients with ankylosing spondylitis have syndesmophytes in the spine. These reflect ossification of the outer layers of the intervertebral discs as well as ossification of the longitudinal ligaments. Trauma may lead to fracture of these sites leading to pseudo joints which become very painful for these patients.

Psoriatic arthritis

General Features: Psoriatic arthritis is an inflammatory arthritis associated with psoriasis. Psoriasis is an inflammatory skin condition which affects 2-3% of the population. It presents with a red scaly rash which often occurs on the extensor surfaces of the elbows and knees, but can involve any part of the body. The commonest type is psoriasis vulgaris, but other forms include guttate psoriasis, flexural psoriasis and the most severe form. Psoriasis is often precipitated by sites of trauma. This is a phenonenom described as the Koebner phenomenon.

25-30% of patients with psoriasis develop a distinct form of arthritis called psoriasis arthritis. PsA affects men and women equally, usually in the 4th decade. It affects both peripheral joints and the spine, and there are some typical extra-articular manifestations including dactylitis, or inflammation of the whole digit, and enthesitis, inflammation at the sites of tendon insertion into bone. Patients with psoriatic arthritis are more likely to have nail changes including nail pits or lifting of the nail from its nail bed, than patients with psoriasis without arthritis.

Etiology and Pathogenesis: The cause of PsA is unknown. Genetic, immunologic andenvironmental factors are implicated in both the etiology and pathogenesis of the condition. Genetic factors are considered most important. A role for genes at the HLA locus has clearly been demonstrated for both psoriasis and psoriatic arthritis. It is still unclear which allele is the most important although most recent studies implicate HLA-Cw*0602. HLA antigens have also been associated with progression of joint damage inpatients with psoriatic arthritis. Other genes have also been identified, but so far it is difficult to ascertain whether these are all related to the skin disease versus the joint disease.

The immunologic abnormalities detected among patients with psoriatic arthritis are similar to those in rheumatoid arthritis. Certain cytokines such as TNF are found to be high both in the serum and joint and skin tissue in patients with psoriatic arthritis. Abnormalities in T cells have also been documented and clearly lead to the inflammatory lesions seen both in the skin and the joints.

Few studies have reported the occurrence of arthritis and lysis of the finger joints (acroosteolysis) following physical trauma in patients with psoriasis. Notably a retrospective study revealed that 9% of patients with psoriatic arthritis compared to only 2% of patients with RA experienced acute illness or trauma before the onset of their arthritis. A traumatic event prior to the diagnosis of psoriatic arthritis was reported in 24.6% in a large cohort of patients with psoriatic arthritis. Patients who developed their arthritis following physical trauma were similar to those who developed PsA without a history of trauma. It is proposed that the trauma-induced arthritis represents a deep Koebner phenomenon therefore suggesting that trauma plays a role in the development of psoriatic arthritis.

Clinical features of Psoriatic Arthritis: Psoriatic arthritis is complex since patients may have peripheral arthritis, axial disease as well as enthesitis and dactylitis in addition to the skin psoriasis. The peripheral arthritis is different from that of rheumatoid arthritis in that distal interphalangeal joints are commonly affected both in the hands and feet. The arthritis tends to be asymmetric although with a large number of joints involved it becomes symmetric. It affects both small and large joints. There is often a reddish or purplish discoloration of the affected joint, which is not usually seen in rheumatoid arthritis. Deformities can develop very quickly in psoriatic arthritis and include both flail joints which result from a total lysis of the joint, to fused joints, which result from ankylosis, or bony bridging across the joint. About half the patients have aspondylitis which in many cases may be asymptomatic and only recognized when x-rays of the spine are taken, or when the spinal deformity occurs. In general, patients with psoriatic arthritis have less pain than patients with rheumatoid arthritis. Dactylitis, orswelling of the whole digit is common is psoriatic arthritis occurring in almost half the patients. Digits with dactylitis have been shown to have more radiographic changes than digits without dactylitis. About 40% of the patients have enthesitis, which involves primarily the Achilles tendon and the plantar fascia and is often associated with bony spurs. Other extra-articular features common to the seronegative spondyloarthritis group are also seen among patients with psoriatic arthritis.

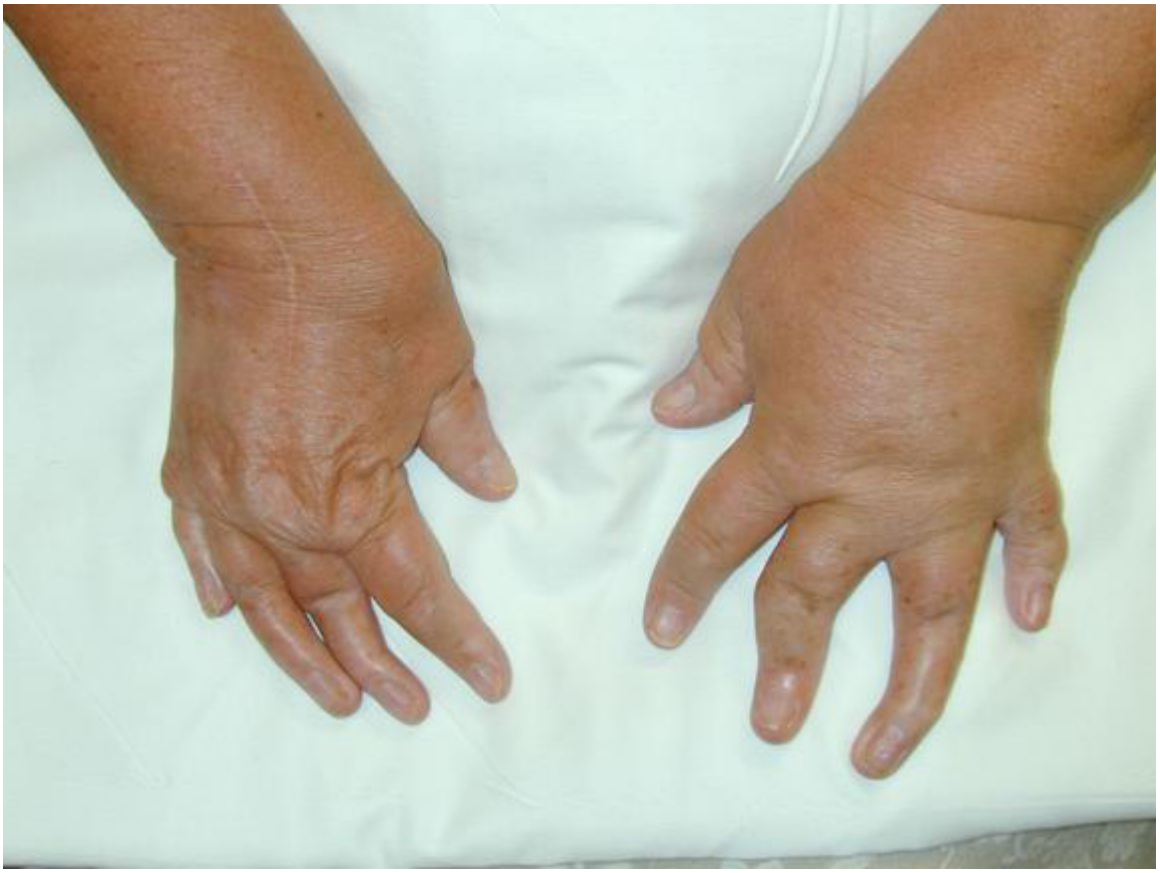


Figure 3 - Psoriatic arthritis hands showing marked deformities.

Diagnosis of Psoriatic Arthritis: The diagnosis of psoriatic arthritis has been difficult because of the lack of criteria. However, recently an international group completed a large study comparing patients with psoriatic arthritis to patients with other forms of inflammatory arthritis and published the CASPAR criteria, which should facilitate the diagnosis of the disease since they were proven both sensitive and specific in established psoriatic arthritis and in new cases. The criteria are based on the presence of inflammatory musculoskeletal disease either peripheral arthritis, spondylitis or enthesitis and 3 points based on the items in the following list, they can be diagnosed as psoriatic arthritis with almost 90% sensitivity and specificity. The features are:

- Current psoriasis which is worth 2 points,
    - ◊ or either a history of psoriasis,
    - ◊ or a family history of psoriasis which is worth 1 point,
- Evidence of nail disease 1 point
- Evidence of dacylitis or a history documented by a rheumatologist – 1 point
- Negative rheumatoid factor – 1 point
- Presence of fluffy periosteal reaction around the joint – 1 point

Natural history: Left untreated psoriatic arthritis is progressive, deforming and destructive in a large proportion of patients. As noted patients develop either flail joints or fused joints which result in marked functional disability. Predictors for progression of joint damage include disease activity and damage as well as some genetic factors. Moreover, patients with psoriatic arthritis are at an increased risk for death. Predictors for early mortality include disease activity and severity at presentation.

Role of Trauma in psoriatic arthritis: As highlighted earlier there appear to be a role for trauma in the development of psoriatic arthritis. However, this remains controversial as there are only a few studies relating trauma to psoriatic arthritis in the literature. It isimpossible to perform a definitive study since it will involve a very large number of individuals who will need to be followed for an extremely long period of time to determine whether trauma leads to the development of arthritis. Not only will this require a large amount of money, but a huge effort on the part of researchers for an extended period of time.

Summary

Inflammatory arthritis is a form of arthritis in which there is clear evidence of inflammation in the peripheral joints, the spine, or the entheses. While there is no direct evidence pointing to trauma in the initiation of these forms of arthritis, except perhaps for psoriatic arthritis, there is some support for exacerbations of inflammatory arthritis by stress, either physical or emotional. This is likely due to the effect of stress on the immune system.

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