

# Psoriatic arthritis: a clinical entity distinct from psoriasis?

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## ABSTRACT

Psoriasis and psoriatic arthritis are complex and heterogeneous clinical entities, whose presentations comprise multiple combinations of subtypes. There are doubts even if they are distinct entities or merely variants of the same disease. Epidemiologically, psoriasis can be considered a common disease because it affects about 2% of the world population. Regarding psoriatic arthritis, there is no consensus in the literature about its true incidence and prevalence in the general population. Genetic, immune, and environmental factors interact culminating in skin and joint manifestations of psoriatic disease. The central role of activated T lymphocytes in the pathogenesis of both psoriasis and psoriatic joints is now recognized. Furthermore, proinflammatory cytokines can be found in increased concentrations in both skin and synovium of patients with psoriatic arthritis. Since 1964, when the relationship between psoriasis and psoriatic arthritis was recognized, many studies have been conducted to better understand the common mechanism of both diseases. The HLA has already been considered the center of the psoriatic arthritis immunopathogenesis; today, TNF- $\alpha$  plays such a role. This paper is a review of various factors associating psoriasis and psoriatic arthritis leading to the hypothesis of a single disease with multiple presentations.

**Keywords:** psoriasis, psoriatic arthritis, interrelation.

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## INTRODUCTION

Psoriasis is a polygenic inflammatory disorder of the skin with triggering factors such as traumas, infections, and medications, which can lead to different clinical manifestations in predisposed individuals. The phenotype represented in 90% of the cases is characterized by the presence of erythematous and scaly plaques with well-defined margins, affecting mainly the extensor surfaces of the limbs such as knees and elbows.<sup>1</sup>

One of its various clinical presentations is arthropathic psoriasis. In Rheumatology, it is called psoriatic arthritis (PsA) and can be defined as a chronic inflammation of the synovial joints associated with psoriasis, usually negative for the rheumatoid factor (RF).<sup>2</sup> It is currently classified in the group of the spondyloarthritides, diseases that share, in addition to the

negativity for RF, clinical manifestations such as arthritis of the peripheral joints and axial skeleton and enthesitis.<sup>3</sup> Psoriasis and PsA are complex and heterogeneous entities that can present as multiple combinations of their subtypes; the possibility that they might be distinct entities or only variants of one same disease has been considered.<sup>4</sup>

## HISTORY

Although several skin diseases have been described in Egyptian papyri, there is no registry of lesions similar to psoriasis in those papyri. In Ancient History, Hippocrates (460–377 b.C.) has meticulously reported several lesions and, according to his classification, scaling and dry eruptions were grouped together under the name of “*lopoi*”. This fact is believed to have been the precursor of grouping leprosy and psoriasis together, with

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the consequent rejection of psoriatic patients in their communities, as reported in the Old Testament.

The confusion between leprosy and psoriasis has remained for centuries. Many psoriatic patients diagnosed as having leprosy received the same modalities of treatment such as social isolation, official declaration of death by the Church, and, in 1313, death by burning at the stake ordered by Philip de Fair.<sup>5</sup>

It was only in the nineteenth century that psoriasis began to be better studied and understood as a clinical entity distinct from leprosy. In 1809, Robert Willan, a British dermatologist, was the first to provide a detailed description of psoriasis and to propose the term “psoriasis”.<sup>1</sup> In 1841, psoriasis was definitively separated from leprosy by Ferdinand von Hebra.<sup>5</sup> In 1818, the descriptions by Alibert associated psoriasis and arthritis for the first time. However, in 1860, Bazin was the first to refer to the disease by using the term “arthritic psoriasis”; in 1888, Bourdillon provided more detailed descriptions of the disease.<sup>6</sup>

Although known since the first decades of the nineteenth century, only in the 1950’s the disease began to be better studied, when Verna Wright acknowledged the association of psoriasis with erosive arthritis and low frequency of RF. In 1959, the same author proposed the term “psoriatic arthritis” and, in 1964, the American College of Rheumatology (then known as the American Rheumatism Association) classified it for the first time as a clinical entity distinct from rheumatoid arthritis (RA).<sup>7</sup>

## EPIDEMIOLOGY

Psoriasis, according to most studies, affects approximately 2% of the world population, but its prevalence can vary from 0%–11.8%, depending on the sample studied and the methods of population analysis.<sup>8</sup> Asians and indigenous peoples seem to have the lowest prevalence.

A study with over 5 million Chinese has revealed a 0.2% prevalence<sup>9</sup> and another study with almost 26,000 indigenous people in Brazil has reported no case of psoriasis.<sup>10</sup> The highest prevalences are seen among the Nordic population, such as 4.8% in Norway.<sup>8</sup> Regarding incidence, few studies have been conducted. The estimated incidence of psoriasis in the United States is of 60.4:100,000 person-years and in the United Kingdom of 140:100,000 person-years.<sup>11</sup>

Even considering variations of the epidemiological design, it is a common disease of universal distribution which affects men and women equally. It can manifest at any age but is currently divided into two age peaks of incidence: the first beginning between 20 and 30 years of age (type 1 psoriasis), and the

second between 50 and 60 years of age (type 2 psoriasis).<sup>8</sup> In approximately 75% of the cases the disease begins before the age of 40 years and although it appears earlier in women, its natural history is similar in both genders, characterized by an intermittent chronic course with remissions that can last 1–54 years.<sup>5</sup> There is no consensus in the current literature regarding the actual incidence and prevalence of PsA in the general population, because only a few studies have been conducted with that purpose.

An overall prevalence of 0.04%–0.1% is estimated, but this might be an underestimation.<sup>3</sup> In the United States its prevalence is estimated as 0.25% of the general population.<sup>12</sup> The prevalence of joint complaints, however, can be as high as 90%, which has been reported by Gisoni in his study conducted with 936 patients hospitalized with psoriasis.<sup>13</sup> Table 1 summarizes the major studies on the prevalence and incidence of PsA.

In Sub-Saharan Africa the prevalence of PsA is affected by the high indices of human immunodeficiency virus (HIV) infection. Historically, seronegative arthropathies have always been rare in that region due to the low prevalence of HLA-B27, whose presence is greater in Caucasian populations. However, a study conducted in Zambia has reported that spondyloarthritides are currently the most common form of arthritis in that population (180/100,000 HIV-positive individuals *versus* 15/100,000 in the general population).<sup>14</sup>

A subsequent study in the same region has revealed that 96% of the patients with PsA were HIV-positive *versus* 30% of the general population.<sup>15</sup> In North America that figure ranges from 0.4%–2%.<sup>6</sup>

Regarding patients with psoriasis who develop arthritis, the numbers vary from 5%–42%.<sup>16</sup> A large and recent German epidemiological study has confirmed the diagnosis of PsA in 20.6% of 1,511 patients with psoriasis.<sup>17</sup> That is currently the most accepted figure (around 20%) for the occurrence of arthritis in patients with psoriasis.

**Table 1**  
Incidence and prevalence of psoriatic arthritis

| Author   | Year | Place         | Prevalence      |
|----------|------|---------------|-----------------|
| Lomholt  | 1963 | Faroe Islands | 0.04%           |
| Alamanos | 2003 | Greece        | 0.06%           |
| Shbeeb   | 2000 | USA           | 0.1%            |
| Author   | Year | Place         | Incidence       |
| Shbeeb   | 2000 | USA           | 6/100,000       |
| Alamanos | 2003 | Greece        | 2.9–3.1/100,000 |
| Soderlin | 2002 | Sweden        | 8/100,000       |

Adapted from Bruce, 2008.<sup>6</sup>

Contrary to RA, which has a predilection for the female population, PsA affects men and women at similar proportions (1:1), the mean age of disease onset being between 30 and 55 years.<sup>6</sup>

## IMPACTS

Psoriasis can be stigmatizing and affect negatively the patients' quality of life.<sup>18</sup> Its physical symptoms are a source of stress and of worsening of quality of life, because 76% of the patients experience scaling and itching all the time. Nevertheless, the clinical severity of the disease assessed by physicians is statistically associated with none of the patients' beliefs about their symptoms, emphasizing the importance of the subjective factor in the course of the disease.<sup>19</sup> The significant presence of other comorbidities such as Crohn's disease, type 2 diabetes mellitus, metabolic syndrome, and mood disorders also contribute to the sensation of psychosocial discomfort and tendency towards isolation.<sup>1</sup>

The impact of psoriasis can also be assessed from the economic viewpoint. In the United States approximately 56 million hours of work are lost by patients with the disease and as much as 3.2 billion dollars are spent per year with its treatment.<sup>20</sup>

## GENETIC AND TRIGGERING FACTORS

Genetic, immune, and environmental factors interact until they culminate in the cutaneous and joint clinical manifestations of the psoriatic disease. Its transmission is believed to be multifactorial, with possibly a polygenic trait and a known important familial aggregation.<sup>21</sup> When both parents have psoriasis, the chance that their child also develops it is 41%.<sup>22</sup> If only the father or the mother has the disease, the transmission chance is 14%; when a sibling is affected, that chance is 6%; and when there is no family history that chance is only 2%.<sup>23</sup> Among twins, the incidence of psoriasis is 65% for monozygous twins and 30% for dizygous twins.<sup>20</sup>

Currently, that genetic predisposition is attributed to the presence of human leukocyte antigens (HLA). Regarding psoriasis, several HLA can be associated, such as HLA-B13, HLA-B17, HLA-B37, HLA-Bw16, HLA-Bw57, and HLA-DR7. However, HLA-Cw6 is the most important.<sup>18,20</sup> The presence of HLA-Cw6 in Caucasian populations represents a 13-fold increase in the relative risk of developing psoriasis; in Japanese, that risk is 25-fold increased.<sup>5</sup>

The major histocompatibility complex (MHC) class I polypeptide-related sequence A (MICA gene) was a *locus* assessed in a study comparing psoriasis and PsA with healthy controls. The results showed that MICA-A9 polymorphism

(corresponding to the MICA-002 allele) was increased only in PsA, while the Cw\*0602 allele was significantly increased in both psoriasis and arthritis. The MICA-002 allele, thus, might be a candidate for the development of PsA.<sup>24</sup>

The following findings have been reported: association of HLA-B27 with pustular psoriasis and acrodermatitis; association of HLA-B13 with guttate psoriasis; and increased frequencies of HLA-B17 in patients with erythrodermic psoriasis.<sup>5</sup>

Although the event triggering the disease is not always recognized, an environmental "trigger" in a predisposed individual might be determinant, because in addition to the genetic factor, environmental and immune elements interact for disease onset.<sup>25</sup>

External factors that act directly on the skin can trigger psoriasis and the positive reaction to the Koebner phenomenon in 25% of psoriatic patients proves that. Positivity for that phenomenon suggests that psoriasis is a systemic disease that can develop locally from a traumatic event on a specific body segment.<sup>5</sup> Infections, both bacterial and viral, should be remembered as important environmental systemic factors that might be related to psoriasis induction and aggravation. Group A streptococcal infections have been associated with the development of guttate psoriasis and the ribosomal RNA of that species has been detected in the blood and synovial fluid of patients with PsA.<sup>3</sup> However, even accepting the immunoreactivity of the streptococcal antigen, it is not clear whether the infection triggers PsA or whether the skin barrier broken by psoriasis leads to exposure to the microorganism and, thus, to a form of reactive arthritis.<sup>26</sup>

In HIV-seropositive populations the clinical manifestations of the cutaneous disease tend to be more severe and exuberant.<sup>27</sup> Regarding the arthropathic form of the disease, HIV-positive patients have a variable course but, in most cases, they tend to show erosions and early deformities, with progressive evolution and refractoriness to conventional therapy.<sup>28</sup>

Several drugs have been implicated as inducers of psoriasis, the major being lithium carbonate, interferon,  $\beta$ -blockers, and antimalarials. Rapid withdrawals of systemic corticosteroids can also be associated with both pustular psoriasis induction and plaque psoriasis aggravation. Other drugs possibly associated, but with a less marked clinical impact, are the angiotensin-converting-enzyme inhibitors and the COX-1 inhibitors (anti-inflammatory drugs).<sup>25</sup>

Other environmental and systemic factors associated with psoriasis are increased alcohol consumption, smoking, and obesity. Their pathological mechanisms, however, have not been completely elucidated.<sup>5</sup>

The increased frequency of PsA in patients with severe psoriasis has supported the association between psychological stress and cutaneous and joint involvement.<sup>29</sup> Psychological stress might play a role, but the real pathogenesis remains unknown.<sup>30</sup>

Rubella vaccination, recurrent oral ulcers, moving house, injury sufficient to require a medical consultation, and bone fractures have also been described as factors associated with the development of arthritis in patients with psoriasis. Subsequent studies, however, are required to confirm those data and to assess the immune mechanisms involved.<sup>31</sup>

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## PATHOGENESIS

The pathogenesis of PsA is complex and has not been totally understood. Currently, the central role of activated T lymphocytes in the pathogenesis of both psoriasis and PA is recognized.

Because of its macroscopic characteristics and the fact of being mainly an epidermal disease, the major biochemical or cellular defect was believed to lie solely on the keratinocyte. The central pathogenesis of psoriasis is in fact related to an abnormal differentiation and proliferation of keratinocytes, but cell aspects, cytokines, chemokines, and elements of the innate and adaptive immune responses are known to be involved in its pathogenesis.<sup>20</sup>

The focus of the research and consequent better understanding of its pathophysiology changed when an improvement was observed in patients diagnosed with psoriasis using cyclosporine to prevent rejection of transplanted organs.<sup>32</sup> That drug inhibits the transcription of messenger RNA for the production of several cytokines of T lymphocytes, whose activation via IL-2 leads to the production of tumor necrosis factor alpha (TNF- $\alpha$ ) and perpetuation of the inflammatory cascade. Thus, part of the scientific community has a tendency to consider psoriasis as an autoimmune disease, although no true autoantigen has been identified so far.

Cells of the innate immune system such as keratinocytes, dendritic cells, neutrophils, monocytes/macrophages, and natural killer (NK) cells are involved in the inflammatory event of the psoriatic joint. Breaking the integrity and function of the keratinocyte can promote an inflammatory response via mechanisms involving T lymphocyte activation and TNF- $\alpha$  signaling.<sup>33</sup>

Increased concentrations of pro-inflammatory cytokines such as TNF- $\alpha$  and IL-1 can be seen in the synovium and skin of individuals with PsA and can account directly for the increase in local growth factors and for the vascular changes

of the disease such as capillary thickening and periarticular inflammatory infiltrates.<sup>5</sup> Biopsies of the bone tissue of psoriatic joints have shown large multinucleated osteoclasts undergoing deep resorption at the bone-pannus junction. There is RANK-L upregulation and decreased osteoprotegerin (OPG) expression.<sup>5</sup> Treatment with anti-TNF- $\alpha$  agents decreases drastically the levels of circulating osteoclast precursors, evidencing the central role played by that cytokine in the bone remodeling dysregulation of PsA.<sup>34</sup>

In addition to the bone and synovial pathology, it is worth noting the role played by blood vessels, whose morphological changes are different from those observed in RA. In PsA, the hyperplasia and hypertrophy of synoviocytes are minimal, while the walls of capillaries and small arteries show important thickening and perivascular inflammatory infiltrate.<sup>5</sup>

That specific vascular pattern and high concentrations of growth factors (TGF- $\beta$ , VEGF, PDGF) suggest that angiogenesis and altered vascular function play an important role at the beginning of the inflammatory process in both skin and joints,<sup>26</sup> supporting the theory of a single systemic disease.

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## CLASSIFICATION AND CLINICAL MANIFESTATIONS

The attempts to classify PsA have been innumerable, but there are natural difficulties of studying a complex and heterogeneous disease which sometimes is similar to RA and other times to ankylosing spondylitis, or even assuming proper characteristics.<sup>35</sup>

Moll and Wright,<sup>2</sup> when classifying the disease for the first time in 1973, used only three elements: inflammatory arthritis, presence of psoriasis, and absence of RF. Later, with a better understanding of the characteristics of the disease, there were at least other five attempts of classification. Over the years other elements such as dactylitis, radiographic changes, family history, enthesitis, and presence of HLA have been added.

Table 2 shows the authors/groups who have attempted to organize knowledge about PsA and their major contributions regarding previous studies.

For the purpose of diagnosis and standardization aiming at clinical studies, the most recent classification is the 2006 Classification Criteria for Psoriatic Arthritis (CASPAR 2006). According to this classification, the presence of arthritis is mandatory for the diagnosis of PsA. Current psoriasis is assigned a score of 2, while all other features are assigned a score of 1: history of psoriasis, family history of psoriasis, nail dystrophy,

**Table 2**

Authors and groups that have proposed classifications for psoriatic arthritis and major characteristics of their studies

| Author(s)/Group            | Year | Major characteristics   |
|----------------------------|------|---|
| Moll; Wright               | 1973 | Arthritis, psoriasis, negative rheumatoid factor  |
| Bennet                     | 1979 | Considers dactylitis, excludes subcutaneous nodules and infections  |
| Vasey; Espinoza            | 1984 | Specific radiographic lesions ("pencil in cup")   |
| ESSG                       | 1991 | Inflammatory spinal pain<br>First to consider family history of psoriasis                                     |
| McGonagle; Canaghan; Emery | 1999 | Enthesitis<br>Association with other arthropathies [SAPHO, chronic recurrent multifocal osteomyelitis (CMRO)] |
| Fournié                    | 1999 | Buttock pain, heel pain, anterior chest wall pain<br>Values the presence of HLA                               |

Adapted from Helliwell and Taylor, 2005.<sup>35</sup>

ESSG: European Spondyloarthropathy Study Group; CMRO: Chronic Multifocal Recurrent Osteomyelitis.

RF negativity, dactylitis, and/or typical radiographic lesions in hands and feet. Patients with a score equal to or greater than 3 in association with the presence of arthritis are classified as having PsA.<sup>36</sup>

However, the 1973 classification of PsA by Moll and Wright continues to be the most traditional and widely used, despite its limitations. The disease is subdivided regarding the pattern of joint involvement into the following subgroups: arthritis mainly of the distal interphalangeal joints; asymmetrical oligoarthritis; symmetrical polyarthritis; spondyloarthropathy; and arthritis mutilans<sup>2</sup> (Figure 1).

It is worth noting that PsA is a chronic and dynamic inflammatory disease, meaning that the same patient can migrate from one subtype to another, or accumulate patterns of involvement. The duration of the disease and the time point at which it is assessed in a certain patient might interfere with its diagnostic classification and count of affected joints, which tends to be mono or oligoarticular at the beginning, and polyarticular at more advanced stages.<sup>6</sup>

Usually, skin lesions precede arthritis in 75% of the patients. The simultaneous beginning of cutaneous-articular disease occurs in 10% of the patients, while arthritis precedes skin lesions in 15% of the patients.<sup>25</sup>

Although the chronic plaque lesion is the most common form of psoriasis, the disease has a large spectrum of cutaneous manifestations. In addition, different variants might coexist in the same patient, but all forms have three characteristics in common: erythema, skin thickening, and scaling.<sup>5</sup>

It is worth considering the individual variations, the drugs used, the patient's environment, and genetic and epidemiological characteristics.<sup>37</sup>

The inflammatory lesions of psoriasis are usually chronic and recurring, although they might also begin suddenly.



**Figure 1**  
Spondylitic form of psoriatic arthritis. Note straightening of the lumbar spine and marked dorsal kyphosis, in addition to erythematous lesions of psoriasis.

Such lesions can be classified according to their morphology, distribution, and presence or absence of pustules. The major



**Figure 2**  
Plaque psoriasis. **A:** Involvement of the dorsum. **B:** Erythematous and scaling plaques in the left breast.

Source: Lima 2010, PhD dissertation.<sup>52</sup>

subtypes are as follows: psoriasis vulgar (Figure 2); guttate psoriasis; erythrodermic psoriasis; pustular psoriasis; and inverted psoriasis.<sup>38</sup>

Palmoplantar pustular disease has been commonly associated with inflammatory bone lesions, receiving the name of SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome.<sup>5</sup>

Nail lesions are very common and can help differentiate initial PsA from RA. They occur in 40%–45% of the patients with psoriasis non-complicated with arthritis, and can affect up to 87% of the patients with PsA.<sup>39</sup>

The oral mucosa can also be affected by a type of migrating annular erythematous lesions (*annulus migrans*), the tongue being the most commonly affected site. The genital region is affected in approximately 30% of the cases.<sup>5</sup>

## EXTRA-ARTICULAR MANIFESTATIONS

In addition to joint manifestations, other organs and systems can be involved in PsA, as follows: dactylitis; enthesitis; peripheral edema; eye inflammations; oral ulcerations, urethritis; aortic valve disease; and nail dystrophy.<sup>3</sup> Subclinical bowel inflammation has been observed via ileocolonoscopy in 16% of the patients with PsA, but such findings have been limited to patients with oligoarticular or axial disease.<sup>40</sup>

The nail apparatus should be approached as an appendix of the musculoskeletal system, rather than of only the skin, considering that it has close anatomical and functional relationship

with the distal phalanges and extensor tendons of the fingers. The association of arthritis of distal interphalangeal joints with nail dystrophy, thus, is not only an anatomical coincidence.<sup>41</sup>

It is worth noting that nail dystrophy and psoriatic lesions of the scalp and intergluteal/perianal region are associated with a greater likelihood of developing PsA.<sup>42</sup>

## DISTINCT DISEASES?

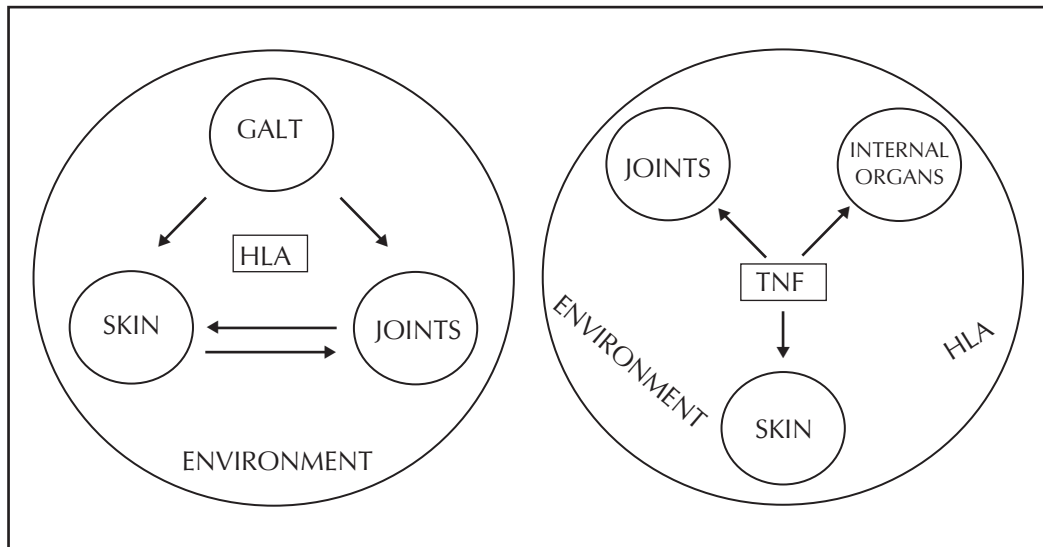
Some systemic diseases have cutaneous and joint manifestations such as systemic lupus erythematosus. Other diseases are predominantly cutaneous and can have systemic and joint manifestations, such as Sweet syndrome.<sup>43</sup> In addition, there is psoriasis, which can have almost imperceptible lesions in nail beds and intergluteal region or affect the whole body surface such as erythrodermic psoriasis. In addition, the joint involvement in psoriasis can range from minimum to polyarticular, severe, and deforming.

Since the relationship between psoriasis and PsA was officially recognized in 1964 by the American Rheumatism Association,<sup>7</sup> a number of studies have been conducted aiming at better understanding the common mechanism of both diseases.<sup>35</sup>

Regarding the immunogenicity of spondyloarthritides, the positive association between the presence of HLA-B27 and the development of that group of diseases is known, specially ankylosing spondylitis, in which positivity for that leukocyte antigen is 90%–95%. Based on that model, HLA has been believed to relate only to spondylitis and other axial diseases.<sup>44</sup> However, in 1977, Eastmond and Woodrow<sup>45</sup> described a group of patients, in whom the presence of HLA-B27 increased the risk of the patient with psoriasis developing not only axial disease, but also peripheral arthritis, including distal interphalangeal arthritis. Those British researchers took the first step to better understand the immunogenetic role of the relationship between psoriasis and PsA.

Another element favoring the relationship between both diseases is the nail involvement associated with arthritis. In 1984, Scarpa et al.<sup>46</sup> identified nail changes in 63% of the patients with PsA as compared with 37% of patients with psoriasis without arthritis. In addition, regarding patients whose arthritis preceded the cutaneous lesions, 88% of them had nail changes prior to the psoriatic lesions.<sup>46</sup>

The association between psoriatic nail and arthritis was also reported by Jones et al.<sup>47</sup> in 1994. McGonagle<sup>48</sup> has recently published articles reporting that although the nail is embryonically related to the skin and traditionally seen as a specialized cutaneous modification, it is actually functionally



**Figure 3**  
 Pathogenic model proposed by Raffaele Scarpa in 1999 with HLA playing the central role (left) and model revision proposed by Scarpa in 2006 (right).  
 Source: Adapted from Scarpa 1999<sup>49</sup> and 2006.<sup>4</sup>

integrated with the musculoskeletal system, anchored to the bone by the entheses.

Thus, the fact that the inflammation of the entheses of the extensor tendon often involves the nail bed explains both the arthritis of a distal interphalangeal joint and the nail dystrophy of the same finger as a single process, rather than distinct diseases of skin and joints.

In the 90's, Scarpa<sup>49</sup> believed that HLA accounted for the multisystemic clinical expression of psoriasis, occupying the center of a theoretical model involving skin, joints, and the gut-associated lymphoid tissue (GALT).

Currently it is known that, in addition to more than one type of HLA, other important molecular elements are involved in the pathogenesis of psoriasis. One of those elements is TNF- $\alpha$ , cytokine capable of participating in the inflammatory cascade activating both epidermal keratinocytes and endothelial cells and synoviocytes. Scarpa has modified his hypothetical model, placing TNF- $\alpha$  in its center, surrounded by environmental and intrinsic elements, such as HLA (Figure 3).<sup>4</sup>

The historical accumulation of knowledge and consequent better understanding of the pathogenic mechanism of PsA have led Scarpa to the following question: "Psoriasis, psoriatic

arthritis or psoriatic disease?"<sup>4</sup> He has assumed they are the same disease, based on findings that confirm the existence of a cutaneous, synovial, and even bowel interconnected inflammatory process.<sup>50</sup>

Studies showing the importance of enthesitis for the diagnosis of systemic inflammation have supported the hypothesis of a single disease. Girolomoni and Gisondi have reported the existence of underdiagnosed enthesopathy confirmed on the ultrasonography of patients with psoriasis, thus suggesting that the disease is multisystemic and not restricted to the skin.<sup>51</sup>

## FINAL CONSIDERATIONS

Dermatology classifies psoriasis as a systemic disease with a number of possible clinical manifestations. One of them is arthropathic psoriasis, that was attributed a specific number in the current International Classification of Diseases, distinct from that used in Rheumatology.

The authors of this review article believe that PsA should be approached as one of several possible clinical presentations of a wide spectrum called psoriasis.

## REFERENCES

- Griffiths CEM, Barker JN. Pathogenesis and clinical features of psoriasis. *Lancet* 2007; 370(9583):263–71.
- Moll JM, Wright V. Psoriatic arthritis. *Semin Arthritis Rheum* 1973; 3(1):55–78.
- Lan GK, Bingham CO. Artrite psoriática. In: Imboden J, Hellmann D, Stone J. *Current: Reumatologia – Diagnóstico e Tratamento*. 2ª ed. São Paulo: McGraw-Hill, 2008.
- Scarpa R, Ayala F, Caporaso N, Olivieri I. Psoriasis, psoriatic arthritis, or psoriatic disease? *J Rheumatol* 2006; 33(2):210–1.
- Van de Kerkhof PCM, Schalkwijk J. Psoriasis. In: Bologna JL, Jorizzo JL, Rapini RP. *Dermatology*. 2.ed. Espanha: Elsevier, 2008.
- Bruce IN. Psoriatic arthritis: clinical features. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH. *Rheumatology*. 4.ed. Philadelphia: Elsevier, 2008.
- Blumberg BS, Bunim JJ, Calkins E, Pirani CL, Zvaifler NJ. ARA nomenclature and classification of arthritis and rheumatism (tentative). *Arthritis Rheum* 1964; 7:93–7.
- Gudjonsson JE, Elder JT. Psoriasis: epidemiology. *Clin Dermatol* 2007; 25(6):535–46.
- Shao CG, Zhang GW, Wang GC. Distribution of psoriasis in China: a nationwide screening. *Proc Chin Acad Med Sci Peking Union Med Coll* 1987; 2(2):59–65.
- Convit J. Investigation of the incidence of psoriasis among Latin-American Indians. In: *Proceedings of the 13<sup>th</sup> Congress on Dermatology*. Amsterdam: Excerpta Medica, 1962; p. 196.
- Huerta C, Rivero E, Rodriguez LA. Incidence and risk factors for psoriasis in the general population. *Arch Dermatol* 2007; 143(12):1559–65.
- Gelfand JM, Gladman DD, Mease PJ, Smith N, Margolis DJ, Nijsten T *et al.* Epidemiology of psoriatic arthritis in the population of United States. *J Am Acad Dermatol* 2005; 53(4):573.
- Gisoni P, Girolomoni G, Sampogna F, Tabolli S, Abeni D. Prevalence of psoriatic arthritis and joint complaints in a large population of Italian patients hospitalised for psoriasis. *Eur J Dermatol* 2005; 15(4):279–83.
- Njobvu P, McGill P, Kerr H, Jellis J, Pobe J. Spondyloarthropathy and human immunodeficiency virus infection in Zambia. *J Rheumatol* 1998; 25(8):1553–9.
- Njobvu P, McGill P. Psoriatic arthritis and human immunodeficiency virus infection in Zambia. *J Rheumatol* 2000; 27(7):1699–702.
- Schur PH. Artrite psoriásica e artrite associada a doenças gastrointestinais. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. *Harrison - Medicina Interna*. 15.ed. Rio de Janeiro: McGrawHill, 2002; p. 2125–7.
- Zachariae H, Zachariae R, Blomqvist K, Davidsson S, Molin L, Mørk C, *et al.* Quality of life and prevalence of arthritis reported by 5,795 members of the Nordic Psoriasis Association. *Acta Derm Venereol* 2002; 82(2):108–13.
- Fortune DG, Richards HL, Main CJ, Griffiths CEM. What patients with psoriasis believe about their condition. *J Am Acad Dermatol* 1998; 39(2 Pt 1):196–201.
- Myers WA, Gottlieb AB, Mease P. Psoriasis and psoriatic arthritis: clinical features and disease mechanisms. *Clin Dermatol* 2006; 24(5):438–47.
- Chandran V, Schentag CJ, Brockbank JE, Pellett FJ, Shanmugarajah S, Toloza SM *et al.* Familial aggregation of psoriatic arthritis. *Ann Rheum Dis* 2009; 68(5):664–7.
- Fitzpatrick TB, Johnson RA, Wolff K, Suurmond D. *Dermatologia – Atlas e texto*. 4.ed. Rio de Janeiro: McGraw-Hill, 2001.
- Andressen C, Henseler T. Inheritance of psoriasis. Analysis of 2035 family histories. *Hautarzt* 1982; 33(4):214–17.
- Marsal S, Armadans-Gil L, Martínez M, Gallardo D, Ribera A, Lience E. Clinical radiographic and HLA associations as markers for different patterns of psoriatic arthritis. *Rheumatology (Oxford)* 1999; 38(4):332–7.
- Sampaio-Barros PD, Azevedo VF, Bonfiglioli R, Campos WR, Carneiro SCS, Carvalho MAP *et al.* Consenso brasileiro de espondiloartropatias: espondilite anquilosante e artrite psoriásica. Diagnóstico e tratamento – primeira revisão. *Rev Bras Reumatol* 2007; 47(4):233–42.
- Antoni CE. Psoriatic arthritis: etiology and pathogenesis. In: Hochber MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH. *Rheumatology*. 4.ed. Philadelphia: Elsevier, 2008.
- Rieger A, Chen TM, Cockerell CJ. Cutaneous manifestations of HIV infection and HIV-related disorders. In: Bologna JL, Jorizzo JL, Rapini RP. *Dermatology*. 2.ed. Espanha: Elsevier, 2008.
- Siqueira-Batista R, Gomes AP, Nacif MS, Guerra JEH, Monte-Alto CR, Lima OAT *et al.* Manifestações reumáticas da síndrome de imunodeficiência adquirida (AIDS). *Rev Bras Reumatol* 2004; 44(5):339–46.
- Bruce IN, Silman AJ. The etiology of psoriatic arthritis. *Rheumatology (Oxford)* 2001; 40(4):363–6.
- Fortune DG, Main CJ, O’Sullivan TJ, Griffiths CE. Quality of life in patients with psoriasis: the contribution of clinical variables and psoriasis-specific stress. *Br J Dermatol* 1997; 137(5):755–60.
- Pattison E, Harrison BJ, Griffiths CE, Silman AJ, Bruce IN. Environmental risk factors for the development of psoriatic arthritis: results from a case-control study. *Ann Rheum Dis* 2008; 67(5):672–6.
- Mueller W, Hermann B. Cyclosporin A for psoriasis. *N Engl J Med* 1979; 301(10):555.
- Ritchlin CT, Haas-Smith SA, Hicks D, Cappuccio J, Osterland CK, Looney RJ. Patterns of cytokine production in psoriatic synovium. *J Rheumatol* 1998; 25(8):1544–52.
- Ritchlin CT. Psoriatic arthritis. Pathology and pathogenesis. In: Klippel JH, Stone H, Crofford LJ, White PH. *Primer on the rheumatic diseases*. 13.ed. New York: Springer, 2008: 178–84.



34. Helliwell PS, Taylor WJ. Classification and diagnostic criteria for psoriatic arthritis. *Ann Rheum Dis* 2005; 64(Supl. 2):ii3–8.
35. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum* 2006; 54(8):2665–73.
36. Sociedade Brasileira de Dermatologia. Consenso Brasileiro de Psoríase. Rio de Janeiro: SBD, 2009, 116 p.
37. Ciocon DH, Kimball AB. Psoriasis and psoriatic arthritis: separate or one and the same? *Br J Dermatol* 2007; 157(5):850–60.
38. Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: epidemiology, clinical features, course and outcome. *Ann Rheum Dis* 2005; 64(Supl 2): ii14–7.
39. Schatteman L, Mielants H, Veys EM, Cuvelier C, De Vos M, Gyselbrecht L *et al.* Gut inflammation in psoriatic arthritis: a prospective ileocolonoscopy study. *J Rheumatol* 1995; 22(4):680–3.
40. McGonagle D, Tan AL, Benjamin M. The nail as musculoskeletal appendage – implications for an improved understanding of the link between psoriasis and arthritis. *Dermatology* 2009; 218(2):97–102.
41. Wilson FC, Icen M, Crowson CS, McEvoy MT, Gabriel S, Kremers HM. Incidence and clinical predictors of psoriatic arthritis in patients with psoriasis: a population-based study. *Arthritis Rheum* 2009; 61(2):233–9.
42. Levin J, Werth VP. Skin disorders with arthritis. *Best Pract Res Clin Rheumatol* 2006; 20(4):809–26.
43. Maksymowych WP. Etiology, pathogenesis and pathology of ankylosing spondylitis. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH. *Rheumatology*. 4.ed. Philadelphia: Elsevier, 2008.
44. Eastmond CJ, Woodrow JC. The HLA system and the arthropathies associated with psoriasis. *Ann Rheum Dis* 1977; 36(2):112–20.
45. Scarpa R, Oriente SP, Pucino A, Torella M, Vignone L, Riccio A *et al.* Psoriatic arthritis in psoriatic patients. *Br J Rheumatol* 1984; 23(4):246–50.
46. Jones SM, Armas JB, Cohen MG, Lovell CR, Evison G, McHugh NJ. Psoriatic arthritis: outcome of disease subsets and relationship of joint disease to nail and skin disease. *Br J Rheumatol* 1994; 33(9):834–9.
47. McGonagle D. Enthesitis: an autoinflammatory lesion linking nail and joint involvement in psoriatic disease. *J Eur Acad Dermatol Venereol* 2009; 23(Supl 1):9–13.
48. Scarpa R. What do rheumatologists think about psoriatic arthritis today? *J Rheumatol* 1999; 26(12):2509–10.
49. Scarpa R, Manguso F, D’Arienzo A, D’Armiento FP, Astarita C, Mazzacca G *et al.* Microscopic inflammatory changes in colon of patients with both active psoriasis and psoriatic arthritis without bowel symptoms. *J Rheumatol* 2000; 27(5):1241–6.
50. Girolomoni G, Gisondi P. Psoriasis and systemic inflammation: underdiagnosed enthesopathy. *J Eur Acad Dermatol Venereol* 2009; 23(Supl 1):3–8.
51. Lima EVA. Avaliação do teste T-SPOT.TB no diagnóstico de infecção tuberculosa latente em pacientes com psoríase. São Paulo, 2010. 153 f. [Tese (Doutorado)] – Programa de Dermatologia da Faculdade de Medicina da Universidade de São Paulo, 2010.