

Psoriasis, Psoriatic Arthritis, or Psoriatic Disease?

In this issue of *The Journal*, Madland, *et al* report results of a 2 week pilot study on a dietary supplementation with seal oil compared to soy oil in patients with psoriatic polyarthritis¹. Despite its short duration, several results of this research are significant. Mainly, 4 weeks after the treatment, subjects taking seal oil dietary supplementation reported improvement in patient's global assessment of disease, with a trend of decreased tender and swollen joint counts. In addition, after seal oil treatment, patients showed a promising shift in serum fatty acid composition, towards a putative antiinflammatory profile. Finally, over 20% of patients had high levels of calprotectin in feces. This point confirms the widespread occurrence of an asymptomatic colitis in patients with psoriatic arthritis (PsA).

Additionally, the relevance of this study lies in the attempt to understand PsA beyond the classic schemes, focusing discussion on the crucial role played by diet and, indirectly, by the bowel in the development of rheumatic diseases.

That environmental factors may play a triggering role in arthritis development has been well described. Among these factors, diet may be considered of primary importance. Ten years ago, a consistent spondyloarthritic involvement was demonstrated in patients with celiac disease, where the presence of gluten in the diet triggers an enteropathy followed by a malabsorptive syndrome². We know that during the course of bowel inflammation patients with Crohn's disease or with ulcerative colitis may experience articular complaints. In these 2 conditions the importance of diet has already been stated.

On the other hand, in more than 30% of patients with psoriasis, we reported the occurrence of arthritis^{3,4}, which may be accompanied by microscopic inflammatory changes of colonic mucosa, even in the absence of bowel symptoms⁵. Inflammatory bowel changes consisted of idiopathic inflammatory bowel disease only in a few cases. Indeed, we found in the majority of patients, based on guidelines suggested by the British Society of Gastroenterology⁶, an unclassified form of colitis completely different from ulcerative colitis (psoriatic colitis?). On the other hand, both

Crohn's disease and ulcerative colitis or celiac disease can be complicated by skin symptoms including pyoderma gangrenosum and dermatitis herpetiformis, as well as psoriasis.

Based on the foregoing our hypothesis of a pathogenetic link between the skin, joints, and gut in spondyloarthritic patients is reliable. It is conceivable that in patients with psoriasis a unique disease exists that may develop and involve, at the same time or in different sequential stages, cutaneous, articular, and intestinal sites.

Psoriasis is a systemic condition with a profound impact on the quality of the life of patients. It has a relapsing clinical trend regarding severity and extent of skin involvement. Clinical evidence, therefore, may be widely variable over time. In fact, there are patients with classical, distinctive lesions and others with minimal active manifestations, as well as those with only a medical history of a previous rash. This cutaneous variability does not affect the clinical expression of joint disease, which is present in 30% of cases, independently from the presence and/or the degree of expression of a clinically evident rash. PsA may also be observed in patients without psoriasis but with a family history positive for a psoriasis in first or second-degree relatives. This last setting characterizes the so-called subset of psoriatic arthritis "sine psoriasis"⁷. In addition, it highlights the importance of genetic factors, which surely play a non-marginal pathogenetic role in the clinical expression of all manifestations of the disease.

Recently, new lines of biological evidence may help to explain all molecular manifestations of the disease. In psoriatic patients the immune system is involved in both the skin and the joints. Despite uncertainty about the factor(s) that either initiates or perpetuates this immune reaction, considerable progress has been made in characterizing the steps of the inflammatory cascade. Epidermal keratinocytes, dendritic antigen-presenting cells, T lymphocytes, endothelial cells, and synoviocytes are the actors directed by various soluble mediators, among which tumor necrosis factor (TNF) plays a fundamental role. TNF induces the production of growth factors, adhesion molecules, and chemotactic polypeptides, which contribute to

See Subjective improvement in patients with PsA after short-term oral treatment with seal oil, page 307

the recruitment of a cellular network colonizing skin^{8,9}, joints^{10,11}, and other sites, such as the bowel^{12,13}.

In 1999, we proposed in an editorial⁴ the schema shown

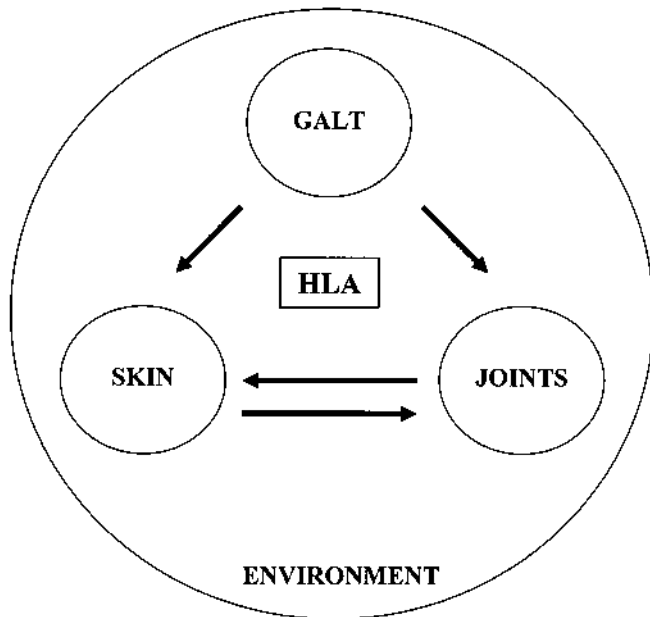


Figure 1. Our schema as proposed in 1999¹⁴. We hypothesized the migration of activated T cells from gut-associated lymphoid tissue (GALT) to trigger sites of inflammation. HLA antigens had a predisposing role and environmental factors influenced the expression of clinical aspects that characterize the multisystemic involvement of spondyloarthropathies.

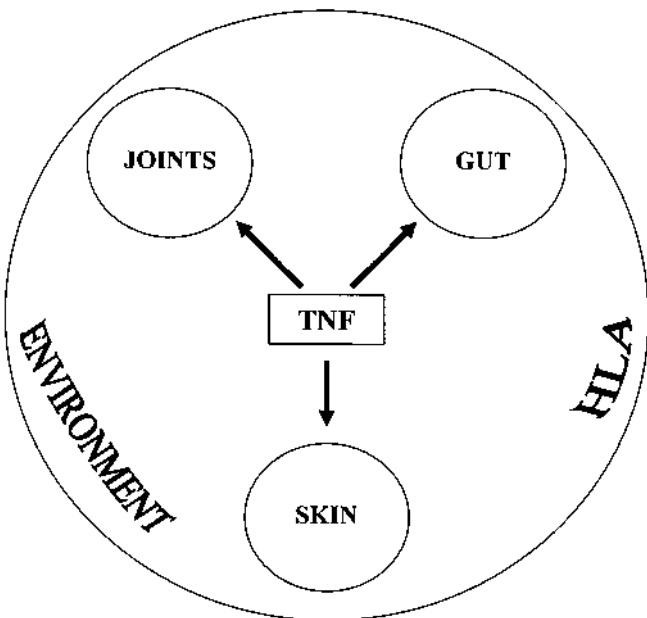


Figure 2. Schema demonstrating the critical role played by TNF in psoriatic disease. By inducing the production of growth factors, adhesion molecules, and chemotactic polypeptides, TNF contributes to the recruitment of the cellular network that colonizes skin, joints, and bowel. HLA antigens (locus B and/or C-related) play the predisposing role, while environmental factors influence the expression of clinical aspects that characterize the multisystemic involvement of psoriatic disease.

in Figure 1. At present, this schema could be modified as shown in Figure 2. TNF activates the inflammatory process of psoriasis in the skin, joints, and into the bowel.

As matters stand, we must pose the question: Is it still meaningful to speak of psoriasis or PsA as 2 distinct clinical manifestations? We indeed believe that it would be better to introduce the concept of “psoriatic disease,” a condition that can be characterized by involvement of several different anatomical sites in the same patient. This would prompt a dermatologist to better consider the effect of arthritis, while a rheumatologist would be able to appreciate the emotional and physical morbidity impact induced by rash. Finally, both dermatologists and rheumatologists should consider the occurrence of bowel inflammation.

We imagine today that, in a model psoriatic arthritis clinic, a project for clinical research should include a dermatologist, a rheumatologist, and a gastroenterologist. In Naples we have experience in this combined approach. Patients are always evaluated by a clinical team utilizing their different approaches. Results are discussed during common clinical rounds, which allows for improvement in our clinical standards. In the past 2 decades we should be aware that many changes have modified our understanding of psoriatic arthritis.

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