

# Psoriatic Disease: Clinical Staging

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**ABSTRACT.** In 2006, the introduction of the concept “psoriatic disease” (PsD) extended the traditional idea of a condition confined to skin and joints. Now we consider PsD a systemic condition, in which the increased activity of tumor necrosis factor acts as the most potent engine for a series of molecular interactions. These lead not only to the genesis of skin and joint symptoms, but also to other clinical aspects such as inflammatory bowel disease, eye involvement, and metabolic syndrome. The blocking of a precise molecular target has dramatically modified therapeutic strategies, making possible adequate control of all the clinical aspects of the condition. Therefore, an expanded clinical staging of patients could now be considered in order to ensure the best therapeutic approach and prognosis. (J Rheumatol Suppl. 2015 Nov;93:24–6; doi:10.3899/jrheum.150629)

## Key Indexing Terms:

PSORIATIC DISEASE

PSORIATIC ARTHRITIS

METABOLIC SYNDROME

DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

TUMOR NECROSIS FACTOR-A BLOCKERS

INFLAMMATORY BOWEL DISEASES

Before the introduction of biologic agents, the management of established psoriatic arthritis (PsA) was aimed at controlling skin and/or joint symptoms. Detection of the arthritic subset was considered to be discriminating in the choice of therapy because the natural history of arthritis significantly varies according to subtype<sup>1</sup>.

There was, in fact, the common idea that patients with distal interphalangeal joint arthritis were adequately controlled by nonsteroidal antiinflammatory drugs (NSAID), whereas those with polyarthritis or those with the mutilans subset required methotrexate (MTX)<sup>1</sup>. Finally, spondylitis symptoms improved when patients were constantly treated with NSAID. Different molecules were suggested for skin and/or joint or for skin or joints, respectively<sup>1</sup> (Table 1).

In 2006, the introduction of the concept PsD extended the traditional idea of a condition confined just to skin and joints<sup>2</sup>. In particular, the new concept was derived from an improved understanding of disease pathogenesis and mainly the involved molecular mechanisms<sup>3,4,5</sup>. These, in turn,

Table 1. Traditional treatments for psoriatic arthritis.

For Skin and Joint	For Skin Only	For Joint Only
Steroids	Retinoids	NSAID
Methotrexate	Cyclosporine	Steroids
Cyclosporine	Methotrexate	Methotrexate
		Gold salts
		Antimalarials
		Sulfasalazine
		Leflunomide

NSAID: nonsteroidal antiinflammatory drugs.

became the main factors influencing the therapeutic approach to patients. Thus, now we consider PsD a systemic condition, in which the increased activity of tumor necrosis factor (TNF) acts as the most potent engine for a series of molecular interactions<sup>6</sup>. These lead not only to the genesis of skin and joint symptoms, but also to other clinical aspects such as inflammatory bowel disease, eye involvement, and metabolic syndrome<sup>2</sup>.

The blocking of a precise molecular target has dramatically modified therapeutic strategies, making possible an adequate control of all the clinical aspects of the condition<sup>7</sup>. Therefore, an expanded clinical staging of patients could now be considered in order to guarantee the best therapeutic approach and prognosis.

At present, the clinical domains recognized for this staging are skin, joint, bowel, eye, and metabolic profile.

In the case of skin, staging is based on the evaluation of the activity and the extension of psoriasis, using the Psoriasis Area Severity Index or body surface area and Nail Psoriasis Severity Index. In the case of articular involvement, we use swollen and tender joint counts (SJC and TJC, respectively)

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for the peripheral pattern versus the Bath Ankylosing Spondylitis Disease Activity Index for the axial pattern. In addition, for involvement of entheses we use the tender entheseal count, and in the case of presence of dactylitis, the appropriate score. Imaging techniques are important for detection and followup of structural damage<sup>8,9,10</sup>, according to clinical findings and anamnestic data<sup>11,12,13,14</sup>.

Clinical clues for the staging of bowel involvement are positive family history of inflammatory bowel diseases, presence of chronic diarrhea, abdominal pain, rectal bleeding, and systemic inflammatory features such as persistent fever, asthenia, and weight loss. In this context, the presence or history of perianal fistula and/or abscesses must be considered<sup>15</sup>.

The staging of eye involvement should include an evaluation of uveitis, ocular pain, photophobia, and blurring of vision.

PsD has also been associated with an increased cardiovascular risk, which seems to be independent of traditional risk factors or therapies<sup>16</sup>. In particular, metabolic syndrome (MetS) — a cluster of cardiovascular risk factors, including dyslipidemia, impaired glucose tolerance, central obesity, and hypertension — has been found to be highly prevalent in patients with PsA<sup>17,18</sup>.

Among these, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) has provided suggestions for the treatment of skin and joint involvement<sup>19</sup>. GRAPPA modulates therapeutic intervention according to 3 main steps: (1) NSAID for joints, and topical treatment for skin when appropriate; (2) for resistant cases, traditional disease-modifying antirheumatic drugs (DMARD) for joints and/or skin; and (3) for nonresponders, biological DMARD for joints and/or skin.

Although traditional DMARD still have a place in the treatment of skin and/or joint symptoms, they are not able to induce complete remission, and are partially effective on other clinical domains of the disease<sup>20,21,22</sup>. In fact, there is no evidence for the effectiveness of methotrexate (MTX), cyclosporine (CSA), and hydroxychloroquine (HCQ) on bowel disease<sup>20</sup>, in which conversely, the use of sulfasalazine (SSZ) is well established<sup>15</sup>. On ocular inflammation, MTX and CSA play effective roles<sup>21</sup>, while inconclusive data have been recorded for SSZ and HCQ<sup>21</sup>. In the case of MetS, the only drug with partial efficacy is MTX, while SSZ has no effect on serum lipids, and inconclusive data are reported for HCQ<sup>22</sup>.

On the other hand, TNF- $\alpha$  blockers seem to effectively control all manifestations of PsD. In fact, these agents are effective in inducing and maintaining remission in patients with inflammatory bowel diseases<sup>15</sup>; they are rapidly effective for the treatment of uveitis associated with PsA and other spondyloarthropathies<sup>21</sup>, and they are cardioprotective in accelerated atherosclerosis<sup>23</sup>.

On the basis of current clinical and therapeutic evidence,

therefore, staging could involve one of 2 different possibilities: (1) PsD confined only to skin and/or joints, and (2) PsD involving skin and/or joints, as well as other clinical domains. Topical therapies and NSAID and/or traditional DMARD represent an appropriate treatment in the case of a disease confined to skin and/or joints. Appropriate lifestyle suggestions should also be provided (stopping smoking, calibrated diet, and moderate physical activity). In the case of refractory response or in the case of a disease complicated by the involvement of other clinical domains (stage 2), TNF- $\alpha$  blockers should be the most appropriate approach, owing to their wider therapeutical spectrum<sup>24,25,26,27</sup>. Increasingly, clinical studies have highlighted the safety and tolerability of anti-TNF blockers, which are mainly linked to a close monitoring by experienced clinicians.

We now realize that we are dealing with a condition that is not simply arthritis in patients with a cutaneous disorder. Rather, we are facing a very complex condition, PsD, in which our knowledge must improve with consideration of multiple pathogenetic and clinical aspects at the same time.

Because of the systemic nature of inflammation in PsD, the definition of a clinical staging accounting for disparate comorbidities needs further investigation and clinical studies. In particular, screening patients for cardiovascular risk, and for ocular and gastrointestinal involvement using an integrated approach, should be developed. This perspective could be the first step toward better defining the multifaceted expression of PsD.

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