

# Psoriatic Arthritis from Wright's Era Until Today

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**ABSTRACT.** This article reviews advances related to psoriatic arthritis (PsA). While the period since Wright's seminal papers is emphasized, his achievements are reviewed in light of knowledge of PsA in his day, as well as knowledge gained since the seminal work of Wright and Moll. Since other presentations focus on pathogenesis and treatment, this article emphasizes the clinical features and prognosis, as well as development of outcome measures. (*J Rheumatol* 2009;36 Suppl 83:4-8; doi:10.3899/jrheum.090209)

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## HISTORICAL PERSPECTIVE – WRIGHT'S ROLE IN THE RECOGNITION OF PSORIATIC ARTHRITIS AS A UNIQUE ENTITY

The first description of psoriatic arthritis (PsA) is attributed to Louis Aliberti, who in 1818 first noted the relationship between psoriasis and arthritis<sup>1</sup>. Pierre Bazin then described psoriasis arthritique in 1860, followed by psoriasis et arthropathies by Charles Bourdillon in 1888. In 1937 Jeghers and Robinson described PsA as a unique entity. However, in 1939, Walter Bauer found "little justification for considering these patients as suffering from a distinct disease entity". Vilanova and Piñol disagreed, and described PsA as an entity in 1951<sup>2</sup>.

However, PsA mainly gained recognition with the seminal studies of the late Prof. Verna Wright of Leeds, England. In 1956 Wright published on psoriasis and arthritis, and reevaluated the subject again in 1959, when he also performed a comparative study of rheumatoid arthritis (RA), psoriasis, and arthritis associated with psoriasis<sup>3,4</sup>. This was followed by a more detailed comparison of patients with RA and PsA<sup>5</sup>. This work paved the way for the American Rheumatism Association (now the American College of Rheumatology) to recognize PsA as a distinct entity in 1964<sup>6</sup>.

John Moll joined Wright in Leeds, where together they continued to make important contributions to the field of spondyloarthritis and PsA. In a review article in 1973 they outlined evidence to support the concept of PsA as a specific disease entity, based on clinical, serological, and radiological as well as epidemiological studies; these confirmed the association between psoriasis and a specific form of arthritis<sup>7</sup>.

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Thus, Wright played a pivotal role in the recognition of PsA as a unique entity, and has made important contributions related to the description of the disease and its features.

## PSORIATIC ARTHRITIS – AN ESTABLISHED ENTITY

Currently, PsA is recognized as an inflammatory musculoskeletal condition associated with psoriasis, usually seronegative for rheumatoid factor. Although its exact prevalence is unknown, estimates vary from 0.02% to 0.25% depending on the type of study (Table 1). There is also variation in the prevalence of PsA among patients with psoriasis (Table 2).

## CLINICAL FEATURES OF PsA

PsA occurs in men and women almost equally. It usually begins in the 4th decade, within 10 years of onset of psoriasis. However, there are some 15% of patients who present with their arthritis prior to recognition of psoriasis (Table 3). The typical features of PsA include the distal joint involvement that occurs in more than half the patients, although sole occurrence is much rarer; oligoarticular presentation; and redness/purplish discoloration over the affected joints. About half the patients with PsA have a spondylitis, which is often less symptomatic than ankylosing spondylitis (AS)<sup>8</sup>. Almost half the patients with PsA have dactylitis, described as inflammation of a whole digit, and about 40% have enthesitis, or inflammation at the insertion of tendons into bone<sup>9</sup>. There is also evidence of tendinitis. Patients with PsA demonstrate less tenderness than those with RA. Radiologically, patients with PsA demonstrate erosive disease, which is distinguished from RA by the presence of periosteal reaction and ankylosis. The sacroiliitis tends to be less symmetrical than that seen in AS, and syndesmophytes tend to skip vertebrae.

## WHAT HAVE WE LEARNED SINCE MOLL AND WRIGHT?

The initial description of PsA by Wright depicted PsA as a mild disease. However, over the past several decades it

Table 1. Prevalence of psoriatic arthritis (PsA). Modified from Setty and Choi. *Curr Rheumatol Rep* 2007;9:449-54; with permission.

Study	Country	Definition	Prevalence, %
Lomholt, 1963	Faroe Is.	Psoriasis with DIP	0.04
Hellgren, 1969	Sweden	Typical PsA features	0.02
van Romunde, 1984	Netherlands	Rheum	0.05
Shbeeb, 2000	USA	Moll & Wright	0.1
Alamanos, 2003	Greece	ESSG	0.06
Trontzas, 2005	Greece	Rheum	0.17
Madland, 2005	Norway	Rheum	0.2
Gelfand, 2005	USA	Self-report	0.25

ESSG: European Spondylarthropathy Study Group; Rheum: rheumatologist diagnosis; DIP: distal interphalangeal.

Table 2. Prevalence of psoriatic arthritis (PsA) in patients with psoriasis.

Study	Center	Patients with Psoriasis, n	PsA, %
Leczinsky, 1948	Sweden	534	7
Vilanova, 1951	Barcelona	214	25
Little, 1975	Toronto	100	32
Scarpa, 1984	Naples	180	34
Stern, 1985	Boston	1285	20
Zaneli, 1992	Winston-Salem, USA	459	17
Barisic-Drusko, 1994	Osijek region	553	10
Salvarani, 1995	Reggio Emilia	205	36
Shbeeb, 2000	Mayo Clinic, USA	1056	6.25
Brockbank, 2001	Toronto	126	31
Alenius, 2002	Sweden	276	48
NPF, 2002	USA	4.4 male	23
Zachariae, 2003	Denmark	5795	30

NPF: National Psoriasis Foundation.

has become clear that the disease is much more severe than previously thought. Although Wright described a mutilating form of arthritis, it was thought to occur in only 5% of the cases, and the majority of patients presented with oligoarthritis. We first noted in 1987 that PsA is a severe disease<sup>10</sup>. Of the first 220 patients registered in our longitudinal observational cohort, 67% had at least one erosion and 20% developed clinical deformities and marked radiological damage resulting in functional disability. Over a 10 year followup it was noted that 55% of the patients developed  $\geq 5$  deformities<sup>11</sup>. Progression of erosions was noted over a 5 year period by McHugh, et al<sup>12</sup>. In a study of PsA patients identified from an early arthritis cohort presenting within 5 months of onset of symptoms,

47% of the patients developed erosive disease within the first 2 years of followup<sup>13</sup>.

It was further shown that polyarticular presentation predicts future deformities and erosions<sup>14,15</sup>. Moreover, the number of actively inflamed joints at each visit as well as elevated erythrocyte sedimentation rate predict progression of clinical and radiological damage at subsequent visits<sup>16,17</sup>. In addition, the number of damaged joints is an independent predictor of subsequent clinical and radiological damage. Digits with dactylitis are more likely to have erosive disease than digits without dactylitis<sup>9</sup>.

Further evidence supporting the concept that PsA is a severe disease comes from studies demonstrating increased mortality among patients with PsA compared

Table 3. Psoriatic arthritis features described in published series.

	Roberts, 1976	Kammer, 1979	Gladman, 1987	Torre-Alonso, 1991	Veale, 1994	Jones, 1994
Site	Leeds	Boston	Toronto	Spain	Leeds	Bath
No.	168	100	220	180	100	100
M/F	67/101	45/55	104/116	98/81	59/52	43/57
Age, yrs	40	39	37	39	34	38
Joints before skin or arthritis before psoriasis	?	30	17	15	?	18
Sacroiliitis	NA	11	26	20	14	16
Arthritis						
Asymmetric	?	53	21	45	43	26
Symmetric	78	28	48	42	33	63
Distal	17	10	12	1	16	1
Back only	?	2	3	7	4	6
Arthritis mutilans	5	7	16	5	2	4

with the general population<sup>18</sup>. Although there appears to be a trend towards improved survival, the standardized mortality ratio is still elevated at 1.36<sup>19</sup>. Causes of death are primarily related to cardiovascular and respiratory problems as well as injuries/poisonings. Predictors for mortality are more active and severe disease at presentation<sup>20</sup>.

PsA impairs quality of life and function as measured by the Health Assessment Questionnaire (HAQ) and the Medical Outcome Survey Short Form 36 (SF-36)<sup>21-23</sup>. It was further demonstrated that the SF-36 is more sensitive to change than other instruments<sup>24</sup>. The HAQ varies over time in patients with PsA. Worsening HAQ scores are associated with female gender, longer disease duration, and higher actively inflamed joint counts, whereas improvement is related to shorter disease duration and lower number of joints involved at onset<sup>25</sup>. Quality of life and function was found to be as impaired in PsA as in RA<sup>26,27</sup>.

#### DEVELOPING PsA CLASSIFICATION CRITERIA

Major advances since Wright's work on PsA have resulted from international collaborations. This began with the development of classification criteria for PsA, the CLASSification of Psoriatic ARthritis (CASPAR) criteria. Philip Helliwell, who was Wright's trainee and colleague, was the leader of the CASPAR group. The CASPAR group collected 588 patients with PsA and 536 controls with other forms of inflammatory arthritis, mostly RA, and through logistic regression analyses and classification and regression trees derived new classification criteria<sup>28</sup>. Thus, widely accepted criteria for the classification of PsA are now available, and subsequent

studies suggest that these criteria may function well as diagnostic criteria<sup>29-31</sup>.

#### GROUP FOR RESEARCH AND ASSESSMENT OF PSORIASIS AND PSORIATIC ARTHRITIS

The formation of the CASPAR group paved the way for the Group for Research and Assessment of Psoriasis and PsA (GRAPPA). GRAPPA includes rheumatologists, dermatologists, methodologists, and radiologists, as well as representation from patient groups, industry, and government agencies. GRAPPA has focused its attention on treatment recommendations, outcome measures, assessment tools, and tissue pathology<sup>32</sup>.

One of the objectives of GRAPPA has been to develop and validate outcome measures for psoriasis and PsA. To achieve this goal, a workshop was carried out within the Outcome Measures in Rheumatology Clinical Trials (OMERACT) in 2004. During that workshop, domains deemed important in the assessment of patients with PsA were identified<sup>33</sup>. A module on PsA was then presented at the 2006 OMERACT meeting. As a result of the deliberation there, a core set of domains to be included in clinical trials and longitudinal observational cohorts was identified. This core set includes the assessment of peripheral joint disease including 68 joints for tenderness and 66 for swelling, the assessment of skin disease, patient global assessment of disease activity, patient global assessment of pain, assessment of physical function, and health related quality of life. Additionally, the following domains were deemed important to include, although not mandatory: dactylitis, enthesitis, spinal disease, nails, fatigue, physician global assessment, acute

phase reactants, and radiological evaluation. A research agenda was set to include evaluation of other imaging tools such as magnetic resonance, ultrasound, and computed tomography, as well as tissue analysis and participation<sup>34</sup>.

It was then important to document the reliability of some of the measures used to assess the domains. The INternational SPondyloarthritis Interobserver Reliability Exercise (INSPIRE) aimed to evaluate peripheral joint and spinal measures in patients with PsA and AS. It showed that the assessment of joint tenderness was reliable, but the assessment of joint swelling was less reliable. Assessment of dactylitis, enthesitis, and spinal measures proved quite reliable in this study<sup>35,36</sup>.

A further reliability study was carried out comparing the assessment of patients with PsA by dermatologists and rheumatologists<sup>37</sup>. It was demonstrated that dermatologists and rheumatologists can assess joint tenderness reliably, similarly to what was found in the INSPIRE study. There was “very good to excellent” agreement on the assessment of tender joint count, Psoriasis Area and Severity Index, nail changes, and the Modified Nail Psoriasis Index.

#### **PATHOGENESIS OF PsA**

Much has been learned about the pathogenesis of PsA: several genetic markers have been identified, and immunological pathways have been elucidated<sup>38,39</sup>. These advances are the topic of another presentation.

#### **FUTURE PROJECTIONS**

Important issues in the management of patients with PsA over the next few years include developing strategies to diagnose PsA early. This can be done by studying patients with psoriasis prospectively for the development of PsA, and developing screening questionnaires to identify patients with PsA. The latter will help determine the incidence of patients with PsA. We also need to learn how to modify the course of the disease. Identifying genetic markers for disease progression will allow us to select only those patients destined to progress for early, aggressive therapy. Other biomarkers may be recognized to identify patients at risk. This type of investigation will likely require international collaboration, and GRAPPA is well suited to pursue this.

My prediction is that within the next 5 to 10 years susceptibility genes for PsA will be identified, and genes for disease expression will also be identified. New therapeutic agents will be developed, possibly with fewer untoward effects than current therapies. The major issues for patients with PsA and their physicians will be comorbidities, which are now emerging as important factors in morbidity and mortality in PsA.

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