

# Chapter 18

## JUVENILE PSORIATIC ARTHRITIS

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An association between psoriasis and arthritis in the adult patient was described almost 200 years ago, but has been recognized in children only since the 1950s.<sup>1-4</sup> Juvenile psoriatic arthritis (JPsA) encompasses a heterogeneous set of arthritic phenotypes characterized by certain hallmark clinical features as well as considerable overlap with other subtypes of juvenile idiopathic arthritis (JIA). It is recognized both in children with frank cutaneous psoriasis as well as those in whom a psoriatic diathesis is suspected on other grounds.

### DEFINITION AND CLASSIFICATION

As classified by the criteria of the International League of Associations for Rheumatology (ILAR), JPsA is arthritis that has its onset before the 16th birthday, lasts for at least 6 weeks, and is associated either with psoriasis or with two of the following: dactylitis, nail pitting or onycholysis, or psoriasis in a first-degree relative.<sup>5</sup> This definition resembles that of the “Vancouver criteria” (Table 18-1).<sup>6</sup> However, under ILAR criteria the diagnosis of JPsA cannot be made if the patient has a positive test for rheumatoid factor, a first-degree family history of an human leukocyte antigen B-27 (HLA-B27)-associated disease, or if the arthritis began in a boy over the age of 6 years who is HLA-B27 positive.

The diagnosis of JPsA is complicated by the presentation of psoriasis in children. Psoriasis in the young child may be subtle, atypical, and transient; initial misdiagnosis as eczema is common.<sup>7-9</sup> Psoriasis occurs in about 0.5% to 1% of children, with a prevalence rising to 2% to 3% in adulthood.<sup>10-12</sup> Since skin disease lags behind arthritis in about half of children with JPsA, sometimes by a decade or more (Table 18-2), the diagnosis may often rest on the presence of dactylitis or family history.<sup>6-8,13-24</sup> Not every patient with arthritis and psoriasis has psoriatic arthritis. Typical seropositive rheumatoid arthritis (RA) with coincidental psoriasis is well recognized.<sup>25</sup> Finally, agents such as methotrexate and tumor necrosis factor (TNF) blockers are effective treatments for cutaneous psoriasis and could potentially forestall its appearance in a child treated for joint inflammation. Confirming that a particular child

does or does not have JPsA is therefore challenging, and diagnostic uncertainty is common.

These challenges have been reflected in the evolution of diagnostic criteria for JPsA. Initially, JPsA was limited to children with chronic arthritis who developed classic psoriasis.<sup>3,7,13-16,26</sup> Recognizing that the psoriatic diathesis may be suggested by features beyond the classic eruption, including dactylitis, nail pits, and a family history of psoriasis, Southwood and colleagues extended the diagnosis of JPsA to patients with such features even in the absence of the typical rash, yielding the “Vancouver criteria” for JPsA (see Table 18-1).<sup>6</sup> These criteria have been validated.<sup>19,23,24</sup> With the development of the ILAR nomenclature, the definition of JPsA was restricted to make it and other subtypes of JIA mutually exclusive. These definitions remain a work in progress.<sup>5,23,24,27-29</sup> Both the Vancouver and ILAR criteria were designed for research, and in practice the diagnosis of JPsA is often used more flexibly.

### EPIDEMIOLOGY

#### Incidence and Prevalence

The incidence and prevalence of JPsA are unknown. Population data, enumerating largely patients with adult-onset psoriatic arthritis (PsA), suggest a prevalence of 0.10% to 0.25% in the United States.<sup>30,31</sup> It occurs in all ethnic groups.<sup>32</sup> The proportion of JIA patients with JPsA varies widely depending on the population studied and the diagnostic criteria employed. Series that recognize patients on the basis of frank psoriasis, or using ILAR criteria, find that JPsA represents approximately 7% (range: 0% to 11.3%) of patients with JIA.<sup>6,8,18,21,24,33-40</sup> Series employing the more inclusive Vancouver criteria identify JPsA in 8% to 20% of patients with JIA.<sup>6,21,24,41</sup>

#### Age at onset and Sex Ratio

The age at onset of JPsA is biphasic (Figure 18-1).<sup>6,21</sup> A first peak occurs during the preschool years, and a second is seen during middle to late childhood. JPsA

is uncommon before the age of 1 year. It is somewhat more frequent in girls than in boys (see Table 18–2), with girls accounting for 60% of cases in larger series.<sup>21,42</sup>

## ETIOLOGY, PATHOLOGY, AND PATHOGENESIS

The cause of JPsA and the reasons for the link between psoriasis and arthritis are unknown.

## PATHOLOGY

### Synovial Pathology

Data concerning the pathology of psoriatic synovium are available largely from adult-onset disease, with rare exception.<sup>43</sup> Gross examination, as performed by arthroscopy, reveals a synovial lining that is less villous than in adult RA but with distinctive tortuous, bushy superficial blood vessels.<sup>44,45</sup> This microvascular pattern resembles that of the psoriatic plaque and is observed also

Table 18–1

#### Vancouver and ILAR criteria for Juvenile Psoriatic Arthritis

	Vancouver	ILAR (Edmonton revision)
Inclusion	Arthritis plus psoriasis or arthritis plus at least two of Dactylitis Nail pits Psoriasis in a first- or second-degree relative Psoriasis-like rash	Arthritis plus psoriasis, or arthritis plus at least two of  Dactylitis Nail pits or onycholysis Psoriasis in a first-degree relative
Exclusion	None	1. Arthritis in an HLA-B27–positive male beginning after the sixth birthday 2. AS, ERA, sacroiliitis with IBD, reactive arthritis, or acute anterior uveitis, or a history of one of these disorders in a first-degree relative 3. The presence of IgM RF on at least 2 occasions at least 3 months apart 4. The presence of systemic JIA 5. Arthritis fulfilling two JIA categories
For both criteria sets, arthritis must be of unknown etiology, begin before the sixteenth birthday, and persist for at least 6 weeks. Under the Vancouver criteria, “definite JPsA” is arthritis plus psoriasis or arthritis plus three minor criteria, while “probable JPsA” is arthritis plus two minor criteria.		

AS, ankylosing spondylitis; ERA, enthesitis-related arthritis; IBD, inflammatory bowel disease; RF, rheumatoid factor.

Table 18–2

#### Clinical series of patients with Juvenile Psoriatic Arthritis

Year	First author	N	F (%)	Definition of JPsA	Follow-up (yr, mean)	Psoriasis (%)	Arthritis Before Rash (%)	FHx of Psoriasis (%)	Dactylitis (%)	Nail Changes (%)	Uveitis (%)
1976	Lambert	43	74	Lambert	11	100	53	40		71	9.3
1977	Calabro	12	58	Arthritis+Psoriasis		100	33		58	92	0
1980	Sills	24	71	Lambert*		71*	58			83	8.3
1982	Shore	60 <sup>†</sup>	58	Lambert	10.8	100	43	42	23	77	8.3
1985	Wesolowska	21	38		4.2		56			86	14.3
1989	Southwood	35	69	Vancouver	4.4	60	48	88	49		17.1
1990	Truckenbrodt	48	44	Arthritis+Psoriasis	5	100	50	42	17	67	10.4
1990	Hamilton	28	57	Arthritis+Psoriasis	8.8	100	21	73	39	71	0
1991	Koo	11	55	Arthritis+Psoriasis		65	36	18		45	18
1996	Robertson	63	70	Vancouver	7		56	85	35		14.3
2006	Stoll	139	59	Vancouver	2	25	29	53 <sup>‡</sup>	37	47 <sup>‡</sup>	7.9
2009	Flato	31	77	ILAR	>15	39	50	75	42	30.4	19.4

Blank = not specified

F = Female

\*Nail disease counted as cutaneous psoriasis

<sup>†</sup>Includes 32 from Lambert 1976.

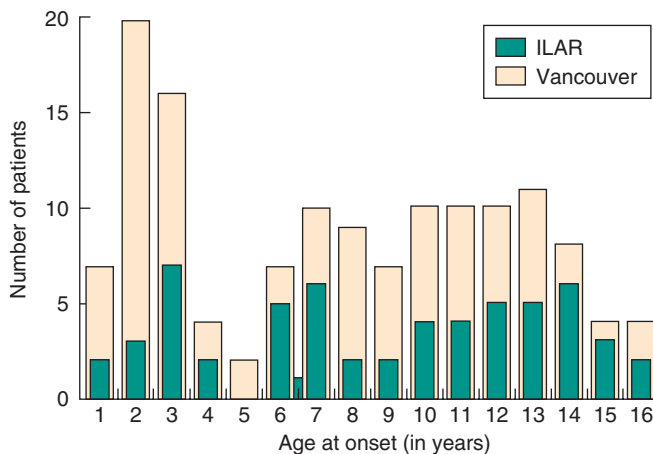
<sup>‡</sup>M. Stoll, P.A. Nigrovic, unpublished data.

Lambert criteria: inflammatory arthritis beginning before 16 years of age, psoriasis preceding or within 15 years of onset, usually negative for rheumatoid factor.

FHx, family history.

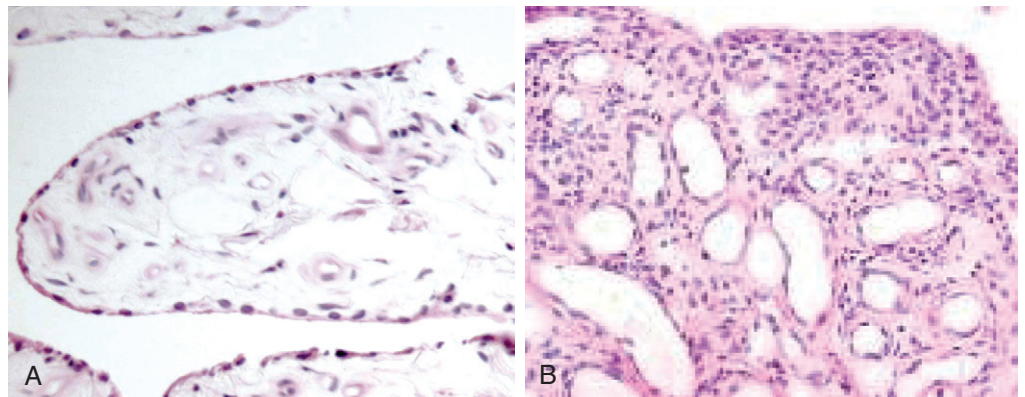
in synovial tissue from the spondyloarthropathies.<sup>44,46</sup> There are histological changes throughout the psoriatic synovium (Figure 18–2). The lining becomes hypertrophic with expansion of both type A (macrophage-like) and type B (fibroblast-like) synoviocytes.<sup>47</sup> The infiltrate in the loose connective tissue beneath the synovial lining is composed principally of lymphocytes and monocyte/macrophage lineage cells, with occasional neutrophils, plasma cells, and mast cells.<sup>48–51</sup> Lymphoid follicles may be observed. Compared with RA, lining hypertrophy and sublining infiltrates are typically less extensive. Infiltrating neutrophils are more prevalent in PsA, but they are not invariably present.<sup>48,49,51</sup> In general, given the variability between patients and within different parts of the same synovium, pathological findings generally are inadequate to define the diagnosis in an individual patient.

Characterization of the psoriatic synovial infiltrate by immunohistochemistry shows that the majority of infiltrating lymphocytes are T cells that express the memory CD45RO phenotype, with CD4 helper cells predominating over CD8 cytotoxic cells.<sup>48,49,52–54</sup> These cells are present at frequencies similar to that in RA, as are CD20<sup>+</sup> B cells, plasma cells, and CD68<sup>+</sup> macrophages. T cell oligoclonality suggests local antigen-driven expansion.<sup>55</sup> CD83<sup>+</sup> dendritic cells are less common than in RA.



**FIGURE 18–1** Age at onset of patients with juvenile psoriatic arthritis. (Data from Stoll M, Lio P, Sundel RP, Nigrovic PA: Comparison of Vancouver and International League of Associations for rheumatology classification criteria for juvenile psoriatic arthritis, *Arthritis Rheum* 59:51–58, 2008.)

**FIGURE 18–2** Synovial pathology in juvenile psoriatic arthritis. **A**, normal synovium with gracile synovial lining layer supported by a loose connective tissue sublining containing small blood vessels. **B**, synovium from 35-year old patient with juvenile-onset psoriatic arthritis, demonstrating lining hyperplasia, mononuclear infiltration of the subsynovium, and striking vascular hyperplasia. (Panel B courtesy of D.L. Baeten, University of Amsterdam, The Netherlands.)



By contrast, increased numbers of macrophages expressing CD163 are identified in PsA and the adult spondyloarthropathies,<sup>49,56</sup> although not as clearly in juvenile-onset disease.<sup>43</sup> CD163 is a scavenger receptor, typically expressed on mature resident tissue macrophages that may help to limit rather than promote inflammation. However, the activity of these cells in the psoriatic synovium is unknown.<sup>56,57</sup>

Complement-fixing immune complexes are not typically found in the psoriatic synovium, and synovial fluid complement levels are usually normal.<sup>58–60</sup> Similarly, citrullinated peptides are observed commonly in the rheumatoid synovium but rarely in PsA.<sup>49</sup>

## Enteseal Pathology

Enteseal sites are not readily accessible to biopsy, but small series in adult patients provide a degree of histological insight.<sup>61–63</sup> A low-grade inflammatory infiltrate is observed, often in association with underlying erosion of bone. This infiltrate is not limited to the surface of the bone and is often more extensive in the bone marrow underlying the enthesis. Such osteitis can be visualized as bone marrow edema by magnetic resonance imaging (MRI).<sup>63–65</sup> Cells observed at the interface include macrophages, lymphocytes (particularly CD8<sup>+</sup> T cells), and occasional neutrophils. Bone healing is commonly evident, with woven bone filling in the defect left by erosions. This new bone often extends beyond the previous bony surface to interface with the ligament.<sup>61</sup> These observations have given rise to the hypothesis that the new bone formation characteristic of the spondyloarthropathies results from recurrent cycles of injury and healing, perhaps enabled by fluctuations in the degree of inflammation.<sup>61,66</sup> Whether such a mechanism underlies the hypertrophic periostitis observed in some patients with JPsA (Figure 18–3C) is unknown.

## PATHOGENESIS

### Environmental Contribution

Both psoriasis and psoriatic arthritis exhibit only limited concordance in monozygotic twins, suggesting that environmental contributions play a pivotal role in the





**FIGURE 18-3** Dactylitis in juvenile psoriatic arthritis. **A**, dactylitis of the third finger (with incidental abrasion). **B**, dactylitis of the second and fifth toes. **C**, radiograph of the hands from the patient in **A**, demonstrating periosteal reaction in the affected digit (arrow).

development of disease.<sup>67-69</sup> The Koebner phenomenon, in which physical trauma precipitates skin disease, is evident in at least one-third of patients with psoriasis.<sup>70,71</sup> There have been reports of psoriatic arthritis being precipitated by physical trauma.<sup>72</sup> Because the entheses are points of mechanical stress, an exaggerated reaction to injury (“deep Koebner phenomenon”) could contribute to clinical enthesitis in JPsA, with potential spread to adjacent structures. Streptococcal infection is a known precipitant for guttate psoriasis, raising the possibility that infection with streptococci or other agents could trigger joint inflammation.<sup>73,74</sup> Indeed, elevated antistreptococcal

antibody titers have been observed in patients with psoriatic arthritis compared with other arthritides.<sup>75</sup> In support of such a role for bacteria, many rodent arthritis models fail to develop joint disease if deprived of normal bacterial flora. Among these is the rat transgenic for human HLA-B27, which develops features reminiscent of PsA including synovitis, spondylitis, and nail dystrophy.<sup>76,77</sup> Varicella infection has been reported to precipitate JPsA,<sup>15</sup> but a survey of childhood arthritis found no correlation between the onset of JPsA and coincident infections with *Mycoplasma*, respiratory syncytial virus, adenovirus, influenza A or B, parainfluenza, rubella, or herpes simplex.<sup>41</sup>

Exacerbation of psoriatic arthritis by emotional stress has also been observed in adults<sup>67</sup> and may potentially be modeled by the male DBA/1 mouse, which develops arthritis, dactylitis, and nail dystrophy with aging, but only if caged with other mice not originally from the same litter.<sup>78</sup>

## Genetic Contribution

There is convincing clinical evidence for a genetic contribution to psoriasis and PsA. More than 50% of patients with childhood-onset psoriasis, with or without JPsA, have a family history of psoriasis (see [Table 18–2](#)).<sup>9,70,79</sup> The risk for both psoriasis and psoriatic arthritis appears to be transmitted more effectively via the paternal line (genetic imprinting).<sup>80,81</sup> A fifty-fold increased risk for PsA was observed in family members of the adults with PsA, suggesting that a propensity for arthritis is inherited over and above the propensity for psoriasis.<sup>67</sup> Similar results were noted in other studies.<sup>82,83</sup>

Association studies have begun to shed light on the genes that explain these strong familial associations.<sup>68,84</sup> In adults, psoriasis with onset age  $\leq 40$  years (Type I psoriasis) is more strongly familial than older-onset (Type II) disease.<sup>85,86</sup> Type I psoriasis is strongly associated with the MHC class I allele HLA-Cw6. This allele is also associated with adult PsA, and possibly with older-onset JPsA in children, but the link appears secondary to risk for psoriasis.<sup>86,87</sup> The results of studies of HLA associations in JPsA have been inconsistent, likely because of differences in definitions employed and variability within JPsA across the pediatric age spectrum.<sup>6,7,17,19,87,88</sup>

Beyond the MHC, JPsA has been linked with single nucleotide polymorphisms (SNPs) near genes involved in the autoinflammatory diseases (MEFV, NLRP3, NOD2, and PSTPIP1).<sup>89</sup> These associations have not emerged in adult genomewide association scans and have yet to be replicated. In adult studies, psoriasis and psoriatic arthritis have been associated with SNPs in a range of genes, including HCP5 (involved with control of viral replication) and genes related to the cytokines TNF, IL-13, and IL-23.<sup>90–92</sup> The functional consequences of these SNPs remain to be determined, but the cytokine findings are of particular interest. TNF blockade is markedly beneficial in psoriasis and psoriatic arthritis. IL-23 is involved in the differentiation of pro-inflammatory Th17 cells, which are increased in frequency in the circulation of patients with PsA and are present in psoriatic plaques.<sup>93–95</sup> Genetic studies have linked both psoriasis and PsA to IL12B, encoding the common p40 subunit of both IL-12 and IL-23, as well as to the IL-23 receptor IL23R. IL-13 suppresses the Th17 axis in favor of differentiation along a Th2 pathway, and the “risk” allele linked to psoriasis is associated with decreased cytokine production. Although no data from psoriatic synovium have been reported to date, murine models suggest that Th17 cells may contribute importantly to arthritis.<sup>96</sup> The implication of these findings is that the Th17 axis may be important in both psoriasis and its associated arthritis. Indeed, the anti-IL-12/IL-23 agent ustekinumab is highly effective for cutaneous psoriasis, although its efficacy for PsA is more modest.<sup>97,98</sup>

## Cytokines and Other Mediators

Data on cytokine expression in psoriatic synovium and synovial fluid exhibit considerable variability. The range of mediators expressed is broadly similar to that in other inflammatory arthritides and includes the classical pro-inflammatory cytokines TNF, IL-1 $\beta$  and IL-6 as well as IL-1 $\alpha$ , the neutrophil chemoattractant IL-8, the IL-2-like cytokine IL-15, IFN- $\gamma$ , and others.<sup>51–53,57,99–102</sup> Pro-angiogenic factors such as VEGF are also elevated,<sup>53,103,104</sup> as are matrix metalloproteinases and their inhibitors.<sup>53,57,105</sup> No pattern of mediators has yet emerged as being specific for PsA, although compared with RA there are typically higher levels of pro-angiogenic factors and lower levels of pro-inflammatory mediators.

## Synthesis: Pathogenesis of Juvenile Psoriatic Arthritis

Despite substantial advances in understanding, much remains to be learned about the pathogenesis of psoriatic arthritis. In the proper genetic context, an environmental trigger such as infection or trauma appears to unleash an inflammatory process involving infiltration of lymphocytes as well as neutrophils and other effectors of innate immunity into entheses and synovium. The target of this immune response remains unknown. Lymphocytes likely play a key role, as suggested by clonal expansion of these cells within the synovium and the requirement for lymphocytes in a murine model of psoriatic arthritis.<sup>55,106</sup> Joint inflammation is accompanied by an exuberant vascular expansion reminiscent of cutaneous psoriasis, with a tendency to promote bone formation as well as injury to cartilage and bone. Whether these principles apply equally to patients with JPsA, including those with early-onset disease, is unknown.

## CLINICAL MANIFESTATIONS

### Subgroups Within JPsA

JPsA is clinically heterogeneous. Age of onset data suggest a biphasic distribution, particularly in JPsA defined under the Vancouver criteria (see [Figure 18–1](#)).<sup>6–8,21,23</sup> This distribution is similar to that of JIA as a whole, with a peak around age 2 to 3 years and a second, less prominent peak in adolescence.<sup>22,38,107</sup> Younger children, presenting before the age of 5 years, tend to be female, ANA positive, and affected by dactylitis, the sausage-like swelling of individual digits.<sup>15,21</sup> This subgroup bears marked clinical and demographic similarity to early-onset oligoarticular JIA, although clinical differences include the tendency to develop dactylitis, to involve the wrists and small joints of the hands and feet, and to progress to polyarticular disease in the absence of effective therapy.<sup>20,24,108</sup> The merit of distinguishing these younger patients from oligoarticular JIA is controversial ([Box 18–1](#)). By contrast, older children exhibit a gender ratio closer to 1:1, with a tendency to enthesitis and axial disease, more closely resembling adult psoriatic arthritis.<sup>8,15,17,21</sup>

**BOX 18–1****Psoriatic Arthritis, or Arthritis with Psoriasis?**

The recognition of psoriatic arthritis in adults as an entity in its own right emerged gradually out of a number of observations. Inflammatory joint disease is encountered at a rate far higher than expected (10% to 20%) among patients with psoriasis.<sup>31,148,149</sup> This arthritis was often clinically distinctive. RF was usually absent or present in low titer, DIP and sacroiliac joints were commonly involved, and radiographs demonstrated new bone formation as well as erosions.<sup>1</sup> Even where arthritis was clinically indistinguishable from RA, it appeared at a younger age and in males and females equally, often clustered within certain psoriatic families.<sup>25,67</sup> Finally, PsA and RA synovial tissue could be differentiated, to some degree, on the basis of distinctive gross and microscopic features (see Pathology). Taken together, these data have provided strong support for the existence of psoriatic arthritis as a distinctive syndrome rather than simply the coincident occurrence of two common diseases.

By contrast, in children the case for JPsA remains controversial.<sup>108,124,150</sup> In most respects patients with JPsA fit somewhere in the spectrum of JIA. The hallmark psoriatic rash may take years to emerge. Absence of rheumatoid factor does not separate JPsA from most other JIA subtypes. Histopathological data are limited, and interpretation of genetic studies is complicated by issues of definition.<sup>21,23,150,151</sup> Finally, patients with JPsA respond to the therapies used in other JIA patients, and generally appear to do equally well.

Nevertheless, there are reasons to suspect that the association between psoriasis and arthritis spans both adults and children.<sup>125</sup> The prevalence of psoriasis in children is 0.5% to 1%; most present in adolescence.<sup>10,11,70</sup> Thus, the identification of a psoriatic diathesis in 7% or more of patients with JIA (of whom 40% to 60% have the

classic rash) is not likely to reflect a chance association. Further, the pattern of arthritis in these children is distinctive in aggregate, if not always in an individual patient. Among younger patients, this includes dactylitis and involvement of small joints in the setting of oligoarthritis; in older patients, it includes an even gender ratio and an appreciable incidence of enthesitis and sacroiliitis.<sup>20,21</sup> Disease outcome may also differ.<sup>24</sup>

Although older-onset JPsA patients rather clearly resemble their adult counterparts, questions remain about arthritis that begins before the age of 5 or 6 years.<sup>22,150</sup> Like patients with early-onset oligoarticular JIA, these children tend to be female, are commonly ANA positive, and are prone to chronic asymptomatic uveitis.<sup>21</sup> Some share expression of the MHC II antigen HLA-DRB1\*0801 (DRw8), associated with early-onset oligoarticular and polyarticular arthritis.<sup>7,152,153</sup> It seems very likely that shared pathophysiological mechanisms underlie these similarities,<sup>22</sup> and it has been proposed that JPsA in this age group is simply a variant of early-onset oligoarticular or polyarticular JIA.<sup>150</sup> However, at least under the Vancouver criteria, the proportion of these patients with a recognizable psoriatic diathesis greatly exceeds the 0.5 to 1.0% prevalence of psoriasis in this age group.<sup>11</sup> Further, young patients with JPsA manifest changes such as nail pits and dactylitis that are highly specific for adult psoriatic arthritis, an association noted even before these features were incorporated into the diagnostic criteria.<sup>7,15,154</sup> Therefore, even among younger children, the psoriatic diathesis seems to carry an elevated risk of an arthritis that is phenotypically distinct from other types of JIA. Clarification of the relationship between JPsA and other types of JIA awaits an improved understanding of the biology of these diseases.

**Table 18–3****Joint involvement in Juvenile Psoriatic Arthritis**

Series	Sills	Shore	Southwood	Truckenbrodt	Robertson	Stoll	Flato
Year	1980	1982	1989	1990	1996	2006	2009
Oligoarticular onset		<b>73</b>	<b>94</b>	<b>85</b>	<b>73</b>	<b>84</b>	<b>68</b>
Cervical spine		32	17		25		
TMJ			34		40	7	
Shoulder		23	9	8		3	
Elbow		43	20	15	30	13	33
Wrist	33	62	43	31	43	25	42
Small hand joints	88		60	31	62		61
MCP		53			43		
PIP		40			51		
DIP	63	42			27		
Sacroiliac joint	29		11	17	5	1	0
Hip	33	38	23	21	32	11	23
Knee	67	77	89	67	84	60	87
Ankle		63	63	50	60	51	71
Small foot joints	67		46	25	56		42
Any peripheral small joint	>88	>53	69	>31	>62	57	65

All numbers indicate percentage of patients

The presence of these clinical subgroups helps to explain the longstanding observation that girls with JPsA present at an earlier age than do boys<sup>7,8,15,19</sup> and corroborates data that HLA associations within JPsA depend on the age at onset of disease, as is also true in other subtypes of juvenile arthritis.<sup>87,107</sup>

**Peripheral Arthritis**

Arthritis in JPsA begins as an oligoarthritis in approximately 80% of children (Table 18–3). Initial presentation as monoarthritis is relatively common, and in some patients the disease begins with dactylitis in the absence of other joint involvement.<sup>15</sup> The knee is affected most





**FIGURE 18–4** Sacroiliitis and hip arthritis in juvenile psoriatic arthritis. This radiograph depicts the pelvis and hip joints of a 23-year-old man with psoriasis who developed psoriatic arthritis at age 15. Note sclerosis at the left sacroiliac joint (arrowheads) and loss of joint space with reactive sclerosis at the hips, left greater than right (arrows).

frequently, followed by the ankle; hip arthritis occurs in 20% to 30% (see [Table 18–3](#)). Even in children in whom arthritis remains oligoarticular, wrists, ankles, and small joints of the hands are more frequently affected than in other subtypes of oligoarthritis.<sup>20,24</sup> Without effective therapy, progression from oligoarticular to polyarticular involvement occurs in 60% to 80% of patients.<sup>6,15,19</sup> Polyarticular onset is observed in 20% of cases, although the number of joints involved is often lower than in other forms of childhood-onset polyarthritis, especially seropositive disease. As a result, joints affected by JPsA are often asymmetrically distributed.<sup>6,109</sup> Distal interphalangeal (DIP) involvement was identified in 30% to 50% of patients in early JPsA series<sup>16–18</sup> but is less common (10% to 30%) in patients diagnosed according to more inclusive criteria.<sup>6,19,21</sup> Fortunately, the highly destructive form of adult PsA known as arthritis mutilans is rare in children.

### Axial Arthritis

Unlike most forms of JIA, JPsA is accompanied by an appreciable incidence of sacroiliitis, affecting from 10% to 30% of patients in some studies (see [Table 18–3](#)). Sacroiliitis affects principally patients with older age at onset.<sup>21</sup> These patients exhibit other features reminiscent of the adult spondyloarthropathies, including a balanced gender ratio, a tendency to manifest enthesitis, and an elevated frequency of the HLA-B27 antigen.<sup>21,87</sup> Patients in this older subgroup resemble adults with psoriatic arthritis, in whom definite radiographic sacroiliitis is detected in 30% to 70%.<sup>110–112</sup> Inflammatory disease of the lumbar spine occurs in less than 5% of children with JPsA.<sup>6,19,21</sup> Axial disease in JPsA is generally milder than in ankylosing spondylitis, with a tendency for asymmetric SI joint involvement and a failure to progress to spinal ankylosis ([Figure 18–4](#)).<sup>113</sup>

### Enthesitis

Enthesitis denotes inflammation localized to the insertion of a tendon, ligament, fascia, or joint capsule into bone. Clinically, enthesitis is diagnosed in children with specific tenderness and occasionally swelling at characteristic sites, in the absence of an alternative, explanation (e.g. trauma). Using this standard, enthesitis is prevalent in patients within the older onset subgroup of JPsA, where it was observed in 57%, compared to 22% in younger patients.<sup>21</sup> This finding is in line with adult PsA, where enthesitis is considered a hallmark feature of the disease and can be documented radiographically in at least one site in almost all patients<sup>114–116</sup> (see [Box 18–2](#)). Typical sites of symptomatic enthesitis include the insertion of the Achilles tendon into the calcaneus and the insertions of the plantar fascia; other sites accessible to examination include the poles of the patellae, the iliac crests, the medial femoral condyles, and lateral epicondyles of the elbow.<sup>115,117</sup> Suspected enthesitis can be confirmed by ultrasound or by MRI.<sup>118</sup> Using the ILAR criteria, most children with arthritis and enthesitis are classified as having enthesitis-related arthritis (See [Chapter 17](#)), although patients with enthesitis may still be diagnosed with JPsA if they fulfill appropriate criteria.<sup>5,23</sup>

### Dactylitis

Dactylitis refers to swelling within a digit that extends beyond the borders of the joints. Such swelling is typically uniform, giving the appearance of a “sausage digit,” but can also be fusiform with accentuation around the PIP joint ([Fig. 18–3A and B](#)). Radiographically, tenosynovitis is often the dominant finding, with or without accompanying synovitis in the nearby joints; edema beyond the tendon sheath is common, suggesting the importance of enthesitis in the full phenotype ([Box 18–2](#)).<sup>119–122</sup> Subperiosteal new bone growth can also contribute to the thickness of the digit ([Figure 18–3C](#)). In children with JPsA, dactylitis is observed in 20% to 40% of patients (see [Table 18–2](#)). Commonly, only one or a few digits are affected, most commonly the second toe and index finger.<sup>19</sup> Dactylitis may be symptomatic or asymptomatic, and in one series it was the only musculoskeletal finding at presentation in 12% of children with JPsA.<sup>15</sup> Onset after trauma has been reported, and may explain the predilection for particular digits.<sup>123</sup> The specificity of dactylitis for psoriatic arthritis is incompletely defined. It has been reported in up to 18% of children with non-psoriatic JIA, although some of these children might actually have had JPsA.<sup>6,124,125</sup> Digital swelling also occurs in children with sickle cell disease, tuberculous osteomyelitis, and sarcoid arthropathy, but these are rarely confused with JPsA.

### Extraarticular Manifestations

#### SKIN AND NAIL DISEASE

Overt psoriasis occurs in 40% to 60% of patients with JPsA.<sup>6,24</sup> In the large majority of patients, psoriasis presents as the classic vulgaris form, although guttate psoriasis is also observed.<sup>7,8,14,15,17</sup> Pustular and erythrodermic variants are rare.<sup>8</sup> This pattern approximates the presentation of psoriasis in childhood in general.<sup>9</sup> Psoriasis in children

## BOX 18–2

## Enthesitis: A Unifying Characteristic of Juvenile Psoriatic Arthritis?

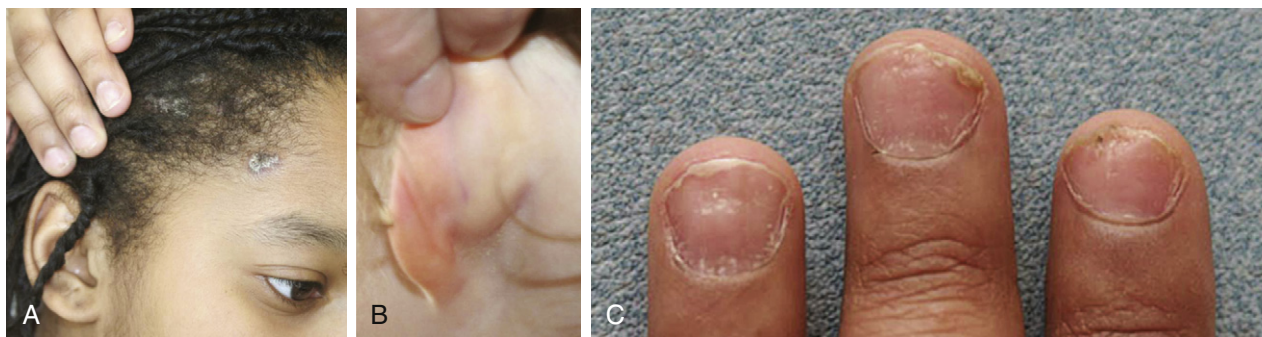
Entheses are subject to substantial mechanical stresses. To dissipate these forces, a number of adaptations have emerged. For example, tendons often become infiltrated with fibrocartilage as they approach the site of insertion into bone, increasing in stiffness in order to limit the concentration of shear stress at the bone/tendon interface. Since the insertion of the joint capsule into bone is itself an enthesis, and tendons and ligaments frequently insert near joints, the synovial lining is usually in intimate contact with entheses.<sup>156</sup>

MRI studies of adults with psoriatic synovitis have identified edema at periarticular entheses.<sup>64</sup> McGonagle and colleagues have proposed that psoriatic arthritis begins at the enthesis and subsequently extends into the joint.<sup>116</sup> Since entheses are frequent sites of microtrauma, this process may be initiated by mechanical injury.<sup>156</sup>

Entheses in the lower extremity are more prone to inflammation, presumably related to mechanical loading, and this may explain the predilection of PsA for joints of the lower extremity (knee, ankle).<sup>115</sup>

Enthesitis also unifies hallmark features of the psoriatic hand. The finger contains a large number of entheses at sites where intrinsic and extrinsic muscles of the hand insert, as well as all along the shaft of the finger where the fibrous tendon sheath is anchored to prevent “bowstringing” with flexion.<sup>155</sup> Ultrasound and MRI have identified inflammation at these entheses in some, but not all, studies.<sup>119–122</sup> Such enthesitis may explain why the “sausage digit” is

rarely observed in RA despite the occurrence of hand tenosynovitis at least as frequently in RA as in PsA.<sup>157</sup> The DIP joint may be particularly susceptible to inflammation originating at entheses, because the joint capsule is largely replaced by ligaments and tendons, residing therefore in unusually close proximity to the synovium.<sup>155</sup> These structures become inflamed in PsA of the DIP.<sup>158</sup> Interestingly, the extensor tendon enthesis extends distally along the DIP to interact with the nail bed. By MRI, thickening of the nailbed is present in almost all adults with PsA; more severe thickening is associated with visible changes in the nails, and these patients are prone to DIP synovitis.<sup>128,159</sup> Indeed, flares at the DIP often coincide with worsening psoriatic nail disease, while psoriasis and arthritis elsewhere are largely uncorrelated.<sup>25</sup> These results suggest that the primary lesion affecting the distal finger is enthesitis, with “spillover” into DIP synovitis when severe. The connection between finger entheses and the nailbed also explains the otherwise puzzling observation that nail changes are much more common in patients with psoriatic arthritis than in those with isolated skin disease (~50% to 80% versus ~10% to 30% in both adults and children)<sup>1,160,161</sup> (see Table 18–2). Taken together, these insights suggest that enthesitis is a distinguishing feature of JPsA not just among older patients, but also among younger children in whom dactylitis and nail changes are common presenting features.<sup>21</sup>



**FIGURE 18–5** Cutaneous manifestations in juvenile psoriatic arthritis. **A**, psoriasis vulgaris on the scalp of a child with polyarticular JPsA. **B**, scaling behind the retracted ear of a 2-year-old girl with knee monoarthritis and a first-degree family history of psoriasis. This rash is suggestive of psoriasis but not diagnostic. **C**, nail dystrophy in JPsA. Findings include multiple nail pits, discoloration, and early onycholysis. This example shows florid changes, but more commonly nail findings are subtle and easily missed.

tends to be subtle, with thin, soft plaques that may come and go.<sup>9,70</sup> Lesions may be isolated to the hairline, umbilicus, behind the ears, or in the intergluteal crease, and thereby escape ready notice (Figures 18–5A and B). Misidentification as eczema is common, and some lesions are in fact ambiguous even to expert examination.<sup>9</sup> There are insufficient data to determine whether psoriasis associated with JPsA differs in age of onset or clinical course from the rest of childhood-onset psoriasis.

One substantial difference between children with JPsA and those with non-arthritic psoriasis is the prevalence of nail changes. Psoriatic changes in the nail surface include pits, onycholysis, horizontal ridging, and discoloration (Figure 18–5C). Nail changes accompany childhood psoriasis in up to 30% of cases.<sup>126,127</sup> By contrast, the prevalence of nail changes in JPsA is approximately 50% to 80%.<sup>8,14,15,21</sup> Nail changes are almost uniformly present in patients with DIP involvement in both adults and children, although nail pits are commonly found in the absence of overt DIP arthritis.<sup>128</sup> In adults, the presence

of nail pits correlates with a more severe arthritis course, but this association is not obvious in children.<sup>129</sup>

### UVEITIS

Chronic uveitis, indistinguishable from that in oligoarticular and polyarticular JIA, occurs in 10% to 15% of children with JPsA (see Table 18–2).<sup>38,130</sup> As in other JIA subsets, young patients with ANA are at highest risk, and standard uveitis screening guidelines apply (see Chapter 20). Acute anterior uveitis can occur in older children, although chronic uveitis is also observed in this subgroup.<sup>8,18,21,23,131</sup> Acute uveitis is associated with the presence of HLA-B27.<sup>132</sup> In one study, the rate of complications of uveitis was higher in JPsA than in other subtypes of juvenile arthritis.<sup>133</sup>

### Other Systemic Manifestations

Children with significant polyarticular JPsA may have the constitutional features of chronic inflammatory disease, including anorexia, anemia, and poor growth.



Histological enteritis and occasionally symptomatic colitis are reported.<sup>134</sup> Fever may rarely occur in very severe cases but should not be ascribed to JPsA without a careful search for alternate causes.<sup>7,25</sup> Amyloidosis is a rare complication of longstanding active disease.<sup>7,16</sup> The SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis) and CRMO (chronic recurrent multifocal osteomyelitis) have been associated with psoriasis and may be related to JPsA.<sup>135</sup> Other rare complications include lymphedema, aortic incompetence, and mitral valve prolapse.<sup>136-138</sup>

## LABORATORY EXAMINATION

Laboratory tests are of limited diagnostic value in JPsA. Inflammatory markers, including ESR and CRP, may exhibit mild to moderate elevation, but are frequently normal.<sup>15,21</sup> Elevation of the platelet count has been noted in younger patients.<sup>21</sup> ANA is found in low or moderate titer in 60% of younger patients and 30% of older patients and is helpful primarily to define uveitis risk for the purpose of ophthalmologic screening.<sup>21</sup> Antibodies against extractable nuclear antigens are usually absent. Rheumatoid factor (RF) is typically absent, and indeed its presence excludes a diagnosis of JPsA under ILAR criteria (see Table 18-1). The presence of psoriasis may be considered incidental in patients with symmetrical polyarthritis who are positive for RF or anticyclical citrullinated peptide antibodies.<sup>25</sup>

## RADIOLOGICAL EXAMINATION

Plain radiographic features of JPsA generally follow a sequence of changes similar to those in other forms of childhood arthritis. In early arthritis, soft tissue swelling around the joint (with or without joint effusion) is the only abnormality. Periarticular osteoporosis may occur within a few months after the onset of joint swelling, and periosteal new bone formation is common in digits affected by dactylitis (see Figure 18-3C). Joint-space narrowing, indicating significant cartilage loss, and erosive disease of bone are usually late features of JPsA (Figure 18-6). Bone remodeling may eventually occur, secondary to persistent periostitis and altered epiphyseal growth, though proliferative new bone formation is less often evident in children than in adults.<sup>65</sup> Sacroiliitis is commonly asymmetric (Figure 18-4).<sup>113</sup> MRI findings in JPsA include synovitis, tendinitis, and bone marrow edema at both articular and nonarticular sites, though the specificity of individual findings for JPsA has not been determined.<sup>65</sup> Both ultrasound and MRI can be used to assess enthesal involvement. In experienced hands ultrasound may be superior.<sup>118</sup>

## TREATMENT

No randomized controlled trials (RCTs) have been conducted in JPsA. Recommendations are therefore extrapolated from trials of therapy in children with polyarticular course JIA,<sup>139-141</sup> from RCTs and clinical practice in adult



**FIGURE 18-6** Radiographic changes in juvenile psoriatic arthritis include soft tissue swelling (dactylitis) of the 4<sup>th</sup> digit, arthritic and secondary degenerative changes of the 4<sup>th</sup> DIP joint, joint space loss at 4<sup>th</sup> and 5<sup>th</sup> PIP joints, multiple erosions of MCP, PIP and DIP joints (solid arrowheads) in the absence of periarticular osteopenia, and fluffy periostitis (open arrowheads).

PsA, and from experience in the treatment of JPsA and other types of JIA.<sup>142</sup> Roles for newer agents, including those that block IL-1, IL-6, and IL-12/23, remain to be defined.

## Peripheral Arthritis

Psoriatic synovitis is potentially destructive of cartilage and bone, and like other types of synovitis may compromise bone growth in the immature skeleton. The goal of therapy is therefore remission, with normalization of physical findings and laboratory markers of inflammation. Efficacy has been demonstrated for nonsteroidal anti-inflammatory drugs (NSAIDs), sulfasalazine, methotrexate, leflunomide, cyclosporine, and the anti-TNF agents.<sup>143</sup> The basic treatment algorithm is similar to that employed in other subtypes of JIA. NSAIDs are often employed initially but typically do not induce remission. Individual large joints can be treated effectively with glucocorticoid injection. In patients with involvement of multiple joints, disease-modifying antirheumatic drugs (DMARDs) such as sulfasalazine or methotrexate are indicated. An inadequate response is addressed by addition of a second DMARD or, increasingly, the addition/substitution of anti-TNF therapy with any of the available agents. TNF blockade is particularly useful when there is axial disease, since no other treatment is effective for inflammation of the spine and sacroiliac joints (see Chapter 17). Anti-TNF agents are also the only medications with demonstrated activity against dactylitis and

enthesitis. Abatacept has not been tested specifically in PsA or JPsA but has been shown to be effective and well tolerated in polyarticular-course JIA.<sup>140</sup>

Several specific considerations apply in the choice of agents for psoriatic disease. Based on anecdote and experience, PsA has been thought to be less responsive to systemic or intraarticular corticosteroids than other types of arthritis. This observation has not been examined rigorously, and both modes of administration are in common use. Substantial doses of systemic corticosteroids can provoke a flare of cutaneous psoriasis when tapered and should be avoided when possible. Similarly, antimalarials can worsen cutaneous psoriasis, although the magnitude of this risk is uncertain.<sup>144,145</sup> In any case, evidence for the efficacy of these agents is limited. Methotrexate has been associated with a higher risk of hepatotoxicity in adults with PsA than in RA.<sup>143</sup> It is not clear that this experience is relevant in JPsA, where methotrexate is typically well tolerated.

## Spondylitis

Treatment of psoriatic spondylitis is based primarily on experience with ankylosing spondylitis.<sup>144</sup> Although axial disease is relatively common in older children and adults with JPsA, it tends to run a milder course. Treatment should be considered in patients who experience axial symptoms or show substantial or progressive limitation of spinal mobility. Continuous treatment with NSAIDs results in measurable radiographic improvement, but the effect is small.<sup>146</sup> Standard DMARDs, including sulfasalazine, methotrexate and leflunomide, are of minimal benefit. Anti-TNF therapy is highly effective for axial disease as assessed both by symptoms and by MRI evidence of inflammation.<sup>144</sup> However, studies in adults have so far failed to show a corresponding reduction in radiographic progression.<sup>66,147</sup>

## COURSE AND PROGNOSIS

The long-term outcome of children with JPsA is incompletely defined. Patients followed at least 15 years demonstrated worse functional outcome than patients with oligoarticular or polyarticular JIA, and 33% still required DMARD therapy.<sup>24</sup> Another study of patients with JPsA followed for at least 5 years demonstrated persistently active disease in 70% and limitations of physical activity in one-third.<sup>19</sup> A more recent study with shorter follow-up documented achievement of clinical remission (on medication) in approximately 60% in both younger and older children, although younger patients required longer to achieve this endpoint.<sup>21</sup> Impaired visual function may also occur, especially if uveitis is not discovered promptly.

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