Recognition and treatment of juvenile-onset spondyloarthritis

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Purpose of review

The purpose of this review is to discuss the classification, diagnosis and management of juvenile-onset spondyloarthritis.

Recent findings

There have been changes in the classification criteria for juvenile-onset spondyloarthritis and magnetic resonance imaging has allowed for earlier detection of disease. Additionally, tumor necrosis factor-α blockers have been shown to be effective in the treatment of ankylosing spondylitis. There is evidence to suggest that early treatment may lead to better response. A high percentage of patients with enthesitis-related arthritis progress to develop ankylosing spondylitis within 10 years after presentation. Patients with juvenile-onset ankylosing spondylitis appear to have poorer functional outcomes.

Summary

Juvenile-onset spondyloarthritis has variable clinical features that may lead to significant impairments. Improved classification criteria exist, but better techniques that are more sensitive are needed to diagnose disease earlier. New therapies appear to improve outcomes, but randomized controlled trials are needed in this population of patients.

Keywords

ankylosing spondylitis, classification, diagnosis, juvenile, spondyloarthritis, therapy

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Abbreviations

AAU	acute anterior uveitis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
DMARD	disease-modifying anti-rheumatic drug
ERA	enthesitis-related arthritis
ESSG	European Spondyloarthropathy Study Group
HLA	human leukocyte antigen
IBD	inflammatory bowel disease
ILAR	International League of Associations for Rheumatology
JIA	juvenile idiopathic arthritis
MRI	magnetic resonance imaging
SEA	seronegative enthesopathy and arthropathy
TNF	tumor necrosis factor

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Introduction

The juvenile-onset spondyloarthritides, like their adult counterparts, are a group of human leukocyte antigen (HLA) B27 associated disorders. Unlike the adult form, in which inflammatory low back pain is the predominant clinical symptom, the juvenile form has peripheral enthesitis and arthritis (predominantly of the lower extremities) as its main clinical features. Factors that relate to the clinical expression of spondyloarthritis include genetic background, race, and ethnicity, age at onset, sex and microorganisms. Classification and diagnosis of the juvenile-onset spondyloarthritides is complex. Patients might initially present meeting criteria for other childhood arthritides. The classification criteria have been revised several times over the past several years. In addition, the diagnosis of juvenile-onset ankylosing spondylitis relies on the same criteria as its adult counterpart. The modified New York criteria require both clinical features and bilateral grade 2 sacroiliitis or unilateral grade 3 or 4 on plain radiographs to meet definitive criteria for ankylosing spondylitis [1]. The inherent difficulty is the low sensitivity of plain film radiography especially early in the disease. Treatment of the disease is based on scarce evidence performed in pediatric populations. Multiple randomized controlled clinical trials have been performed in the adult ankylosing spondylitis population. It is inferred that children with juvenile-onset spondyloarthritis and juvenile-onset ankylosing spondylitis will respond similarly and case–controlled studies support this concept.

Classification

The juvenile-onset spondyloarthritides are a group of diseases that are associated with the HLA-B27 allele and begin at 16 years of age or younger. They are predominately characterized by arthritis and enthesitis. The arthritis is more commonly in the lower limbs and usually asymmetric. Both undifferentiated and differentiated forms are recognized.

They are classified either as the enthesitis-related arthritis (ERA) subgroup of juvenile idiopathic arthritis (JIA) from the International League of Associations for Rheumatology (ILAR) or by the European Spondyloarthropathy Study Group (ESSG) classification criteria as is used in adults (Table 1).

Revisions to the ILAR classification of JIA were made for a second time in 2004 [2]. The revision was performed to better define homogeneous, mutually exclusive

categories of idiopathic childhood arthritis based on clinical and laboratory manifestations that could be used for research purposes. The newer classification criteria define patients as having ERA if they have arthritis or enthesitis in addition to two of the following: the presence of or a history of sacroiliac joint tenderness or inflammatory lumbosacral pain; the presence of HLA-B27 antigen; onset of arthritis in a male patient older than 6 years of age; acute anterior uveitis (AAU); history of ankylosing spondylitis, ERA, sacroiliitis with inflammatory bowel disease (IBD), reactive arthritis, or AAU in a first-degree relative. Exclusions are psoriasis or history of psoriasis in the patient or first-degree relative; the presence of IgM rheumatoid factor on at least two occasions 3 months apart, and the presence of systemic JIA.

The ESSG criteria require inflammatory back pain or synovitis in addition to one of the following: family history, psoriasis, IBD, urethritis, cervicitis, acute diarrhea, alternating buttock pain, enthesopathy, or sacroiliitis. There are no exclusions for the ESSG criteria. They are inclusive of psoriatic arthritis, reactive arthritis and IBD, all of which are excluded by the ILAR classification criteria thereby being more inclusive of other subgroups.

The undifferentiated forms include those patients meeting ESSG or Amor criteria or seronegative enthesopathy and arthropathy (SEA) syndrome. The ESSG and Amor criteria have been validated in juvenile-onset disease [3,4]. It was found that these performed well at distinguishing juvenile spondyloarthritis from other forms of juvenile idiopathic arthritis but did poorly at dividing the undifferentiated spondyloarthritides from the broader group of spondyloarthritis. The ESSG criteria were developed for adults with inflammatory back pain, but inflammatory back pain has low sensitivity in children and the more common manifestation, enthesitis, is only a minor criterion by the ESSG classification system. Because of these difficulties with the classification, Burgos-Vargas *et al.* [5] recommended either deleting the family history of psoriasis as an exclusion criterion or maintaining psoriatic arthritis as an exclusion criterion but then demand HLA-B27 absence and no clinical manifestations of spondyloarthritis. A study was done to assess the adequacy of various classification criteria [6]. The authors compared ESSG, Amor, Garmisch-Partenkirchen, SEA syndrome, and atypical spondyloarthritides classification criteria. They reported that none were sufficient for the classification of juvenile-onset spondyloarthritis and illustrated the need for a new set of criteria with both high specificity and better sensitivity so that earlier disease may be recognized. The most recent classification criteria are those of the ILAR group.

Patients are included in the ILAR classification system with SEA syndrome. This syndrome occurs predominantly in HLA-B27 positive boys in late childhood who present with peripheral arthropathy and enthesopathy with a negative IgM rheumatoid factor and antinuclear antibodies. A portion of patients with SEA syndrome progress to ankylosing spondylitis or related spondyloarthritides.

Differentiated spondyloarthritis includes ankylosing spondylitis, reactive arthritis, arthropathy associated with IBD, and that associated with psoriasis. Psoriatic arthritis, however, is a separate category within the JIA classification scheme, unlike the adult spondyloarthritides. SEA syndrome can progress to ankylosing spondylitis. The pattern of symptoms, however, is very different from the adult form of the disease. The appearance of sacroiliac joint and spinal disease in this form of ankylosing spondylitis usually takes 5–10 years after initial symptom presentation [7,8]. Therefore, a definite diagnosis can take several years leading to a delay in diagnosis. The SEA syndrome may be self-limited, or differentiate to ankylosing tarsitis, psoriatic, reactive arthritis or the IBD-related arthritides [8]. Studies suggest that persistent, severe disease of at least five joints in the first year of disease is a risk factor for progression to ankylosing spondylitis [9]. There appears to be a second subset of patients who develop juvenile- onset ankylosing spondylitis. Burgos-Vargas *et al.* [10] described this cohort in a case–control study in which they noted that in addition to the patients with SEA syndrome who progressed to ankylosing spondylitis, there was a subset of patients who had axial symptoms initially. In addition, they manifested radiographic changes earlier than those with the initial SEA syndrome. These patients appeared more like patients with adult-onset ankylosing spondylitis, and although less common, these patients are more likely to get a diagnosis earlier.

Diagnosis

In order to effectively treat and follow the spondyloarthritides, a confirmatory diagnosis needs to be made. Even in the adult form of the disease, there is a delay of 5–10 years between the first symptoms of the disease and actual diagnosis [11]. This is due, in part, to a low awareness among the non-rheumatologic community. The definitive diagnosis is still made using the modified New York criteria that rely on radiographic findings of sacroiliitis by plain radiography. Radiographic sacroiliitis may be a relatively late finding after the first symptoms appear. It has been argued that a diagnosis should be made in the pre-radiographic stage without the essential radiographic findings, where these may rather be a measure of disease severity or chronicity [12]. Magnetic resonance imaging (MRI) has increased sensitivity for sacroiliitis as compared with plain film radiography. In a prospective study of 185 children, MRI was found to be significantly more sensitive for detecting sacroiliitis than radiography [13]. In addition, there is no radiation exposure. Limitations to this imaging technique include

Table 1 Classification criteria for spondyloarthritides

ILAR classification for JIA sub-category enthesitis-related arthritis[a]	ESSG criteria for spondyloarthritis	Modified Amor criteria for spondyloarthritis
Includes undifferentiated SEA syndrome and differentiated spondyloarthritis except psoriatic arthritis		
Arthritis or enthesitis with at least 2 of the following:	Inflammatory spinal pain or synovitis, asymmetric or predominantly lower limbs and one or more of the following:	Diagnosis of spondyloarthritis if 6 or more points are accrued
The presence of or a history of sacroiliac joint tenderness or inflammatory lumbosacral pain.	Positive family history	Inflammatory back pain (1 point)
The presence of HLA-B27 Antigen	Psoriasis	Unilateral buttock pain (2 points)
Onset of arthritis in a male over 6 years of age	Inflammatory bowel disease	Alternating buttock pain (2 points)
Acute (symptomatic) anterior uveitis (AAU)	Urethritis, cervicitis, or acute diarrhea within one month before arthritis	Enthesitis (2 points)
History of ankylosing spondylitis, enthesitis-related arthritis, sacroiliitis with IBD, Reiter's syndrome, or AAU in a first-degree relative	Buttock pain alternating between right and left gluteal areas	Peripheral arthritis (2 points)
Exclusion criteria	Enthesopathy	Dactylitis (2 points)
Psoriasis or a history of psoriasis in the patient or in a first-degree relative	Sacroiliitis	AAU (2 points)
IgM rheumatoid factor		HLA-B27 positivity of family history of spondyloarthritis (2 points)
Presence of systemic JIA		Good response to nonsteroidal anti-inflammatory drugs (2 points)

ILAR, International League of Associations for Rheumatology; JIA, juvenile idiopathic arthritis; ESSG, European Spondyloarthropathy Study Group; SEA, seronegative enthesopathy and arthropathy; HLA, human leukocyte antigen.
[a] Other sub-categories within JIA include systemic arthritis, oligoarthritis, polyarthritis (RF negative), psoriatic arthritis, undifferentiated arthritis (arthritis that fulfils criteria in no category or in two or more categories).

cost and access. Bollow *et al.* [14] studied 130 children with joint complaint to ascertain the frequency and determinants of sacroiliac joint involvement in spondyloarthritis. They found acute sacroiliitis without chronic changes was only detected by MRI. MRI was also more sensitive in detecting chronic changes. Those subjects with acute sacroiliitis by MRI were also noted to have significantly longer disease duration, higher C-reactive protein and more back pain on a visual analogue scale. In early-onset disease, the delay in diagnosis may be due to all of the above and because only a portion of patients progress on to the differentiated form with axial disease. This progression has a 5–10-year delay to presentation. Differentiating early-onset spondyloarthritis from JIA may be difficult because of the classification criteria and because of the different stages of disease in spondyloarthritis. In the early stages, juvenile-onset spondyloarthritis might actually meet criteria for JIA. This is because early on, there are recurrent bouts of peripheral arthritis and enthesitis with a lack of axial disease. In comparing these two groups of patients it was found that there were certain early clinical characteristics that differentiated the two diseases and supported the diagnosis of early-onset spondyloarthritis within the first year of symptoms. Those included the presence of enthesopathy and tarsal disease in children who have lower, but not upper, extremity arthritis [9]. Prieur *et al.* [3] prospectively assessed 310 consecutive patients for their rheumatic complaint to determine the sensitivity and specificity of different signs of spondyloarthritis. The study found that the sensitivity was 84% and 69.7% and the specificity was 96.1% and 92.2% for the Amor and ESSG criteria respectively.

Clinical manifestations

Peripheral enthesitis and arthritis are the major clinical features in the juvenile-onset spondyloarthritides. In addition to these manifestations some patients will also have involvement of the spinal and sacroiliac joints. The arthritis of early-onset spondyloarthritis is most commonly of the lower extremity. At presentation, there is usually an asymmetric monoarthritis or oligoarthritis. The clinical course of the arthritis is variable. There may be a single episode of monoarthritis that resolves or the development of a symmetric polyarthritis with joint destruction [15••]. AAU is a common extra-articular manifestation that occurs in juvenile-onset spondyloarthritis, but it occurs in less than 27% of patients [16]. Subclinical IBD may occur in juvenile-onset spondyloarthritis like it does in adults. Other manifestations are much less common but may include cardiac involvement (conduction disease, valvular disease) and pulmonary disease [17,18].

Management and treatment

As with all chronic diseases affecting children, spondyloarthritis is best managed by a multidisciplinary team. Care might become challenging in the adolescent years

when compliance can become an issue. The importance of a transitional care program has been demonstrated by Shaw *et al.* [19] in a cohort of patients with JIA. The basis for the treatment of spondyloarthritis stems from expert guidelines and evidence-based medicine. The expert guidelines come from the ASAS (Assessment in Ankylosing Spondylitis International Working group) consensus statement and the subsequent update [20••,21]. These guidelines, however, refer specifically to patients with a definitive diagnosis of ankylosing spondylitis, and do not make definitive statements on the wider spondyloarthritis category. In addition, these are not specific to the pediatric population. To date, there is no consensus statement for the pediatric groups. The updated guidelines focus on the use of anti-tumor necrosis factor (TNF)-α agents in patients with ankylosing spondylitis. The recommendations are the following: a definitive diagnosis of ankylosing spondylitis should be made; sustained disease activity for ≥4 weeks with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 on a scale of 0–10; failure of at least two nonsteroidal anti-inflammatory drugs (NSAIDs) during a 3-month period, and failure of intra-articular steroids and sulfasalazine if peripheral features predominate. In addition, it is recommended that monitoring while on anti-TNF-α therapy should include the following: the BASDAI and expert opinion. If patients are non-responders, change in or cessation of therapy should be considered at 6–12 weeks. Response was defined as improvement by 50% or 2 points (on a scale of 0–10) for the BASDAI and an expert opinion of continuing therapy.

Unlike adult subjects with spondyloarthritis, the juvenile cohort has a greater amount of peripheral enthesopathy. This enthesopathy is usually refractory to traditional disease-modifying anti-rheumatic drugs (DMARDs).

In an open-label pilot study, 10 subjects with juvenile spondyloarthritis (meeting the criteria for ERA) were studied with anti-TNF-α therapy (either etanercept or infliximab) after failing NSAIDs and DMARDs. All participants demonstrated improvement as evidenced by a reduction in their active joint count, tender entheseal count, markers of inflammation, C-HAQ scores, and concomitant anti-rheumatic medications. The response was sustained in all subjects at 1 year [22•]. Another study [23] examined the long-term efficacy of etanercept in treating patients with ERA refractory to DMARDs. This was an open-label trial in eight subjects. Within 2 months, there was significant improvement in active joint count, hemoglobin, and erythrocyte sedimentation rate. These results were sustained through the 2 years of the trial. In the adult studies, patients who are younger in age with shorter disease duration appear to respond better to anti-TNF-α therapy [24].

Prognosis and outcomes

Unfortunately, there are few data on the prognosis of juvenile spondyloarthritis especially in the era of biologic agents. With respect to the undifferentiated spondyloarthritis (or SEA syndrome) 50–75% of patients progress to juvenile-onset ankylosing spondylitis by 5–11 years after initial presentation [25,26]. Rudwaleit *et al.* [24] found that pain, both axial and at peripheral sites, was the most common symptom in juvenile spondyloarthritis. They reported that it was also closely related to disease activity. Interestingly, pain at peripheral sites increased with physical activity compared with lumbar pain that increased with rest. In another study, female participants with juvenile ankylosing spondylitis were found to have higher Childhood Health Assessment Questionnaire scores than those with other arthritis subtypes after 7 years [27]. Hip joint involvement appears to be closely related to poorer prognosis [28]. A Norwegian study [29] prospectively looked at predictors of disability in patients with juvenile rheumatoid arthritis and juvenile spondyloarthritis compared with healthy controls. Although health status and disease activity improved over time, patients with a diagnosis of SEA syndrome, juvenile ankylosing spondylitis, and rheumatoid factor-positive polyarthritis had poorer health than the other subtypes. Of note, in this study only seven of 197 subjects had spondyloarthritis. In a prior Norwegian study, Flato *et al.* [30] found that about 40% of children with juvenile spondyloarthritis develop functional disability after 10–15 years. Recently, a cross-sectional study compared functional outcomes in juvenile-onset ankylosing spondylitis patients ($n = 326$) with adult-onset patients ($n = 2021$). A postal survey identifying clinical features, demographics and functional outcomes as assessed by Bath Ankylosing Spondylitis Functional Index was used. The study found that, in addition to a significantly increased delay to diagnosis in the early-onset cohort, the early-onset ankylosing spondylitis participants also had significantly worse functional outcomes [31].

Conclusion

Improved classification criteria specific to juvenile-onset spondyloarthritis are needed to help more accurately determine what disease a patient has and therefore target treatments appropriately. We have sensitive tools to diagnose disease by imaging, but these tools are expensive and not necessarily helpful in the early stages of disease. It is not, however, part of the diagnostic criteria at this point. As we continue to learn more about the genetics and pathophysiology of this disease, we will have a better understanding of its relation to and distinction from the adult forms. With new and improving therapies, we continue to change the course of spondyloarthritis.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 569).

1 Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis A proposal for modification of the New York criteria. Arthritis Rheum 1984; 27:361–368.

2 Petty RE, Southwood TR, Manners P, *et al.* International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol 2004; 31:390–392.

3 Prieur AM, Listrat V, Dougados M. Evaluation of the ESSG and the Amor criteria for juvenile spondyloarthropathies (JSA): study of 310 consecutive children referred to one pediatric rheumatology center. Arthritis Rheum 1990; 33:D195.

4 Prieur AM, Listrat V, Dougados M, *et al.* Criteria for classification of spondyloarthropathies in children. Arch Fr Pediatr 1993; 50:379–385.

5 Burgos-Vargas R, Rudwaleit M, Sieper J. The place of juvenile onset spondyloarthropathies in the Durban 1997 ILAR classification criteria of juvenile idiopathic arthritis International League of Associations for Rheumatology. J Rheumatol 2002; 29:869–874.

6 Kasapcopour O, Demirli N, Arisoy N, *et al.* Evaluation of classification criteria for juvenile-onset spondyloarthropathies. Rheumatol Int 2005; 25:414–418.

7 Burgos-Vargas R, Clark P. Axial involvement in the seronegative enthesopathy and arthropathy syndrome and its progression to Ankylosing Spondylitis. J Rheumatol 1989; 16:192–197.

8 Tse S, Laxer R. Juvenile spondyloarthropathy. Curr Opin Rheumatol 2003; 15:374–379.

9 Burgos-Vargas R, Vazquez-Mellado J. The early clinical recognition of juvenile-onset Ankylosing Spondylitis and its clinical differentiation from juvenile rheumatoid arthritis. Arthritis Rheum 1995; 38:835–844.

10 Burgos-Vargas R, Vazquez-Mellado J, Cassis N, *et al.* Genuine ankylosing spondylitis in children: a case-control study of patients with early definite disease according to adult onset criteria. J Rheumatol 1996; 23:2140–2147.

11 Feldtkeller E, Khan MA, van der Heijde D, *et al.* Age at disease onset and diagnosis delay in HLA-B27 negative vs positive patients with Ankylosing Spondylitis. Rheumatol Int 2003; 23:61–66.

12 Rudwaleit M, Khan MA, Sieper J. The challenge of diagnosis and classification in early Ankylosing Spondylitis: do we need new criteria? Arthritis Rheum 2005; 52:1000–1008.

13 Bollow M, Braun J, Hamm B, *et al.* Use of contrast-enhanced MR imaging to detect sacroiliitis in children. Skeletal Radiol 1998; 27:606–616.

14 Bollow M, Biedermann T, Braun J, *et al.* Use of dynamic magnetic resonance imaging to detect sacroiliitis in HLA B-27 positive and negative children with juvenile arthritides. J Rheumatol 1998; 25:556–564.

15 •• Weisman M, Reveille M, van der Heijde D. Ankylosing spondylitis and the spondyloarthropathies. In: Burgos-Vargas R, editor. A companion to rheumatology, 3rd ed. Mosby: St Louis; 2006. pp. 94–106.

This is an outstanding book chapter review on juvenile-onset spondyloarthritis.

16 Burgos-Vargas R, Pacheco-Tena C, Vazquez-Mellado J. The juvenile-onset spondyloarthritides: rationale for clinical evaluation. Best Pract Res Clin Rheumatol 2002; 16:551–572.

17 Huppertz H, Voight I, Muller-Scholden J, *et al.* Cardiac manifestations in patients with HLA B-27-associated juvenile arthritis. Pediatr Cardiol 2000; 21:141–147.

18 Camiciottoli G, Trapani S, Ermini M, *et al.* Pulmonary function in children affected by juvenile spondyloarthropathy. J Rheumatol 1999; 26:1382–1386.

19 Shaw KL, Southwood TR, McDonagh JE. British Society of Pediatric and Adolescent Rheumatology. Growing up and moving on in rheumatology: a multicenter cohort of adolescents with juvenile idiopathic arthritis. Rheumatology (Oxford) 2005; 44:806–812.

20 •• Zochling J, van der Heijde D, Braun J, *et al.* ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis 2006; 65:442–452.

This is the most recent consensus statement based on evidence and expert guidelines for the management of ankylosing spondylitis in adult patients. There is no current statement for pediatric patients.

21 Braun J, Davis J, Dougados M, *et al.* For the ASAS working group. First update of the international ASAS consensus statement for the use of anti-TNF agents in patients with Ankylosing Spondylitis. Ann Rheum Dis 2006; 65:316–320.

22 • Tse SM, Burgos-Vargas R, Laxer RM. Anti-tumor necrosis factor-α blockade in the treatment of juvenile spondyloarthropathy. Arthritis Rheum 2005; 52:2103–2108.

This was one of the few studies in the literature assessing the efficacy of anti TNF-α blockade for the treatment of juvenile-onset spondyloarthritis. This was an open-label pilot cohort study.

23 Henrickson M, Reiff A. Prolonged efficacy of Etanercept in refractory enthesitis-related arthritis. J Rheumatol 2004; 31:2055–2061.

24 Rudwaleit M, Listing J, Brandt J, *et al.* Prediction of a major clinical response (BASDAI 50) to tumor necrosis alpha blockers in ankylosing spondylitis. Ann Rheum Dis 2004; 63:665–670.

25 Cabral DA, Oen KG, Petty RE. SEA syndrome revisited: a long-term follow-up of children with a syndrome of seronegative enthesopathy and arthropathy. J Rheumatol 1992; 19:1282–1285.

26 Burgos-Vargas R, Clark P. Axial involvement in the seronegative enthesopathy and arthropathy syndrome and its progression to ankylosing spondylitis. J Rheumatol 1989; 16:192–197.

27 Gare BA, Fasth A. The natural history of juvenile chronic arthritis: a population based cohort study II Outcome. J Rheumatol 1995; 22:308–319.

28 Garcia-Morteo O, Maldonado-Cocco JA, Suarez-Almador ME, Garay E. Ankylosing spondylitis of juvenile onset: comparison with adult onset disease. Scand J Rheumatol 1983; 12:246–248.

29 Selvaag AM, Lien G, Sorskaar D, *et al.* Early disease course predictors of disability in juvenile rheumatoid arthritis and juvenile spondyloarthropathy: a 3 year prospective study. J Rheumatol 2005; 32:1122–1130.

30 Flato B, Aasland A, Vinje O, Forre O. Outcome and predictive factors in juvenile rheumatoid arthritis and juvenile spondyloarthropathy. J Rheumatol 1998; 25:366–375.

31 Stone M, Warren RW, Bruckel J, *et al.* Juvenile-onset ankylosing spondylitis is associated with worse functional outcomes than adult-onset ankylosing spondylitis. Arthritis Rheum 2005; 53:445–451.