Enthesalgia in Childhood: Site-Specific Tenderness in Healthy Subjects and in Patients with Seronegative Enthesopathic Arthropathy

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ABSTRACT. ***Objective.*** The presence of pain over an enthesis defines enthesitis and is a major (or sole) clinical feature of childhood spondyloarthropathies. However, the presence or degree of tenderness of the entheses in healthy children is unknown. We studied the prevalence of enthesalgia and pain thresholds over entheses in healthy children and whether these sites are different from those in patients diagnosed with seronegative enthesopathic arthropathy (SEA syndrome).

Methods. We examined 234 schoolchildren aged 8 to 16 years for enthesalgia; those reporting tenderness were compared to randomly selected patients with SEA syndrome previously diagnosed in a tertiary outpatient clinic.

Results. Enthesalgia in at least one site was found in 68 children (29%). Schoolchildren had fewer sites than patients (mean 1.2 ± 2.8 sites vs 8.1 ± 4.5 sites; $p < 0.0001$). Enthesalgia was not associated with age, sex, or self-reported activity level. In schoolchildren, pressure thresholds were higher with age ($p < 0.0001$), and in boys ($p = 0.014$), and were decreased in those with enthesalgia ($p = 0.003$). The metatarsal heads had the lowest pain thresholds. Significant sites specific for SEA patients were: plantar fascial insertion ($p < 0.0001$), Achilles tendon insertion ($p = 0.001$), sacroiliac joint ($p = 0.002$), and inferior pole of the patella ($p = 0.003$). Of these 8 sites, only 10% of schoolchildren reported tenderness in 3 sites compared to 56% of children with SEA syndrome.

Conclusion. Enthesalgia is not rare in children; metatarsalgia or a limited number of tender entheses should not define enthesitis. Enthesalgia in 3 of the 8 specific tender entheses noted above may better define childhood enthesitis. (J Rheumatol 2003;30:1335–40)

Key Indexing Terms:

CHILD ARTHRITIS JUVENILE RHEUMATOID ARTHRITIS
TERMINOLOGY PREVALENCE SPONDYLOARTHROPATHY

Enthesalgia, pain at an enthesis, is a prominent symptom and sign of the seronegative spondyloarthropathies (SpA) in children, many of whom do not have the typical radiographic evidence of sacroiliitis and limited back mobility signs of ankylosing spondylitis (AS)[1-3]. Some children will present with enthesalgia without chronic arthritis[2-7]. Enthesitis defines one of the forms of juvenile idiopathic arthritis (JIA)[8], which has been adopted by the World Health Organization, and is proposed to define SpA[9]. Therefore the diagnosis rests on finding tenderness at these tendon and ligament insertions. This tenderness is presumed to represent enthesitis, that is, inflammation of the entheses.

There have been enthesopathic indexes described to quantify enthesitis, but these are not in frequent use[10]. There are no data regarding tenderness at entheses in healthy children. One study of 18 children with Osgood-Schlatter syndrome revealed 6 children with enthesalgia at sites other than the tibial tuberosity[11], and enthesalgia has been reported in up to 9% of children with polyarticular juvenile rheumatoid arthritis (RA)[2] and 11% of adults with RA[12]. We studied the prevalence of tender entheses in schoolchildren and pain thresholds at each enthesis site and at control sites. Both the specific site and number of enthesalgic sites in the schoolchildren were compared with a randomly selected group of children who had been referred to a tertiary pediatric rheumatology clinic and diagnosed with enthesitis.

MATERIALS AND METHODS

After informed consent was obtained, 234 schoolchildren, aged from 8 to 16 years, from local private and public schools were examined for the presence of enthesalgia at selected entheses and pain thresholds at the selected entheses were determined. Children were excluded if, by parental report, they had ever had arthritis, had sought care for foot or back pain, had had surgery on the foot or leg, or had a family history of AS. Family history of psoriasis or inflammatory bowel disease was not obtained. Enthesalgia was defined as present when the subject reported pain when approximately 3 to 4 kg of pressure was digitally applied by a single observer (DDS) over an enthesis. Each child was asked to report pain during the examination rather than wait for a spontaneous report. This was done prior to pain threshold measurements. The examiner repeatedly tested himself by blindly pushing on the pressure gauge to confirm that between 3 and 4 kg of pressure was applied.

Pain thresholds were established when pain was reported by the subject

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when pressure was applied to control sites and entheses using a pressure gauge with a 1 cm^2 rubber tip (3M, Boston, MA, USA) and increasing the pressure by about 1 kg/s up to a maximum of 11 kg. The following entheses were studied: plantar fascia insertion on all metatarsal heads, plantar fascia insertion on the calcaneus, Achilles tendon insertion, tibial tuberosity, inferior pole of the patella, greater trochanter, and the lower sacroiliac (SI) joint (at the inferior insertion of the dorsal iliosacral ligament). Control points included thumbnail of the non-dominant hand, superior posterior iliac spine, mid-tibia, calcaneus, and proximal great toe phalange.

Activity level was by self-report with the following descriptors: not active (no physical education, mostly indoors), a little active (indoors a lot), regular activity (physical education, or occasional sports), pretty active (plays sports pretty often; outdoors a lot), very active (always in sports or dancing). Activity level was verbally confirmed at the time of examination.

At the time of the study, 160 patients diagnosed with seronegative enthesopathic arthropathy (SEA) syndrome[2] were being followed in the pediatric rheumatology clinic. All had enthesalgia, defined as self-reported tenderness over the entheses noted above with digital palpation of between 3 and 4 kg by the same observer (DDS). Digital control points including mid-tibia and proximal great toe phalange were negative in all SEA syndrome patients. Once 68 schoolchildren with enthesalgia were identified, 68 of these 160 patients with SEA syndrome were randomly selected using a random number table. To limit bias, retrospective data regarding the number and location of enthesalgic sites were obtained from the charts from the patient's initial evaluation and compared to that obtained on the schoolchildren.

Statistical analyses. Means for continuous variables were compared between subgroups by independent t tests. Ordinal variables were analyzed by Mann-Whitney rank-sum tests and nominal data by Pearson's chi-square. Paired t tests were used to compare pressure thresholds from site to site within individuals. Testing for association between 2 continuous variables was done using Pearson correlation coefficient. All tests were 2-sided. Significance was defined as $p < 0.05$. Our institutional review board approved this study.

RESULTS

Sixty-eight (29%) of the 234 schoolchildren reported at least one enthesis to be tender to digital palpation, the total number of tender entheses was 292; the mean number of sites was 1.2 ± 2.8 per child, n = 234 (Table 1). The presence of enthesalgia was not associated with age ($p = 0.773$, independent t test) or sex ($p = 0.205$, chi-square).

By far the most common site was the metatarsal heads (Table 2); however, pressure thresholds data for the entheses and control sites (Table 1) show that the metatarsal heads have a lower pain threshold than most control sites, especially the second and third metatarsal heads, which are typically compared to either the mid-tibia or proximal phalange of the great toe. For example, the mean pain threshold of the third metatarsal head was significantly lower than the proximal great toe phalange, $p < 0.0001$, paired t test (Table 1). In schoolchildren, mean pressure thresholds in all sites combined were higher with age ($p < 0.0001$, Pearson's correlation) and for boys relative to girls ($p = 0.014$, independent t test).

We compared the mean pain thresholds of the schoolchildren with and without enthesalgia. The mean pain thresholds of both the entheses and control sites were lower in those reporting enthesalgia ($p = 0.001$ and $p = 0.008$, respectively, independent T test; Table 1). However, non-dominant thumbnail pain thresholds were almost identical between the groups.

The schoolchildren reported a high level of activity (Table 1); greater than regular activity was reported by 72%. The level of activity reported was not associated with enthesalgia ($p = 0.285$, Mann-Whitney rank-sum).

The 68 children who reported enthesalgia led us to ask just how many tender entheses constitute an abnormal number and if any specific site was more predictive of SEA syndrome. The number of sites for the schoolchildren and the patients with SEA is shown in Figure 1. The frequency of tenderness at each site is shown in Table 2. Figure 1 would indicate somewhere between 4 and 7 sites differentiate schoolchildren and children with SEA syndrome. The percentage of schoolchildren diagnosed with SEA syndrome reclassified if the number of sites is prescribed and the percentage of children defined as having enthesitis is shown in Table 3. Again, the cutoff appears to fall between 4 to 7 sites.

Since the presence of enthesalgia was not rare, we compared those with enthesalgia to an equal number of children diagnosed with SEA syndrome (Table 4). There was no difference in the age or sex of the 2 groups.

The children presenting to the pediatric rheumatology clinic and diagnosed with SEA syndrome were more likely to have more enthesalgic sites. Metatarsalgia was relatively common and there was little difference between the groups in tibial tuberosity and greater trochanter tenderness. Figure 2 shows the number of tender entheses after eliminating these 3 sites. This graph would indicate that 3 to 4 sites differentiate the schoolchildren from our patients with SEA syndrome. Using these 8 sites, the percentage of children diagnosed with SEA syndrome reclassified if the number of sites is prescribed; the percentage of schoolchildren defined as having enthesitis is shown in Table 5. Again, the cutoff appears to fall between 3 and 4 sites, with perhaps 3 the best cutoff number.

In the entire population of 234 schoolchildren, the mean number of these 8 sites that were tender was 0.2 ± 0.7. The mean number of tender sites in schoolchildren reporting enthesalgia was 1.1 ± 1.4, and in children with SEA syndrome, 2.1 ± 1.9.

DISCUSSION

Establishing a diagnosis of enthesitis is important both for determining treatment and patient education. The vast majority of these children have postactivity limb pain and, perhaps, low back pain that is unrecognized as inflammatory[2,3,13]. Frequently these children are presumed to have post-traumatic musculoskeletal pain, growing pains, or psychogenetic pain and therefore are not treated appropriately. Most children with SEA syndrome or enthesopathic JIA will benefit from nonsteroidal antiinflammatory medication[14].

Table 1. Subject characteristics and pressure thresholds (kg/cm^2 ± 1 SD)* for control sites and entheses in 234 schoolchildren and those reporting and not reporting at least one tender enthesis.

	All Subjects, n = 234	Subjects Reporting Enthesalgia, n = 68	Subjects Not Reporting Enthesalgia, n = 166
Mean age, yrs	11.8 ± 2.2	11.9 ± 2.2	11.8 ± 2.2
Sex: girls:boys (% girls)	140:94 (60)	45:23 (66)	95:71 (57)
Activity level**	4.1 ± 0.8	4.2 ± 0.8	4.0 ± 0.8
No. of tender entheses	1.2 ± 2.8	4.3 ± 3.8	0
Control sites			
Non-dominant thumbnail	3.6 ± 1.7	3.5 ± 1.8	3.6 ± 1.7
Posterior-superior iliac spine	5.1 ± 2.5	4.2 ± 1.9	5.4 ± 2.7
Mid-tibia	4.0 ± 1.7	3.6 ± 1.4	4.2 ± 1.8
Calcaneus, plantar surface	5.9 ± 2.6	5.3 ± 2.2	6.1 ± 2.7
Proximal great toe phalange	4.5 ± 2.1	3.9 ± 1.6	4.7 ± 2.3
Mean of all control sites	4.6 ± 2.0	4.1 ± 1.5	4.8 ± 2.1
Entheses tested			
Metatarsal			
First	4.0 ± 1.9	3.3 ± 1.2	4.3 ± 2.1
Second	3.9 ± 1.8	3.2 ± 1.1	4.1 ± 2.0
Third	3.8 ± 1.8	3.1 ± 1.1	4.0 ± 2.0
Fourth	4.0 ± 1.9	3.4 ± 1.3	4.3 ± 2.1
Fifth	4.4 ± 2.0	3.8 ± 1.4	4.7 ± 2.1
Plantar fascia on calcaneus	5.2 ± 2.4	4.6 ± 1.9	5.4 ± 2.5
Achilles tendon	6.2 ± 2.7	5.4 ± 2.3	6.5 ± 2.8
Tibial tuberosity	5.6 ± 2.7	4.9 ± 2.3	5.8 ± 2.8
Patella, inferior pole	4.4 ± 2.3	3.6 ± 1.8	4.7 ± 2.4
Greater trochanter	4.5 ± 2.3	3.9 ± 1.8	4.8 ± 2.5
Sacroiliac, lower third	5.5 ± 2.7	4.7 ± 2.3	5.8 ± 2.8
Mean of all entheses	4.7 ± 2.0	4.0 ± 1.4	5.0 ± 2.2

* Results mean of both right and left sides. ** Activity level: 1 = not active; 2 = a little active; 3 = regular activity; 4 = pretty active; 5 = very active (see text).

Enthesalgia is generally interpreted as representing enthesitis and is an important sign in the diagnosis of children with SEA syndrome. However, we found significant enthesalgia in schoolchildren, especially metatarsalgia. This may be due, in part, to the amount of digital pressure applied during the examination, since the plantar fascial insertion on the metatarsal heads has a lower pain threshold than control sites. The pressure one applies to entheses to establish the presence of enthesalgia has not previously been studied. We tend to apply between 3 and 4 kg of pressure digitally when checking for enthesalgia, and thus some of the children classified as having enthesitis may not be significantly different from schoolchildren. Metatarsal enthesalgia has to be differentiated from arthritis; this may be difficult, but enthesalgia is usually posterior to the joint and only on the plantar surface.

Enthesalgia in schoolchildren, as it turns out, is not uncommon, with 29% of children reporting at least one tender enthesis. Widespread enthesalgia was uncommon, especially in the limited sites of the plantar fascia insertion at the calcaneus, the Achilles tendon insertion, the inferior pole of the patella, and the SI joints. These sites may be more selective of SEA syndrome than using the metatarsal heads, tibial tuberosity, and greater trochanter. Although the SI joint tenderness may represent arthritis and not just a manifestation of enthesitis, it has not been studied in children presenting with SEA syndrome or in normal children[15,16]. It seems that tenderness at 3 of the 8 selected entheses should be used to define SEA syndrome or enthesopathic JIA. The frequency with which we observed metatarsalgia may reflect that the metatarsal heads have low pain thresholds. This data would caution against defining the enthesitis of SEA syndrome or enthesopathic JIA solely on the basis of metatarsal head tenderness.

On a practical side, reclassifying our population of children with SEA syndrome as Table 5 suggests using 3 or more specific sites means only 56% would be classified as having enthesitis. Therapeutically, all the children would still be treated for metatarsalgia or other painful entheses as symptoms warrant; however, 44% would not be included as having SEA syndrome. This may be helpful if the latter group does not go on to develop a spondyloarthropathy. The longterm outcome of the children with SEA syndrome in our study is not known. It would be useful to know if they develop enthesalgia at multiple sites, limited range of motion of the lower spine or chest, inflammatory bowel disease, or other identifiable features of SpA. This, however, will take longterm followup. The 56% who would be classi-

Table 2. The frequency of tender entheses by site in 234 schoolchildren and in 68 children with seronegative enthesopathic arthropathy (SEA) syndrome.

Site	No. Reported as Tender	
	Schoolchildren, n = 234 (%)	SEA Syndrome Patients, n = 68 (%)
Metatarsal head		
1st right	23 (9.8)	23 (33.8)
1st left	13 (5.6)	18 (26.5)
2nd right	21 (9.0)	38 (55.9)
2nd left	20 (8.5)	39 (57.4)
3rd right	23 (9.8)	42 (61.8)
3rd left	29 (12.4)	43 (63.2)
4th right	18 (7.7)	36 (52.9)
4th left	26 (11.1)	40 (58.8)
5th right	9 (3.8)	15 (22.1)
5th left	17 (7.3)	21 (30.9)
Plantar fascial insertion on the calcaneus		
Right	12 (5.1)	34 (50.0)
Left	7 (3.0)	40 (58.9)
Achilles tendon insertion on the calcaneus		
Right	2 (0.8)	14 (20.6)
Left	1 (0.4)	14 (20.6)
Tibial tuberosity		
Right	3 (1.3)	5 (7.4)
Left	4 (1.7)	4 (5.9)
Inferior pole of the patella		
Right	13 (5.6)	23 (33.8)
Left	16 (6.8)	28 (41.2)
Greater trochanter		
Right	3 (1.3)	10 (14.7)
Left	4 (1.7)	8 (11.8)
SI joint, lower third		
Right	12 (5.1)	27 (39.7)
Left	14 (6.0)	31 (45.6)

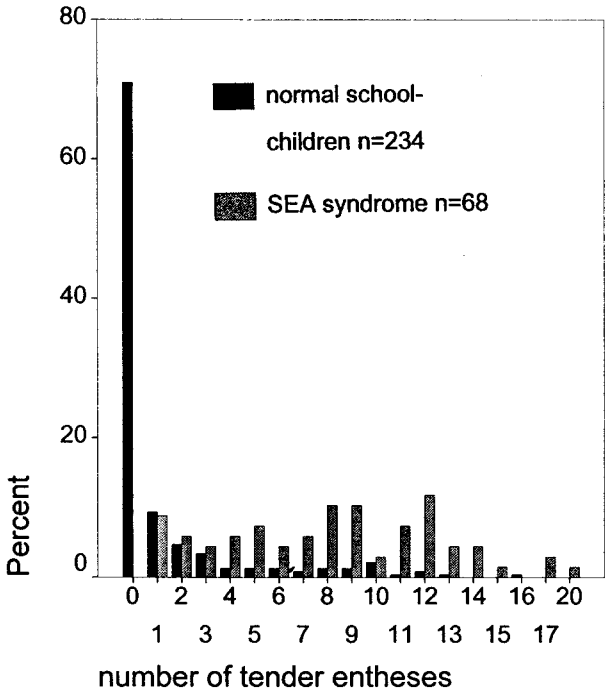


Figure 1. Number of tender entheses in schoolchildren and in children with seronegative enthesopathic arthropathy (SEA) syndrome.

fied as having enthesitis may better define a more uniform group of patients and thereby increase our prognostic accuracy.

There is currently no gold standard to accurately calculate sensitivity and specificity of enthesalgia at each enthesis since early SpA is a clinical diagnosis and the presence of enthesalgia at any site is a criterion. This might be explored by prospectively examining over time the entheses of children of patients with AS who are HLA-B27 positive. There may be a difference in children who do and those who do not have the HLA-B27 gene or in those who eventually develop AS[17,18].

We did not take into account the presence of HLA-B27 as part of SEA syndrome in the group of children with enthesalgia, since most of these children were untested. Therefore whether or not having the HLA-B27 gene predisposes to more enthesalgic sites is unknown. One would expect about 8% of the schoolchildren to be HLA-B27 positive given the population demographics of the Pacific Northwest. Similarly, we did not perform pressure threshold studies on the children with enthesalgia of SEA syndrome, so it is unknown if those presenting to a tertiary clinic have lower pressure thresholds, that is, are more tender. However, we have many children with SEA syndrome who have exquisitely tender entheses.

Although a limitation of our study design, we analyzed enthesalgia data retrospectively obtained on all children with SEA syndrome actively being followed in the clinic, because of the subjective nature of enthesalgia. All entheses are specifically examined at each visit. We used the first clinic examination, since that is when the physician is confronted with establishing a diagnosis. However, children presenting to our clinic with musculoskeletal pain may have a tendency to have enthesitis overdiagnosed or tenderness overreported. Pressure measurements may help limit this bias.

In summary, these data suggest that the presence of enthesalgia may be seen in one-third of schoolchildren and that pathologic enthesalgia involves multiple and specific sites. In order to be classified as SEA syndrome or enthesopathic JIA, enthesitis might better be defined as the presence of tenderness in 3 or more entheses, limited to the plantar fascia insertion at the calcaneus, the Achilles tendon insertion, the inferior pole of the patella, or the SI joints. Metatarsalgia is common and should not, in itself, be used to establish the enthesitis of SEA syndrome or enthesopathic JIA. Criteria for various forms of SpA or JIA should clearly

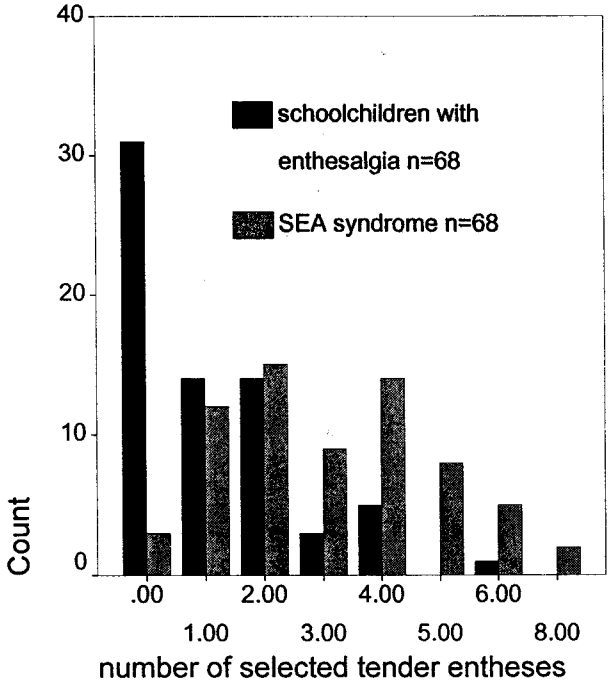
Table 3. Percentage of children diagnosed with SEA syndrome who would still be diagnosed as having enthesitis, and the percentage of schoolchildren defined as having enthesitis, if one requires a particular number of tender entheses to define enthesitis.

No. of Tender Entheses To Define Enthesitis	Percentage of the 68 Children with SEA Syndrome Still Classified As Having Enthesitis	Percentage of Schoolchildren Defined As Having Enthesitis	
		All 234	The 68 with Enthesalgia
1	100	29	100
2	91	20	68
3	85	15	51
4	81	12	40
5	75	10	35
6	68	9	31
7	63	8	26
8	57	7	22
9	47	5	18
10	37	4	10

Table 4. Characteristics of 68 schoolchildren who reported at least one tender enthesis and 68 randomly selected patients with SEA syndrome.

	Schoolchildren with Enthesalgia	Patients with SEA Syndrome	Significance*
Mean age, yrs	12.0 ± 2.2	12.5 ± 2.8	0.197**
Sex:girls:boys (% girls)	44:24 (65)	42:26 (62)	0.722
No. of sites with enthesalgia	4.3 ± 3.8	8.1 ± 4.5	< 0.0001**
No. of individuals with tenderness, at each enthesis***			
Metatarsal	50	51	0.844
Plantar fascia on calcaneus	13	46	< 0.0001
Achilles tendon	3	17	0.001
Tibial tuberosity	6	7	0.771
Patella, inferior pole	18	33	0.008
Greater trochanter	4	11	0.055
SI joint, lower third	16	33	0.002

* By Pearson chi-square except where noted otherwise; ** analysis by independent t test. *** Combining metatarsal heads and right and left sites.



define enthesitis by site, number of sites, pressure thresholds, and other variables as compared to healthy age matched control subjects.

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Figure 2. Number of selected tender entheses in schoolchildren with enthesalgia and children with seronegative enthesopathic arthropathy (SEA) syndrome. Selected entheses include the plantar fascial insertion on the calcaneus, Achilles tendon insertion on the calcaneus, inferior pole of the patella, and the sacroiliac joint.

Table 5. Considering only the 8 selected sites*, the percentage of children diagnosed with SEA syndrome who would still be diagnosed as having enthesitis, and the percentage of schoolchildren defined as having enthesitis, if one requires a particular number of tender entheses to define enthesitis.

No. of Tender Entheses To Define Enthesitis	Percentage of the 68 Children with SEA Syndrome Still Classified As Having Enthesitis	Percentage of Schoolchildren Defined As Having Enthesitis	
		All 234	The 68 with Enthesalgia
1	96	16	54
2	78	10	34
3	56	4	13
4	43	2	9
5	23	1	1

* Selected entheses include the plantar fascia on the calcaneus, Achilles tendon insertion, inferior pole of the patella, and the SI joint.

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