# Pediatric Complex Regional Pain Syndrome

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**Abstract:** Complex regional pain syndrome (CRPS) is a relatively new diagnostic entity in pediatrics. There is debate as to what constitutes the most effective treatment for pediatric CRPS. This study presents the patient characteristics, clinical course, and treatment outcome of 20 children diagnosed with CRPS at a major children's hospital during a 4-year period. The results showed that pediatric CRPS occurs predominantly in girls (90%) in later childhood and adolescence (mean age, 11.8 [range, 8–16 years]). It affects mainly the lower limbs (85%), with a predilection for the foot (75% of all cases), and was frequently initiated by minor trauma (80%). In many cases, there was a lengthy time to diagnosis (mean, 13.6 weeks) that delayed the institution of treatment, which consisted of intensive physiotherapy and psychological therapy. Most children (70%) required adjuvant medications (amitriptyline and/or gabapentin) for analgesia and to enable them to participate in physiotherapy. A high percentage of children had complete resolution of symptoms using this treatment regime (mean, 15.4 weeks [range, 3 days to 64 weeks]), but 40% required treatment as a hospital inpatient and 20% had a relapse episode. In conclusion, pediatric CRPS is under-recognized by clinicians, resulting in diagnostic delays, but has a favorable outcome to noninvasive treatment in that complete resolution of symptoms and signs occur in most patients. However, the lengthy period to achieve symptom resolution in some children and a high relapse rate support the need for further research into other treatment modalities.

**Key Words:** children, complex regional pain syndrome, pediatric, prognosis, reflex sympathetic dystrophy, treatment

(*J Pediatr Orthop* 2007;27:567–572)

Causalgia, reflex sympathetic dystrophy (RSD), Sudeck atrophy, and shoulder-hand syndrome are pain disorders characterized by constant, intense limb pain associated with vasomotor and sudomotor abnormalities. First described by Mitchell et al[1] during the American Civil War, these syndromes are now conceptualized as variants of a single entity: complex regional pain syndrome (CRPS).[2] The main characteristics of CRPS are (1) the presence of continuing pain that is disproportionate to the inciting event, and (2) the evidence of edema, skin blood flow changes, or abnormal sudomotor activity in the region of the pain.[2,3] There are 2 types of CRPS: (1) CRPS type 1 (previously known as *reflex sympathetic dystrophy*) occurs without a definable nerve lesion, and (2) CRPS type II (previously known as *causalgia*) refers to cases where a definable nerve lesion exists. The pathophysiology of CRPS is not completely understood[4,5] and there is still debate as to what constitutes best treatment. Usually, this consists of active physical therapy, psychological therapy (cognitive-behavioral regimen), and other pain-relieving measures, including pharmacotherapy (analgesics, anticonvulsants, antidepressants) and, occasionally, sympathetic blockage and spinal analgesia.

Studies focusing on children with CRPS are on the rise. Once considered rare among children, it is now thought that this may have been caused by under-recognition of the disorder. Pediatric CRPS differs in many respects from adult CRPS.[6–9] In children, the lower limb is more commonly affected, and significant trauma is a much less frequent precipitating event than in adults. Children are also considered to have a better response to noninvasive treatment,[7,10] and psychosocial factors are thought to play a greater role.[8,10–12] Therefore, treatment that has been reported to be successful in adults may not necessarily apply to children. This study presents the patient characteristics, clinical course, and outcome of the cases of 20 children diagnosed with CRPS at a major children's hospital.

## METHODS

A review of medical records of children diagnosed with CRPS and who were treated in the pain clinic at the Children's Hospital at Westmead during a 4-year period between January 1, 2001, and December 31, 2004, was performed. This study was approved by the hospital ethics committee. The diagnosis was made in all cases by a consultant orthopaedic surgeon or pain specialist on the basis of clinical evaluation. Only children who met the diagnostic criteria of CRPS[3] were included in the study. Twenty patients met these inclusion criteria.

The medical records of these children were used to obtain demographic data, information on clinical presentation and possible precipitating events, details of the various consultations made and investigations required prior making a diagnosis. Any significant past history, family history, or psychosocial problems were also noted. The time taken to make a diagnosis was calculated from the date of reported onset of symptoms to the time when the patient was first seen in the pain clinic. The time to symptom resolution was calculated from the date the patient was first seen in the pain clinic to the time when symptoms were noted to be completely resolved. We noted the number of patients who required a hospital admission, the total number of days spent in hospital, the nature of the treatment received, and the

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None of the authors received financial support for this study.
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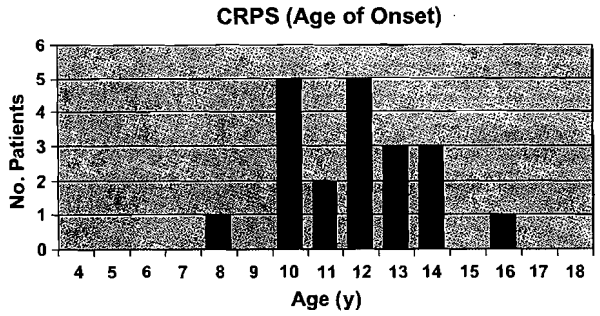


**FIGURE 1.** Age of onset.

number of relapses. We defined a relapse as a recurrence of symptoms after being symptom-free for at least 3 months.

The treatment for all children consisted of an intensive physiotherapy program, supervised by an experienced pediatric physiotherapist. This consisted of a graded exercise program with the aim of increasing muscle strength, weight bearing, and the range of motion in joints. Hydrotherapy, proprioception training, massage, and tactile desensitization techniques were used. Children were also routinely referred for psychological assessment and intervention. Any psychiatric disorder or psychosocial issues documented by the psychologist were recorded. A cognitive behavioral approach was used which focused on improving skills in managing pain and other stressful situations. Children were taught anxiety management skills, which included relaxation therapy, assertiveness training, and problem solving.

Simple analgesia (paracetamol, nonsteroidal anti-inflammatory drugs, and/or codeine) was frequently prescribed, supplemented by adjuvant analgesia to enable the children to participate in physiotherapy. The adjuvant analgesia was prescribed by a pain consultant and consisted of either a tricyclic antidepressant (amitriptyline, 10–20 mg at night) or an anticonvulsant (gabapentin, 300 mg nocte, up to 300 mg 3 times daily).

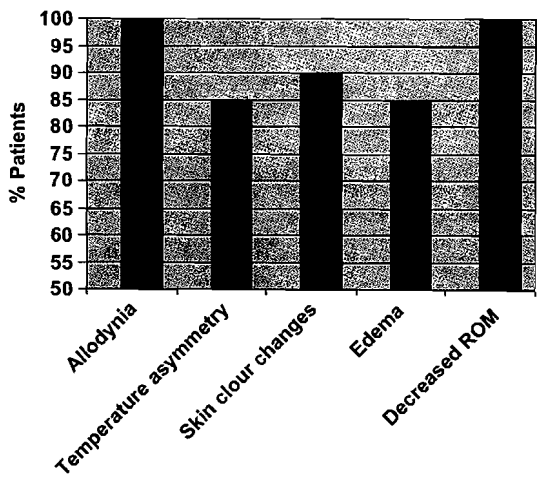


**FIGURE 2.** Frequency of symptoms and signs.

**TABLE 1.** Investigation Modalities and Frequency

| Investigation | Frequency |
|---|---|
| Radiograph | 19 |
| Bone scan | 14 |
| MRI (limb) | 7 |
| MRI (spine) | 2 |
| CT (limb) | 2 |
| CT (abdomen/pelvis) | 1 |
| Blood pathology | 5 |
| Ultrasound | 3 |
| Doppler studies (limb) | 3 |
| Arthroscopy (knee) | 1 |
| Electrocardiogram | 1 |
| Angiogram | 1 |
| Nerve conduction study | 1 |

There were no strict criteria for hospital admission. Patients who were admitted either had no improvement with outpatient treatment or had a brief exacerbation of pain, which was deemed to be better managed in hospital. The aim of admission was to improve pain control and to provide more intense physiotherapy. A daily timetable that consisted of attending school, hydrotherapy, physiotherapy, and gym sessions was formulated for each child. Resocialization with other adolescents was encouraged through attendance at adolescent groups, and independence was fostered by teaching them skills in areas such as self-care. Anxiety management skills were reinforced, and visiting hours were strictly enforced to lessen any secondary gain from family focus on pain.

The children were followed up until their symptoms had resolved and, again, 3 months later. If they remained asymptomatic at this final visit, they were discharged from the pain clinic.

## RESULTS

Twenty children were diagnosed and treated with CRPS type I at the Pain Clinic in The Children's Hospital at Westmead between 1 January 2001 and 31 December 2004. No cases of CRPS type II were encountered during this period. Follow-up was possible in 18 children until their symptoms had completely resolved. Of the 2 children lost to follow-up, 1 child was referred, at parental request, to a pain clinic closer to their place of residence. The other patient was transferred to an adult pain service when she turned 18 years old.

### Demographics

The age at onset ranged from 8 to 16 years, with a mean of 11.8 years (SD, ±1.8 years) (Fig. 1). Eighteen girls (90%) and 2 boys (10%) were affected. The mean age of onset was 12.1 years in girls and 8.9 years in boys.

### Clinical Presentation

The lower limb was affected in 17 children (85%). The foot was affected in 15 children, the ankle in 1 child, and the knee in another. In 10 children, the left side was affected. In

**TABLE 2.** Time to Symptom Resolution Based on Treatment Received

| Treatment | No. Patients | Time to Diagnosis | Time Symptom Resolution | Relapsers | No. Patients Admitted | No. Patients Lost to Follow-up |
|---|---|---|---|---|---|---|
| Physiotherapy alone | 1 | 17 wk | 64 wk | — | — | — |
| Physiotherapy + medications | 1 | 9 d | 15 wk | — | — | — |
| Physiotherapy + psychological | 5 | 17.6 wk (2–41 wk) | 16.7 wk (4–25 wk)* | — | 1 | 1 |
| Physiotherapy/psychological/ medications | 13 | 12.7 wk (2 d to 41 wk) | 11.0 wk (3 d to 26 wk)* | 4 | 7 | 1 |

*Calculations exclude patient lost to follow-up.

the 3 cases (15%) where the upper limbs were affected, 2 cases involved the right wrist and hand, and the other involved the entire left arm.

Sixteen children (80%) reported a precipitating episode of trauma, which was relatively minor in all cases. The common reported mechanisms of injury included falls (n = 6) and sprains (n = 6), with 8 cases occurring during sporting or recreational activities and 3 cases during school. Only 1 case involved a radiologically proven fracture (tip of the distal fibula). Of the 4 children (20%) who could not recall a precipitating event, 3 reported waking up with symptoms of CRPS.

Two children with CRPS of the foot had a past history of Sever disease affecting the same foot. Three children had reported an earlier episode where symptoms were possibly related to CRPS.

The frequency of symptoms and signs is illustrated in Figure 2. All patients reported a continuing pain that was disproportionate to the precipitating event. All patients had allodynia and a decreased range of movement in the affected limb. Most children also exhibited edema, temperature asymmetry, and skin color changes. Trophic changes of the hair, nails, or skin or any sweating changes were not included because they were inconsistently noted in the patient records.

## Clinical Course

The mean time to diagnosis was 13.6 weeks (range, 2 days to 41 weeks). The number of specialists consulted before the patient was seen in the pain clinic averaged 2.7 (range, 1–6). The specialist fields consulted included orthopaedics, pediatrics, rheumatology, neurology, accident and emergency, and general practice.

All children underwent some form of investigation before the diagnosis of CRPS was made (Table 1). The most common investigation modalities used were plain radiography in 19 children (95%), 3-phase technetium bone scan in 14 (70%), and a magnetic resonance imaging (MRI) in 9 (45%) children. Each child had a mean of 3.0 investigations. Because most children reported an episode of trauma, radiographs were often performed as the first-line investigation modality, primarily to exclude a fracture. Only 1 patient had a fracture (distal fibula). When radiographs were performed later in the course of the disease, generalized osteopenia was almost universally observed. Bone scans were conducted within 3 months from the onset of symptoms. Diffuse hypoperfusion was the most common pattern (n = 7), followed by a normal scan (n = 6), then by diffuse hyperperfusion (n = 1). An ultrasound scan of the wrist showed generalized edema in the subcutaneous tissue; otherwise, all other investigation modalities revealed no abnormalities.

Once the diagnosis was made, patients were treated in a multidisciplinary fashion. Children received intensive physiotherapy (20 children [100%]), psychological intervention (18 children [90%]), and adjuvant analgesics (14 [70%]) (Table 2). Two families declined psychological evaluation and intervention. Thirteen children received amitriptyline, and 3 received gabapentin. Two patients received both amitriptyline and gabapentin. The administration of these medications tended to be commenced early to facilitate physiotherapy and was weaned when symptoms had subsided. No adverse effects were noted, and no patients received nerve blocks.

Eight children (40%) were treated as a hospital inpatient at some stage during their illness. Of these, 1 child required 2 admissions into hospital, 1 child a third, and another required a fourth admission. The total number of days spent in hospital of each of these patients is shown in Figure 3. The mean stay for each admission was 14.3 days (range, 4–24 days).

## Outcome

Two girls (age, 10 and 16 years) were lost to follow-up. Their mean time to diagnosis was 15.5 weeks (13–18 weeks), and only the 16-year-old reported a precipitating history of trauma. Each had seen 3 specialists and had 4.5 (range, 4–5) investigations performed, which all showed no abnormalities.

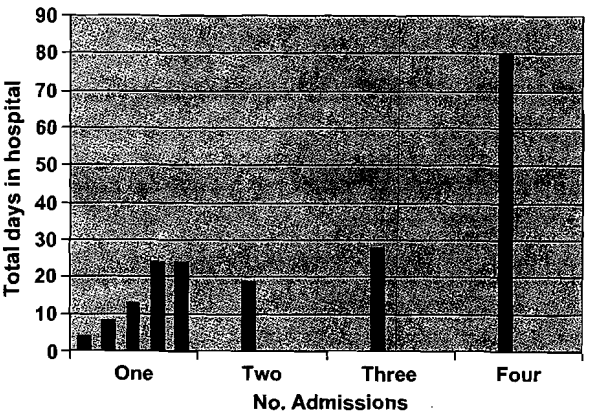


**FIGURE 3.** Time as inpatient.

TABLE 3. Time to Symptom Resolution Based on Time to Diagnosis

| | Time to Diagnosis, mean (range) | No. Patients | Time to Symptom Resolution, mean (range) | No. Relapsers | No. Patients Admitted | No. Patients Lost to Follow-up |
|---|---|---|---|---|---|---|
| <3 Mo | 5.0 wk (2 d to 9 wk) | 10 | 10.6 wk (4–25 wk) | 2 | 2 | — |
| >3 Mo | 22.2 wk (12–41 wk) | 10 | 21.5 wk (3 d to 64 wk)* | 2 | 6 | 2 |

*Calculations exclude patients lost to follow-up.

They were treated for 23 months (range, 22–24 months) in the clinic and were still symptomatic at the time of transfer. The 16-year-old received only physiotherapy and psychological intervention. She was admitted to hospital on 4 occasions for a total of 80 days. The 10-year-old received physiotherapy, psychological intervention, and amitriptyline and had been admitted to hospital 3 times for a total of 28 days.

Four children (3 girls and 1 boy; mean age, 11.6 years [range, 9–13 years]) experienced a relapse. We defined a relapse as a recurrence of symptoms after being symptom-free for at least 3 months. They relapsed after a mean of 28.8 weeks (range, 16–37 weeks) from the end of the first episode (mean length of first episode, 7.7 weeks [range, 3 days to 23 weeks]). One child had a second relapse 6 months after the first relapse ended. Each relapse (total, 5) lasted, on average, 12.8 weeks (range, 7–19 weeks). The mean time to diagnosis was 8 weeks (range, 2 days to 15 weeks). The foot/ankle was affected in all cases, and each patient received physiotherapy, psychological intervention, and adjuvant analgesia during both initial and relapse episodes. Two children reported a precipitating episode of trauma to account for the first episode. With regard to the relapse episode, only 1 child reported a precipitating episode of trauma. Three children were admitted once to hospital (mean length of stay, 13.7 days [range, 4–24 days]). All 4 children were asymptomatic at final follow-up.

Fourteen children (13 girls and 1 boy; mean age, 11.7 years [range, 8–13 years]) had only 1 episode of CRPS, with all children having complete resolution of their symptoms at final follow-up. The mean time to diagnosis was 14.9 weeks (range, 1–41 weeks), and the mean time to symptom resolution was 17.6 weeks (range, 4–64 weeks). Two patients had 1 hospital admission, and 1 patient had 2 admissions (mean length of stay for each admission, 12.8 days [range, 8–24 days]).

This group included 3 children who had a repeat occurrence after being asymptomatic for about a month. By our definition, they were not considered relapsers. Because the weaning of adjuvant analgesia only began when the symptoms had subsided, it is possible that they had not fully recovered and that medications were masking the symptoms during this period. Only in 1 child was the recurrence precipitated by an episode of trauma.

## Outcome Summary

Symptoms and signs resolved together in all cases. The mean time to resolution of symptoms (single episode and relapse groups) was 15.4 weeks (range, 3 days to 64 weeks) for the first episode of CRPS and 12.8 weeks (7–19 weeks) for each subsequent relapse episode. Notably, these figures exclude the 2 children lost to follow-up who had the most resistant form of CRPS and were still symptomatic up to 2 years from commencement of treatment.

The mean times to symptom resolution (for the first episode) based on time to diagnosis (Table 3), bone scan result (Table 4), and treatment received (Table 2) are shown.

# DISCUSSION

Complex regional pain syndrome was once considered very uncommon in children.[10] The growing number of case series and clinical outcome studies is evidence of our increasing awareness and recognition of pediatric CRPS. The differences between pediatric and adult CRPS have been reported,[6–9] but it is still not clear what constitutes the most effective treatment for pediatric CRPS.

The current study found that pediatric CRPS had a strong affliction both for girls and for the lower limb, especially the foot. It tended to affect older children (mean age, 11.8 years), with no child younger than 8 years affected. It was also found to be frequently precipitated by an episode of trauma, which is almost always minor in nature. These findings are very similar to those of previous reports.[6–9,12] In adult CRPS, there is a less marked female predominance; it affects mainly the upper limbs and is almost always triggered by an episode of trauma.[13] Up to half of pediatric CRPS cases may not report a precipitating episode of trauma.[6,7] Estrogen-dependent pain responses may explain sex differences in CRPS, but its rarity in early childhood and the marked

TABLE 4. Time to Symptom Resolution Based on Bone Scan Result

| Bone Scan | No. Patients | Time to Diagnosis, mean (range) | Time to Symptom Resolution, mean (range) | No. Relapsers | No. Patients Admitted | No. Patients Lost to Follow-up |
|---|---|---|---|---|---|---|
| Hypoperfusion | 7 | 9.2 wk (1–15 wk) | 12.2 wk (3 d to 26 wk) | 2 | 4 | — |
| Normal | 6 | 12.9 wk (3–18 wk) | 28.4 wk (4–64 wk)* | 1 | 3 | 2 |
| Hyperperfusion | 1 | 34 wk | 16 wk | — | — | — |

*Calculations exclude patients lost to follow-up.

predilection for the lower limbs in children have not been adequately explained.[14]

A troublesome finding in almost all studies on pediatric CRPS has been the delays in diagnosis. Average delays of up to a year were not uncommon a decade ago.[8,9] Our study and a more recent one[7] have shown marked improvement, but still less than ideal, with an average delay of about 3 months. Murray et al[7] noted that in 15% of children, it still took more than 12 months to come up with a diagnosis and, in the current study, it took more than 6 months to come up with a diagnosis in 3 children (15%). It is clear from both studies that despite our increased awareness of the disorder in children, it still remains a diagnostic challenge, with most patients having seen a number of specialists and having been subjected to multiple investigations before a diagnosis is made. In CRPS, trophic changes tend to occur as the disease progresses; thus, treatment is most likely to be effective when commenced early. We noted that in children who were diagnosed early (<3 months), symptom resolution occurred much more rapidly than in those diagnosed later (10.6 vs 21.5 weeks, respectively). Later diagnosis was also associated with a higher rate of hospitalization and included the 2 patients lost to follow-up, who were still symptomatic after 2 years of treatment.

Pediatric CRPS is a clinical diagnosis and investigations are generally only useful to exclude other pathology. In some series, fractures have been demonstrated in up to 14% of cases,[9] but this is uncommon.[6,8] In the current study, only 1 patient had a fracture; however, when radiographs were performed later in the course of the disease, diffuse osteopenia, secondary to disuse, was almost universally observed. One child even had a knee arthroscopy, which could potentially have exacerbated the condition. Bone scanning in adult CRPS often shows diffuse hyperperfusion, but this is the least common pattern in pediatric CRPS. Children tend to exhibit diffuse hypoperfusion or even a normal scan,[6,15] and our results agree with these findings. Thus, diffusely abnormal findings can be helpful in diagnosing pediatric CRPS, but a normal scan does not exclude it. We also investigated the role of bone scan as a possible prognostic indicator. Those with diffuse hypoperfusion achieved symptom resolution much quicker (time to symptom resolution, 12.2 weeks) than did those with normal scans (time to symptom resolution, 28.4 weeks). The 2 patients lost to follow-up, who were still symptomatic at 2 years, had normal bone scans and were not included in the calculations. If included, the difference between groups would even be greater. Ultimately, it is difficult to determine whether there is a real difference, considering the small numbers and the number of uncontrolled variables in each group.

After diagnosis, all children commenced intensive physiotherapy and were referred for psychological evaluation and intervention. Some studies have reported that abnormalities are frequently detected after psychological evaluation; recurring themes include the presence of family dysfunction, lack of self-assertiveness, nonverbalization of feelings, and performance pressure in school and sports.[8,10,11] In the current study, no psychiatric disorder was evident. Eleven children (55%) were labeled as high achievers on their psychological profile, a characteristic that has been recognized in other studies.[7,9] The main purpose of psychological intervention in this study was to improve skills in managing pain and in other stressful situations. However, the quality of treatment received and the ultimate effect on outcome is very difficult to measure, but it does seem to be an important adjunct to physiotherapy.[6,12]

Good results have been achieved with physiotherapy as the primary mode of treatment, but better results are observed when combined with psychological intervention. Dietz et al[16] reported on 5 cases of RSD and summarized 80 cases in the literature. They stated that noninvasive, nonpharmacological therapy was successful in 78% of the patients discussed in the literature. In their own study, 4 of 5 patients were treated successfully by means of an outpatient physiotherapy program. With physiotherapy and psychological intervention, 11 of 15 patients available for long-term follow-up were functioning normally, with no significant sequelae.[15] In another study where the focus was on intense physiotherapy but where 77% of patients had been referred for psychological counseling, 43 of 49 (88%) patients had no symptoms of CRPS after a mean follow-up of 5 years.[6] No medications were used in that study.

However, compliance with physiotherapy is often difficult without some form of analgesia. Most patients in the current study received simple analgesia, and 70% also received adjuvant analgesia (amitriptyline, gabapentin). Both these medications were found to be effective in improving pain with minimal adverse effects. When commenced early, there was good compliance with physiotherapy. Adjuvant analgesia was continued until symptoms were either minimal or had completely subsided, after which its administration was slowly weaned. In adults, amitriptyline and gabapentin are reported to be efficacious in treatment of CRPS[17,18]; in a study of RSD in children, 23 (56%) of 41 patients who received tricyclic antidepressants and 5 (42%) of 12 patients who received anticonvulsants had reported substantial improvement in symptoms. Using an alternate form of analgesia (nonsteroidal anti-inflammatory drugs [in 41% of patients], combined with physiotherapy and psychological intervention [in 20% of patients]), the median time to recovery was 7 weeks (range, 1–140 weeks); however, 10% of patients still reported problems beyond a year.[7]

The current study also had good results with a combination of physiotherapy, psychological intervention, and pharmacotherapy. Twelve of 13 children at final follow-up had complete resolution of symptoms and for the first episode of CRPS, this occurred in 11.0 weeks. However, all the relapsers and almost all patients who required hospitalization were included in this group. With regard to those who received only physiotherapy and psychological intervention, 4 of 5 patients were completely asymptomatic at final follow-up, and this occurred in 16.7 weeks. However, 2 children were still symptomatic at 2 years despite either treatment regime. The relapse rate (20%) was relatively high but was lower than in other studies, which have reported relapse rates of 27.5% to 36%.[6,7,12] These studies used predominantly physiotherapy and psychological intervention. Furthermore, we found relapse episodes to be more resistant to treatment,

with relapse episodes lasting longer than does the initial episode (12.8 vs 7.7 weeks, respectively) despite receiving similar treatment.

Retrospective studies of multimodal therapy have not clearly shown invasive treatment to provide additional benefit. In a study using physical therapy, transcutaneous electrical nerve stimulation, psychological counseling, and systemic medications and where 19% of patients had a sympathetic block, the average duration of symptoms was 9 months, with 9 (25%) of 36 patients still having symptoms at final follow-up.[8] In another study, 38 (54%) of 70 children continued to have some degree of residual pain and dysfunction at final follow-up[9] when physical therapy, transcutaneous electrical nerve stimulation, psychological therapy, sympathetic blocks, and pharmacotherapy (tricyclic antidepressants, anticonvulsants, and corticosteroids) were used. However, the investigators found sympathetic blocks to be highly effective, with 14 (38%) of 37 patients having complete resolution and another 14 (38%) having substantial improvement in symptoms. Many studies, including ours, have reported good compliance with physiotherapy without the need of a sympathetic block, but their role in cases that prove resistant to conservative treatment has not been clearly defined.

In conclusion, significant delays in diagnosis of CRPS in children are still evident despite our apparent increased awareness of the disorder. Prompt recognition will avoid many unnecessary consultations and investigations, and early referral to a specialist pain service for initiation of treatment may lead to quicker resolution of symptoms. Pediatric CRPS appears to have a good prognosis because a high percentage of patients are expected to have complete resolution of their symptoms and signs without the need for any invasive treatment. However, the condition is not benign, with many patients requiring a long period of treatment, and the relapse rate is high. Study weaknesses include the small sample size, with 10% loss on follow-up, and the retrospective nature of the study. There was no control group and, thus, it is possible that symptom resolution was not caused by treatment. Patient selection bias was a factor, and it is possible that milder forms of CRPS were either not referred or resolved without treatment. Finally, some children in the study may come to have a relapse in the future or may already have had a relapse but presented elsewhere. Both scenarios would increase our reported relapse rate.

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