

Reflex Sympathetic Dystrophy in Children

CLINICAL CHARACTERISTICS AND FOLLOW-UP OF SEVENTY PATIENTS*

BY ROBERT T. WILDER, M.D., PH.D.†, CHARLES B. BERDE, M.D., PH.D.†, MICHAEL WOLOHAN, M.D.†,
MARIE ANN VIEYRA, PH.D.†, BRUCE J. MASEK, PH.D.†, AND LYLE J. MICHELI, M.D.†, BOSTON, MASSACHUSETTS

Investigation performed at Children's Hospital, Boston

ABSTRACT: We report on the experience with our first seventy patients who had reflex sympathetic dystrophy and were less than eighteen years old (average age, 12.5 years). In our series, the patients were predominantly girls (male to female ratio, 11:59) and the lower extremity was involved most often (sixty-one of the seventy patients). The average time from the initial injury to the diagnosis was one year, which indicates that the syndrome remains under-recognized in patients in this age-group. Conservative treatment with physical therapy, transcutaneous electrical nerve stimulation, psychological therapies including cognitive-behavioral management and relaxation training, and tricyclic antidepressants was effective in improving the average scores for pain and function for forty patients. Sympathetic blocks were helpful for twenty-eight of thirty-seven patients. Thirty-eight of the seventy patients in the series continued to have some degree of residual pain and dysfunction. Reflex sympathetic dystrophy in children differs in presentation and clinical course from the syndrome in adults. It is best treated in a multidisciplinary fashion.

Reflex sympathetic dystrophy, a disorder characterized by pain in an extremity associated with autonomic dysfunction, has been recognized since the time of the American Civil War¹⁸. Common symptoms include burning pain, hyperalgesia (increased sensitivity to noxious stimuli), allodynia (pain provoked by stimuli not usually considered painful, such as light touch), dysesthesia, and paresthesia. Frequent findings related to the autonomic nervous system include cyanosis, mottling, increased sweating, abnormal growth of hair, diffuse swelling not confined to the vicinity of joints, and coldness. If not adequately treated, atrophy of muscles, demineralization of bone, and contractures may ensue.

The diagnostic criteria for reflex sympathetic dystrophy have varied²⁷. Some physicians base the clinical diagnosis on the presence of chronic pain with neuropathic descriptors (burning, allodynia, dysesthesia, hyperalgesia to cold) in an extremity that has objective signs of

sympathetic dysfunction (coldness, cyanosis, mottling, increased sweating), after the exclusion of other orthopaedic, rheumatological, or neurological diagnoses. Other clinicians restrict the diagnosis of reflex sympathetic dystrophy or the related term, sympathetically maintained pain, to patients whose pain is relieved temporarily by selective sympathetic blocks with a block of the sympathetic chain with a local anesthetic, a regional block with guanethidine (or related blocking agents) given intravenously, or the systemic intravenous administration of phentolamine⁴. The term *causalgia* is generally used for patients who have a similar spectrum of pain descriptors and autonomic abnormalities in association with direct trauma to a major nerve trunk²¹.

Methods of treatment vary widely and are matters of controversy and debate. The treatments described for reflex sympathetic dystrophy have included immobilization and elevation of the extremity, vigorous mobilization and physical therapy²⁵, transcutaneous electrical nerve stimulation²³, steroids, tricyclic antidepressants, anticonvulsants, non-steroidal anti-inflammatory drugs²⁵, injections of calcitonin, vasodilators, and beta-adrenergic antagonists. Temporary block of the sympathetic nervous system with local anesthetic, regional anesthetic (guanethidine or bretylium given intravenously⁶), and chemical⁶ or operative sympathectomy⁷ have also been used. As Schutzer and Gossling²⁶ pointed out, the response to therapy is variable, and few forms of treatment have been examined in prospective clinical trials.

In recent years, reflex sympathetic dystrophy has been recognized with increasing frequency in children. Pillemer and Micheli²² reported on twenty patients who were seen in the Sports Medicine Clinic at Children's Hospital, Boston, in whom reflex sympathetic dystrophy developed after an injury that was sustained during organized sports. The current study includes two of these patients. These authors hypothesized that the stress of sports activities may help to precipitate or perpetuate reflex sympathetic dystrophy in children. Olsson et al.²⁰ reported the cases of fifty-five children who had reflex sympathetic dystrophy and were treated with a regional sympathetic block given intravenously. Some authors¹³ have suggested that reflex sympathetic dystrophy is under-reported, and probably substantial numbers of cases are undiagnosed or misdiagnosed.

We report on the clinical course and responses to treatment of seventy children and adolescents who had

*No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. No funds were received in support of this study.

†Children's Hospital, 300 Longwood Avenue, Boston, Massachusetts 02115. Please address requests for reprints to Dr. Berde, Pain Treatment Service.

reflex sympathetic dystrophy and were followed for a minimum of two years. The objective of the study was to determine the characteristics of the patients and the course of reflex sympathetic dystrophy in a group of younger patients who were evaluated and treated by a consistent algorithm. We sought to examine the roles of sports, dance, and related activities in the development and exacerbation of this syndrome and to assess the role of sympathetic blocks in the treatment of reflex sympathetic dystrophy in children and adolescents.

Materials and Methods

The charts of 121 patients who had chronic non-arthritic pain in an extremity and were seen in the Pain Treatment Service or the Orthopaedic Division of Sports Medicine at Children's Hospital, Boston, between February 1986 and June 1989 were reviewed. Patients were excluded if they were eighteen years old or older at the time of the onset of symptoms.

A decision was made to base the diagnosis on a clinical evaluation rather than on a response to testing of sympathetic function or to sympathetic blocks, because a variety of underlying neurophysiological abnormalities may produce a similar clinical presentation¹⁹. The diagnosis of reflex sympathetic dystrophy was made on the basis of the presence of at least two descriptors typical of neuropathic pain and two physical signs of autonomic dysfunction. The neuropathic pain descriptors were burning, dysesthesia, paresthesia, mechanical allodynia, and hyperalgesia to cold. The autonomic signs were cyanosis, mottling of the skin, hyperhidrosis, edema, and coolness of the extremity (at least 3 degrees Celsius). Seventy-two patients met these criteria. We were able to obtain long-term follow-up data on seventy (97 per cent) of these seventy-two patients. The other two did not cooperate and sought treatment elsewhere.

The patients were managed according to an algorithm of treatment that represents a compromise between the view favored in the pediatric literature, which emphasizes vigorous physical therapy and psychological treatment³, and the belief expressed in the adult anesthesia and pain-clinic literature, which supports the aggressive use of sympathetic blocks⁴ (Fig. 1). Our goals were to use an initial treatment that was least invasive or had the fewest side-effects and to progress to other modes of treatment if the patient did not respond. Thus, we initially offered physical therapy, transcutaneous electrical nerve stimulation, and techniques for cognitive and behavioral management of pain. For the patients who did not respond to these treatments, non-steroidal anti-inflammatory drugs and tricyclic antidepressants were added to the regimen. Patients who did not improve after the additional treatment were offered a trial of sympathetic blocks. Finally, patients who continued to have dysfunction despite all of the aforementioned treatments were offered trials of several classes of medications on an individual basis; the medications included alpha and

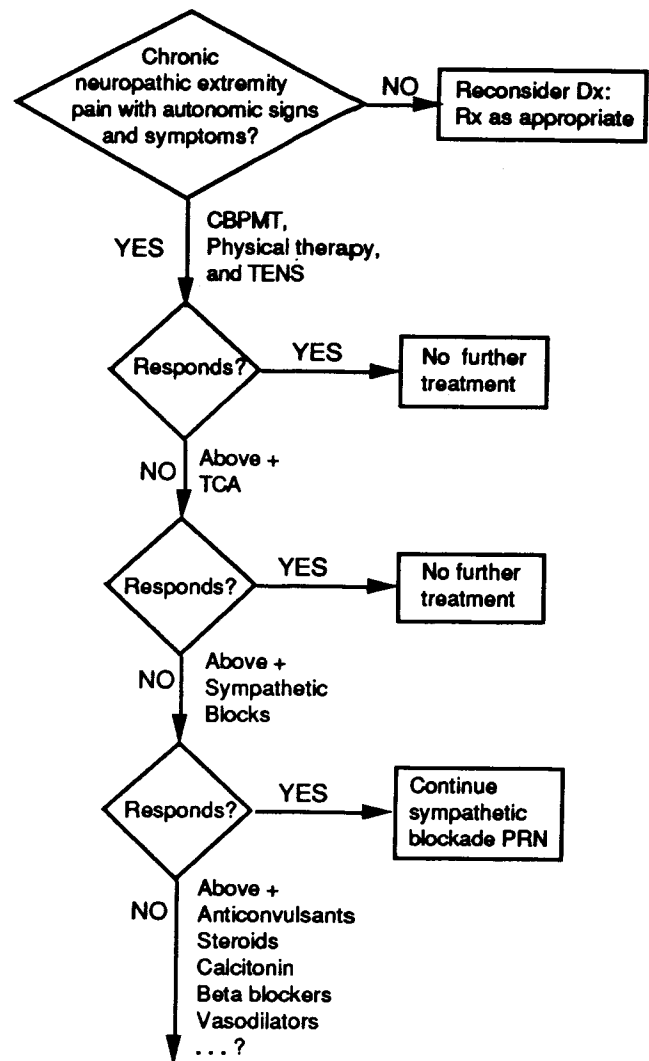


FIG. 1

Algorithm of treatment of patients who had reflex sympathetic dystrophy. Dx = diagnosis, Rx = therapy, CBPMT = cognitive-behavioral pain-management techniques, TENS = transcutaneous electrical nerve stimulation, and TCA = tricyclic antidepressants.

beta-adrenergic antagonists, anticonvulsants, calcium-channel blockers, and steroids. Through our multidisciplinary pain service, all of the patients were strongly urged to accept evaluation and care by the departments of behavioral medicine, physical therapy, orthopaedics, and anesthesia.

Physical therapy was employed for all patients. Some severely affected patients initially would not permit touch or passive movement of the affected extremity. For these patients, initial treatment focused on desensitization to tactile stimuli and on the use of heat and the whirlpool, followed by passive range-of-motion exercises. A therapeutic trial of transcutaneous electrical nerve stimulation was introduced early in the course of physical therapy and a variety of stimulation parameters were used, such as placement according to dermatomes or to the points used for acupuncture and variable frequencies, as needed. For patients who found transcuta-

neous electrical nerve stimulation to be beneficial, a unit was provided for use at home. As soon as was tolerated by the patient, physical therapy emphasized active strengthening and physical conditioning of the affected limb. This usually occurred within two weeks of the start of therapy, but there was great variation. At least twenty-three patients were already capable of performing such exercises when they began therapy, and thirty-seven patients were unable to make substantial progress in this area until nerve blocks were performed to desensitize the affected extremity. For patients who had involvement of a lower extremity, progressive weight-bearing was a prominent goal. Patients who had a tight Achilles tendon were given specific stretching exercises. Recommendations regarding progression of physical therapy were made in conjunction with orthopaedic consultation.

Four patients who did not progress with weight-bearing and in whom a tight heel cord impeded gait received a trial of walking in a weight-bearing below-the-knee cast, at the discretion of the attending orthopaedic surgeon. The average time in the cast was ten weeks. These four patients and two others also received a bivalved cast or an ankle-foot orthosis.

A psychological assessment was performed in order to (1) diagnose psychiatric conditions, including depression, anxiety, somatoform illness, conversion disorder, psychogenic pain disorder, Münchhausen syndrome, or post-traumatic stress disorder; and (2) evaluate factors that might interfere with the patient's motivation to get well, such as family dysfunction, litigation, or unrealistic demands on performance in school and sports. Unless specifically contraindicated by formal psychological assessment, patients were then offered a structured program of behavioral management of pain consisting of six to ten sessions. This program included relaxation training, with or without temperature or electromyographic biofeedback; cognitive-behavioral therapy to improve skills in the management of stressful situations; and intervention in the behavioral patterns of the family to eliminate reinforcement of behaviors such as repeated avoidance of social obligations, school, and family responsibilities and to promote healthy behaviors such as the use of relaxation techniques and distracting activity to cope with pain. In some patients, treatment was longer because more serious psychopathology (such as sexual abuse or severe depression) was revealed.

Three pediatric anesthesiologists who served as attending physicians in the pain clinic prescribed medications according to the following indications. Non-steroidal anti-inflammatory drugs were used in patients who had not previously had a trial of such medications, and they were continued in patients who reported benefit and had no intolerable side-effects. Opioids were prescribed in association with brief painful events, such as a change of a cast, but were not generally recommended for ongoing pain¹; a tapering schedule was followed by patients who had been taking opioids regularly

at the time of referral. Tricyclic antidepressants were administered to patients who were unresponsive to physical and behavioral therapies and who met one or more of the following criteria: symptoms suggestive of depression, such as loss of energy, poor appetite, and loss of interest or pleasure in usual activities; substantial sleep disturbance; or unremitting, severe pain. Prospective, blinded clinical trials have shown tricyclic antidepressants to be efficacious for several types of neuropathic pain^{16,17}. For sleep disturbance, amitriptyline was used; if somnolence in the morning or a dry mouth became bothersome, trials of either doxepin or desipramine were begun. For all three agents, the dosage began at 0.1 to 0.2 milligram per kilogram of body weight, orally, at bedtime; this dosage was advanced, as limited by side-effects, to 0.5 to one milligram per kilogram of body weight per day. Electrocardiography was encouraged for patients who were receiving tricyclic antidepressants in the range therapeutic for depression (more than one milligram per kilogram of body weight per day). Electrocardiography and cardiac evaluation were mandatory for any patient who had a history of syncope, chest pain, palpitations, cardiac murmur, or thyroid disease.

Sympathetic blocks with a local anesthetic, or in selected patients, with a regional anesthetic (guanethidine or bretylium, administered intravenously), were given to patients who were unresponsive to conservative management. The decision to employ sympathetic blocks was based on physical signs of progressive sympathetic dysfunction along with worsening dysfunction of the limb and an inability to progress with active physical therapy and strengthening programs, rather than on the patient's report of pain. Descriptions of techniques for sympathetic blocks in children and their results are subjects of separate reports^{2,14}. In general, we preferred sympathetic blocks with a local anesthetic given through an indwelling catheter placed in the lumbar epidural space, lumbar paravertebral area, brachial plexus (axillary approach), or pleural space. Continuous techniques often were chosen instead of repeated single injections because several doses could be given before physical therapy and the number of painful or anxiety-provoking procedures with a needle was reduced. As most patients were girls, consideration was also given to limitation of exposure to radiation. The catheter was typically maintained for seven to ten days, during which time patients had physical therapy twice a day as well as regular psychological consultation. When a lumbar epidural block was used, we most commonly infused diluted bupivacaine (0.1 per cent, 0.15 to 0.25 milliliter per kilogram of body weight per hour). With a dose in this range of concentrations, usually patients were able to walk with assistance, although proprioception and balance often were diminished. If urination was difficult, the infusion was discontinued for three hours two or three times daily to permit urination; catheterization of the bladder was thus avoided for all but one patient. Early in our series,

one patient needed intermittent catheterization of the bladder, but an indwelling bladder catheter was not used in any patient. For severely affected patients, supplemental injections of a more concentrated local anesthetic (0.25 per cent bupivacaine, 0.5 milliliter per kilogram of body weight) often were given initially to permit passive mobilization.

Thirty patients were admitted to the hospital for a sympathetic block and more intensive physical and behavioral therapy. While they were in the hospital, a structured program of behavioral management was instituted. All patients wore street clothes during the day and had regularly scheduled activities including study hall, art, physical therapy (twice daily), and behavioral therapy for relaxation training, as well as cognitive-behavioral and biofeedback training. Independence in activities of daily living was strongly encouraged, even for patients who had substantial dysfunction of a limb. Admissions were routed to two orthopaedic/general surgery units where the nurses were highly experienced with behavioral management of chronic pain.

For patients who did not improve with these treatments, another medication, including anticonvulsants, vasodilators⁸, or prednisone¹², was given orally, in structured individualized trials.

Neurodestructive sympathectomy (either operative or chemical [injection of phenol into the sympathetic ganglia]) was done in three patients whose condition deteriorated despite all of the aforementioned treatments. The criteria for consideration of sympathectomy included active participation in physical therapy, a sufficient trial of psychological treatment and a reasonable level of psychological functioning, adequate trials of medications, repeatedly favorable temporary responses to (but not prolonged benefit from) sympathetic blocks with a local anesthetic, and physical signs of severe sympathetic dysfunction, including atrophy and extreme swelling, particularly in association with unresolved cellulitis or lymphangitis in the foot.

Follow-up information was obtained at visits to the clinic and, for patients who were no longer returning to the clinic, by structured interviews of patients and parents over the telephone.

Patients and parents were asked to rate the child's pain both before and after treatment on a scale of 0 to 10 points, with 0 indicating no pain and 10, the worst imaginable pain. This form of rating scale has been shown to possess valid psychometric properties for children five years old and older¹⁵. Function before and after therapy was rated on a scale of 0 to 5 points (Table I). The patient's ability to perform in work, school, or sports was also evaluated in a formal questionnaire. Finally, we attempted to evaluate responses to different modalities of treatment. Since multiple treatments were employed simultaneously, responses to treatment were recorded, by an investigator who was not involved in the treatment, through review of the assessments made at visits to the

TABLE I
SCORE FOR FUNCTION

| Score | Lower Extremity | Upper Extremity |
|-------|--|--|
| 0 | Wheelchair-bound | No movement |
| 1 | Crutches | Movement, unable to eat or write |
| 2 | Cane | Can eat and write |
| 3 | Unrestricted walking | Can eat and write without difficulty |
| 4 | Can swim and cycle, some athletic restrictions | Can swim and cycle, some athletic restrictions |
| 5 | No restrictions | No restrictions |

clinic and interviews with the patient.

The patient's age, sex, sports activity, type of injury (if any), duration of symptoms, level of disability, treatment, and response to treatment were reviewed. The average scores for pain and function before and after treatment were tabulated. A variety of pre-treatment parameters were tested for significance in prediction of the outcome.

Statistical Methods

The chi-square test, Kruskal-Wallis analysis of variance, Mann-Whitney U test, Wilcoxon rank sum, Kendall tau, or linear regression was used to test for differences among subgroups and statistical trends. A p value of less than 0.05 was considered statistically significant.

Results

Fifty-nine patients (84 per cent) were girls and eleven (16 per cent) were boys. The mean age was 12.5 years (range, five to seventeen years) (Fig. 2).

The average time from the onset of symptoms to the initial visit to a physician was twelve days. For all but three patients, the onset of symptoms was attributed to an antecedent activity or injury; in forty-eight patients (69 per cent), the injury was vague and seemingly minor, such as a sprain or a twist. Although plain radiographs

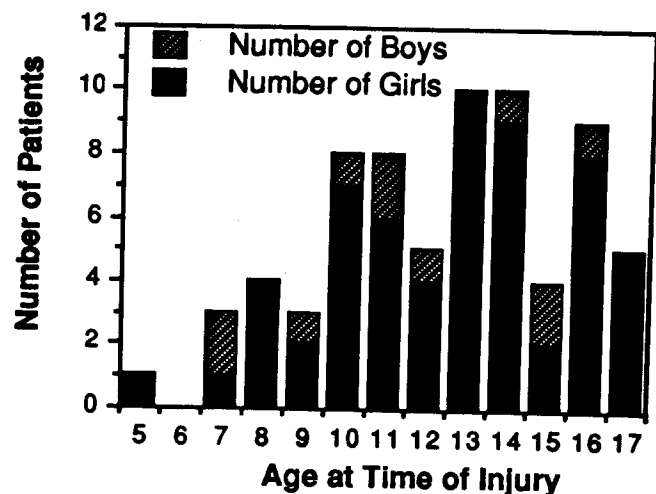


FIG. 2

Age and sex distributions of patients who had reflex sympathetic dystrophy.

TABLE II
COMPARISON OF SYMPTOMS AT INITIAL VISIT AND AT FOLLOW-UP

| Sign or Symptom | At Initial Visit | At Follow-up |
|----------------------|------------------|--------------|
| Pain | 70 (100%) | 43 (61%) |
| Mechanical allodynia | 60 (86%) | 20 (29%) |
| Edema | 54 (77%) | 18 (26%) |
| Cold extremity | 54 (77%) | 22 (31%) |
| Cyanosis | 51 (73%) | 16 (23%) |
| Mottling of skin | 45 (64%) | 27 (39%) |
| Hyperalgesia to cold | 44 (63%) | 19 (27%) |
| Hyperhidrosis | 22 (31%) | 3 (4%) |

were made for sixty-eight patients (97 per cent) and bone-scanning was performed for forty-three patients (61 per cent), only ten patients (14 per cent) had an identifiable fracture or meniscal tear as the initiating injury. Nonetheless, fifty-two patients (74 per cent) had the affected extremity immobilized for an average of seven and one-half weeks before they were referred to the pain-treatment service. For seven patients (10 per cent), the symptoms of reflex sympathetic dystrophy followed an operative procedure on the involved extremity: bunionectomy (one), arthroscopy of the knee (two), excision of an osteochondroma (one), resection of a calcaneonavicular coalition (one), and excision of an osteosarcoma complicated by recurrent infection and the need for additional procedures (two). The interval from the onset of symptoms to the time of diagnosis of reflex sympathetic dystrophy averaged twelve months (range, one to sixty months).

In half (thirty-five) of the patients, the injury was sustained during a supervised sports activity. Twenty-one injuries occurred during an individual sport: ballet (seven injuries), gymnastics (three injuries), ice-skating (three injuries), swimming (two injuries), and cheerleading and skiing (one injury each). Four patients were injured while running. Fourteen injuries occurred during a team sport: soccer (six injuries), basketball (two injuries), field hockey (two injuries), and football, ice hockey, softball, and volleyball (one injury each). However, sixty of the seventy children, including many in whom the injury was not directly related to a sports activity, were involved in organized sports.

Reflex sympathetic dystrophy was much more common in the lower extremity than in the upper extremity. In sixty-one (87 per cent) of the seventy patients, the lower extremity was affected: twenty-five patients had involvement of the foot; twenty-three, the ankle; and twenty-six, the knee. All were involved to about the same extent. Of the nine patients (13 per cent) in whom an upper extremity was affected, the hand was involved in five patients; the wrist, in five; and the elbow, in four. Involvement of the proximal joints, either the hip (three patients) or the shoulder (three patients), was less common. Twenty-two patients had involvement of more than one joint or limb when they were first seen by us.

All patients had pain on the initial visit, with an

average score for pain of 8.7 points (Fig. 3-A). Other symptoms included allodynia in sixty patients (86 per cent), coldness of the extremity in fifty-four (77 per cent), edema in fifty-four (77 per cent), cyanosis in fifty-one (73 per cent), mottling of the skin in forty-five (64 per cent), sensitivity to cold in forty-four (63 per cent), and hyperhidrosis in twenty-two (31 per cent) (Table II). On the average, each patient had six of the eight signs and symptoms. The original score for function averaged 1.5 points (Fig. 3-B).

The median duration of follow-up was three years (range, two to eight years). During follow-up, there was a general reduction in the percentage of patients who had pain, allodynia, and each of the sympathetic findings, although moderate degrees of pain and sympathetic dysfunction persisted for many patients (Table II). At the latest follow-up, the average score was 2.7 points for pain (Fig. 4-A) and 4.1 points for function (Fig. 4-B). When the thirty-two patients who had no pain or other symp-

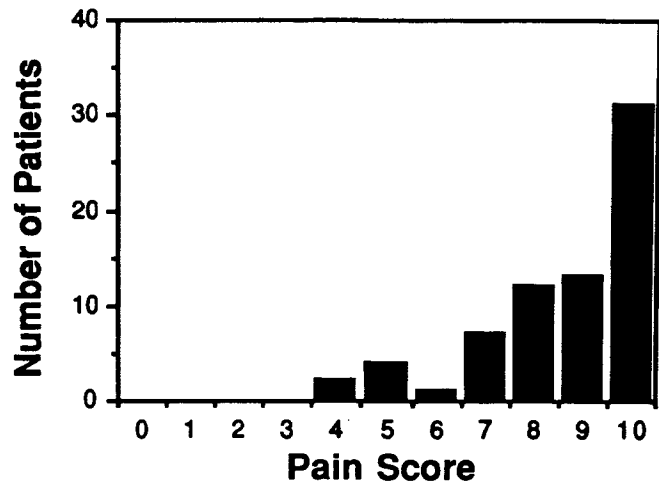


FIG. 3-A

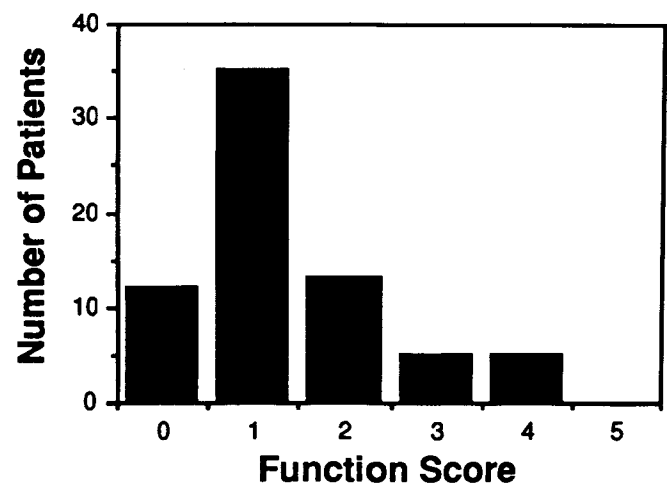


FIG. 3-B

Figs. 3-A and 3-B: Scores for pain and function when the patients were first seen at the Pain Treatment Service. Pain was reported on a linear-analog scale marked from 0 to 10. Scores for function were based on the scale in Table I.

toms of reflex sympathetic dystrophy at the time of follow-up are excluded, the average score in the remaining thirty-eight patients was 5.0 points for pain and 3.6 points for function. Sixty patients (86 per cent) were involved in organized sports before the onset of symptoms; only thirty-one (44 per cent) were playing sports at the latest follow-up. Sixty-seven patients (96 per cent) were either regularly in school or at full-time work at the time of follow-up.

The numbers of patients who used each modality of treatment were as follows. Sixty-four patients (91 per cent) participated in physical therapy, fifty (71 per cent) received non-steroidal anti-inflammatory drugs, sixty-one (87 per cent) had transcutaneous electrical nerve stimulation, and forty-four (63 per cent) were involved in biofeedback or relaxation training. Forty-one patients (59 per cent) took tricyclic antidepressants, thirty-seven (53 per cent) were given a sympathetic block, fifteen (21 per cent) used opioids, twelve (17 per cent) received anticonvulsants, eight (11 per cent) took prednisone, and

TABLE III
PERCEIVED RESPONSE TO TREATMENT*

| Treatment | Status of Reflex Sympathetic Dystrophy | | |
|---|--|----------|--------------------|
| | Completely Resolved | Improved | Unchanged or Worse |
| Physical therapy (n = 64) | 17 (27%) | 27 (42%) | 20 (31%) |
| Transcutaneous electrical nerve stimulation (n = 61) | 4 (7%) | 27 (44%) | 30 (49%) |
| Techniques for behavioral management of pain (n = 44) | 2 (5%) | 23 (52%) | 19 (43%) |
| Non-steroidal anti-inflammatory drugs (n = 50) | 3 (6%) | 17 (34%) | 30 (60%) |
| Tricyclic antidepressants (n = 41) | 2 (5%) | 21 (51%) | 18 (44%) |
| Opioids (n = 15) | 0 | 6 (40%) | 9 (60%) |
| Corticosteroids (n = 8) | 0 | 0 | 8 (100%) |
| Anticonvulsants (n = 12) | 0 | 5 (42%) | 7 (58%) |
| Sympathetic blocks (n = 37) | 14 (38%) | 14 (38%) | 9 (24%) |
| Chemical/operative sympathectomy (n = 3) | 0 | 1 (33%) | 2 (67%) |

*Five patients reached limiting orthostatic hypotension with the use of vasodilators before any improvement was seen. One patient improved with the use of a vasodilator.

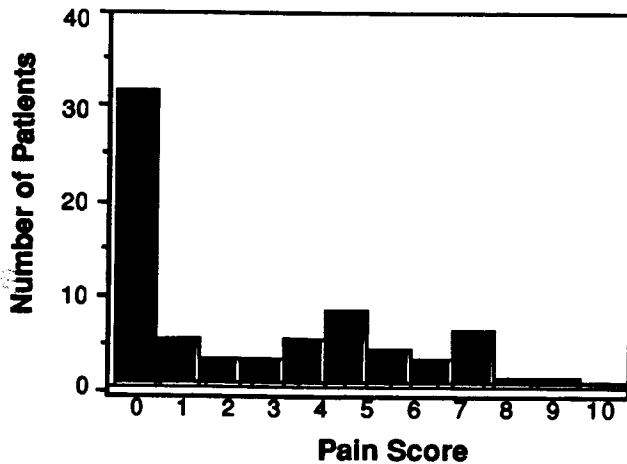


FIG. 4-A

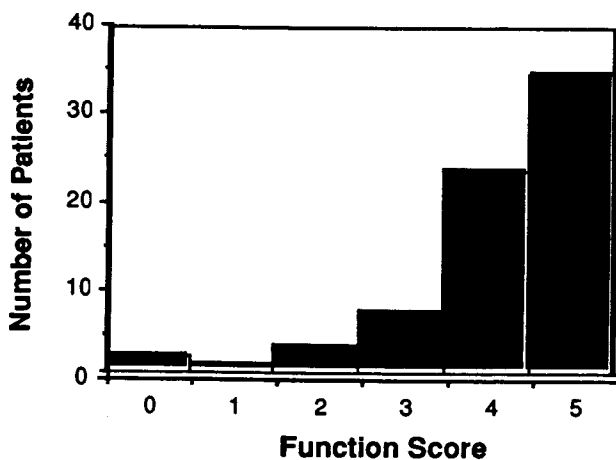


FIG. 4-B

Figs. 4-A and 4-B: Scores for pain and function at follow-up at an average of two and one-half years after the patients were first seen by us. Pain was reported on a linear-analog scale marked from 0 to 10. Scores for function were based on the scale in Table I.

three (4 per cent) had sympathectomy (operative in two patients and chemical in one). Twenty patients (29 per cent) had an operation, most often arthroscopy. Immobilization in a weight-bearing cast or partial immobilization with a splint for use at night was prescribed for six patients (9 per cent). Although the symptoms occasionally improved during the period of immobilization and elevation, patients who wore a cast commonly reported that the symptoms were worse after the cast was removed.

There was a wide variation in the perceived response of the patients to different modes of therapy (Table III). Two-thirds of the patients who had physical therapy judged it to be helpful. Most reported improvement in function despite transient increased intensity of pain during therapy. Four patients reported complete and long-lasting resolution of pain with the use of transcutaneous electrical nerve stimulation, and twenty-seven patients reported some degree of improvement. In contrast, twenty-five patients reported no improvement, and five had a considerably worse score for pain after transcutaneous electrical nerve stimulation. Many of the twenty-seven patients reported initial improvement in pain with transcutaneous electrical nerve stimulation but a decrease in the effectiveness with continued use.

Forty-four patients (63 per cent) were evaluated by the behavioral medicine program and received therapy. The remaining patients already were receiving psychological treatment, refused treatment, or had had psychological treatment elsewhere. Twenty-five (57 per cent) of the patients who participated in behavioral management reported a definite benefit and continued to use skills learned in therapy during periods of stress and pain. The

remainder usually disengaged from treatment rapidly. The patients' descriptions of the positive effectiveness of the techniques for cognitive-behavioral management of pain were predictive of the outcomes, including the score for pain, the score for function, and the number of autonomic signs present at follow-up ($p < 0.01$ for each parameter).

Although various non-steroidal anti-inflammatory drugs usually were prescribed for the treatment of reflex sympathetic dystrophy, 60 per cent of our patients did not report a reduction in pain with this class of drugs. One patient had clinically important gastritis associated with chronic use of non-steroidal anti-inflammatory drugs.

Despite the enthusiasm of Kozin et al.¹², trials with prednisone (two milligrams per kilogram of body weight per day initially, with tapering initiated after two weeks) did not produce improvement in the scores for pain or function in any of the eight patients for whom they were prescribed. No major steroid-induced complications occurred, however.

Of the forty-one patients for whom tricyclic antidepressants were prescribed, two had a nearly complete resolution of pain and symptoms, twenty-one (51 per cent) reported a substantial improvement in the symptoms and improved sleep at night, and eighteen reported little or no reduction in symptoms. Although minor reactions such as somnolence or dry mouth were common, they often resolved with continued use, and there were no severe or life-threatening reactions. One patient reported having palpitations, which stopped after the drug was changed. Another patient had episodic palpitations during treatment with amitriptyline; the palpitations and syncope persisted after the drug was discontinued. The resting electrocardiogram was normal, and evaluation with a Holter monitor was also normal. Subsequent electrophysiological evaluation two years after treatment for reflex sympathetic dystrophy disclosed a re-entrant tachycardia.

For all patients who used opioids, the drug had been initially prescribed by a referring physician. We tried to reduce or discontinue administration after referral to our pain service. Opioids did not resolve the neuropathic pain of reflex sympathetic dystrophy in any of our patients, and nine of the fifteen patients who used opioids found them completely ineffective in the reduction of pain (Table III).

Sympathetic blocks appeared to be highly effective in the treatment of reflex sympathetic dystrophy in many, but not all, of the patients in whom they were tried. Although sympathetic blocks were generally used only for patients who had severe disease that was unresponsive to less invasive forms of therapy, fourteen (38 per cent) of the thirty-seven patients in whom a block was done reported complete resolution of the symptoms, and an additional fourteen (38 per cent) patients had substantial improvement. Even with this form of therapy, however, nine (24 per cent) of the thirty-seven pa-

tients had no response. No life-threatening reactions occurred with sympathetic blocks, and there were no convulsions, infections, or episodes of hypotension. Early in the series, a lumbar paravertebral 18-gauge catheter (Becton-Dickinson, Rutherford, New Jersey) broke during removal from the patient; a subcutaneous incision was made to remove it. After that, all lumbar infusions were given through a polyamide epidural-type 20-gauge catheter that was inserted through a five, six, or seven-inch (thirteen, fifteen, or eighteen-centimeter) Tuohy needle, and this problem has not recurred.

Two patients had operative sympathectomy. One of them had reported that pain was reduced after repeated temporary sympathetic blocks with a local anesthetic but that the symptoms promptly recurred within days after the injection. In this patient, sympathectomy, performed more than one year after the onset of symptoms, did not improve the scores for pain or function immediately, despite substantially improved circulation. The scores improved steadily over the following eight months with continued vigorous physical therapy and renewed psychological treatment. A second patient had operative sympathectomy because of severe circulatory insufficiency and swelling in the leg associated with recurrent cellulitis. Sympathectomy did not relieve the ongoing pain but it did prevent recurrence of infection. The patient remained unable to walk and had severe pain for an additional year, and then improved steadily with ongoing physical therapy; at follow-up, the score for function was 3 points and the average score for pain was 3 to 5 points.

One patient had bilateral chemical sympathectomy with phenol. This patient also had severe swelling, hypoperfusion, and recurrent infection. Four courses of infusion of a local anesthetic along the sympathetic chain produced good but temporary improvement in both pain and circulation. Blocks with phenol were done on each side separately with use of biplane fluoroscopy and contrast medium. There was a reduction of pain of more than 50 per cent immediately and at the three-year follow-up, as well as long-term improvement of circulation and resolution of infection.

To determine whether any clinical features of the disease or the patient at the time of presentation were prognostic of the outcome, we examined the predictive values of several presumed risk factors. These risk factors included the time to the initial visit and to the diagnosis of reflex sympathetic dystrophy, the age at the time of the injury, the sex of the patient, whether the injury was related to a supervised sport, the number of original sympathetic signs at the time of the diagnosis, whether or not the extremity was immobilized, and the number of school days missed during the year after the injury. The measurements of outcome that were included in the statistical analysis were the duration of symptoms, the latest scores for pain and function, the number of remaining autonomic signs, and the degree of current involve-

ment in sports. Among the presumed risk factors, only the patient's age at the time of the injury and the number of school days missed during the first year after the injury were statistically associated with changes in the indicators of outcome. Younger patients had a milder course than older ones. A younger age correlated with less pain, better function, fewer remaining signs of autonomic dysfunction on follow-up, and a shorter total duration of symptoms ($p < 0.01$ for each parameter). Younger patients were also more likely to return to sports: the mean age of the thirty-one patients who returned to sports was eleven years, and the mean age of the thirty-nine patients who did not return to sports was thirteen years and seven months ($p < 0.01$) at the time of the injury. The number of days of school missed during the first year after the injury was also predictive of outcome. The patients who missed fewer days had less pain, better function, and fewer autonomic signs at the time of follow-up ($p < 0.01$). The days of school that were missed did not correlate with the total duration of symptoms.

Discussion

There have been many reports on reflex sympathetic dystrophy in adults but few series, particularly in the orthopaedic literature, have included children. Ruggeri et al.²⁴ cited one study of 506 cases in which no patient was less than fifteen years old; these authors suggested that reflex sympathetic dystrophy in children is not a well recognized entity. In their case report of a ten-year-old child who had reflex sympathetic dystrophy, Carron and McCue⁵ stated that in their experience with more than 300 affected patients, no patient was less than sixteen years old. Bernstein et al.³ reported the largest series of reflex sympathetic dystrophy in a pediatric journal, to our knowledge — that of twenty-four cases in twenty-three children. These authors followed twenty patients who had a mean age of 12.4 years for an average of two and one-half years. In 1985, Rush et al.²⁵ stated that the cases of only fifty-seven children who had reflex sympathetic dystrophy had been reported to date.

The relative scarcity of reports on reflex sympathetic dystrophy in children has been taken to imply that the syndrome is rare in children. We suggest, as did Bernstein et al.³ and Lemahieu et al.¹⁵, that this disorder is not as rare in children as was once thought and that perhaps many cases are undiagnosed or misdiagnosed. Because, in our series, the average interval between the onset of symptoms and the first visit to the physician was ten days but the average interval to the time of diagnosis of reflex sympathetic dystrophy was twelve months, it appears that the diagnosis is often delayed in children. We suggest that the diagnosis of reflex sympathetic dystrophy in children is best made on the basis of a carefully taken history and a physical examination. It should be suspected whenever the severity or character of the pain does not fit the pattern of injury and the pain is associated with extreme sensitivity to light touch (allodynia);

episodic mottling, cyanotic discoloration of the skin, or swelling; or a difference in the skin temperature between the injured extremity and the contralateral one.

Several authors have suggested that reflex sympathetic dystrophy is much more benign in children than in adults. Bernstein et al.³ reported excellent responses to treatment among twenty children who were followed for a mean of 2.4 years: twelve patients had no complaints, five had occasional discomfort at the involved site, and two had moderate discomfort with intermittent swelling. One patient had a full recurrence after more than five years. Of the ten patients in the series of Kesler et al.¹¹, eight became free of symptoms, one continued to have mild episodic pain, and one had persistent pain. Ruggeri et al.²⁴ reported that all six of their patients had considerable improvement in symptoms. The report by Rush et al.²⁵ demonstrated that appreciable sequelae can occur. In contrast, Greipp et al.¹⁰ presented a much more pessimistic view of the disorder. In their questionnaire-based study, persistent pain and disability were the rule rather than the exception; pain was present at follow-up in 96 per cent of the patients. It is possible that a questionnaire-based study could be biased toward more severely affected patients.

Kesler et al.¹¹ and Ruggeri et al.²⁴ both suggested that trophic changes are not part of the symptom complex in children. Rush et al.²⁵ demonstrated that trophic changes can indeed occur. They described the cases of three patients who had substantial trophic changes, as well as a leg-length discrepancy, as a result of reflex sympathetic dystrophy during childhood. Bernstein et al.³ stated that there is "a rarity of chronic trophic changes" in reflex sympathetic dystrophy in children. Trophic changes were demonstrated at the time of referral to our program in ten of the seventy patients, and changes developed during treatment in an additional five patients. With treatment, these changes resolved or remained with only minor residua in thirteen of the fifteen patients. The two patients who continued to have severe atrophy declined to participate in multidisciplinary care and were particularly resistant to physical therapy and behavioral management. They sought treatment elsewhere.

Radiographs demonstrated fractures in only ten patients (14 per cent). The radiographic findings characteristic of advanced reflex sympathetic dystrophy in adults are typically not seen in children. Although bone-scanning has been reported to be helpful in the diagnosis of reflex sympathetic dystrophy in adults, studies have shown that the findings can vary in children who have reflex sympathetic dystrophy⁹. We suggest that the role of plain radiography and bone-scanning in the work-up of a child who apparently has reflex sympathetic dystrophy is not to make the diagnosis but rather to rule out other conditions such as stress fracture, infection, osteoid osteoma, or some other neoplasm²⁹.

The responses of the patients to treatment were highly variable and difficult to predict. Physical therapy

has been reported by many to be the mainstay of treatment in children. Bernstein et al.³ reported excellent results with physical therapy as the primary mode of treatment. They reported that twelve of twenty patients were free of symptoms after an average of 2.4 years of follow-up. We concur that physical therapy is the mainstay of treatment; 94 per cent of our patients participated in physical therapy. An obvious goal of physical therapy is to improve function, and our study showed that most of the patients progressed from no weight-bearing to unassisted walking.

Transcutaneous electrical nerve stimulation has been described as highly effective in the treatment of children who have reflex sympathetic dystrophy¹¹. Our results varied. Four of the sixty-one patients who had this therapy obtained complete relief of pain and symptoms and twenty-seven had some benefit; however, twenty-four patients reported no effect from transcutaneous electrical nerve stimulation, and six patients stated strongly that the treatment increased the pain. Because transcutaneous electrical nerve stimulation is very safe, with minimum complications or side-effects, we think that it should be attempted in most patients.

Thirty-seven (53 per cent) of our patients had at least one sympathetic block, generally because of persistently poor circulation, dysfunction of the limb, and an inability to tolerate physical therapy. We think that sympathetic blocks are appropriate when a patient has a clear clinical diagnosis of reflex sympathetic dystrophy, demonstrates persistent or progressive lack of use of the extremity, and cannot tolerate physical therapy. Failure of sympathetic blocks was common among patients who refused to cooperate with physical therapy and behavioral treatment. An intravenous phentolamine test may be a less painful or invasive way to demonstrate sympathetic dependence of pain than sympathetic blocks with a local anesthetic or a regional block with guanethidine given intravenously. However, the positive and negative predictive values of these procedures remain a subject of dispute²⁰. Patients who are unresponsive, even temporarily, to sympathetic blocks should still receive a vigorous multidisciplinary program that includes physical therapy and behavioral management. It is not appropriate to reject them from treatment on the grounds that the diagnosis of reflex sympathetic dystrophy is excluded by a negative response to a sympathetic block. Additional randomized prospective trials in children and adolescents are needed to determine if sympathetic blocks should be employed early in the course of treatment or if they should be used only after failure of conservative management involving physical therapy and techniques from behavioral medicine.

Ruggeri et al.²⁴ stated that there are no data to support the use of corticosteroids in the treatment of reflex sympathetic dystrophy in children. Steroids were used for a small minority of our patients; none of them reported a clear benefit. Given the risks and potential

side-effects of steroids, we suggest that they not be used routinely in the treatment of children who have reflex sympathetic dystrophy.

Previous investigators have retrospectively explored the psychological aspects of reflex sympathetic dystrophy²⁸. As with many chronic-pain conditions, it is difficult to determine, either for populations or for individual patients, the extent to which psychological factors cause or perpetuate the condition, or whether they are the result of chronic pain. A recent prospective evaluation of psychological factors was performed in a subgroup of our patients who had reflex sympathetic dystrophy and in control populations³⁰; we failed to detect statistical differences between the patients who had reflex sympathetic dystrophy and control groups by a variety of psychological measures of individual and family functioning. In our study population, there were no cases of major psychosis, and evidence for somatoform or factitious disorders was generally lacking. For certain patients, it appeared to all clinicians involved that pressures of academics or organized sports; substantial family stress such as divorce, marital conflict, or sibling rivalry; or concurrent illness amplified both the severity of symptoms and the reaction of the family to the symptoms of reflex sympathetic dystrophy²². The high prevalence of involvement of our patients in organized sports and dance was striking, and this association has been underemphasized in many previous reports. Although psychological antecedents and consequences of reflex sympathetic dystrophy are difficult to quantify, 60 per cent of our patients participated in psychological treatment, including biofeedback, relaxation training, cognitive-behavioral therapy, and individual or family psychotherapy. Many of these patients had favorable results. This supports our belief that such techniques should be an integral part of care.

The outcomes in our series were less favorable than in the series of Bernstein et al.³ or Kesler et al.¹¹ but were more favorable than those in the series of Greipp et al.¹⁰. Our data suggest that the severity of reflex sympathetic dystrophy in children and adolescents varies widely — some patients have relief of symptoms with physical therapy in several weeks, and others have persistent, disabling symptoms for several years, despite multiple types of conservative or invasive therapies. Although treatment produced substantial improvement in pain and function in the group as a whole, many patients still had considerable pain and dysfunction at the time of the latest follow-up (Figs. 3-A through 4-B). Only thirty-two patients (46 per cent) were free of symptoms at follow-up. Fewer than half of the patients who were competing in sports before the onset of symptoms returned to those sports after treatment. Several patients had a major disruption of their life and that of their family. Ninety-four per cent of the patients reported that the illness had adversely affected their schoolwork, due to absences from school totaling as much as one year. Three parents stopped working because of a perceived or real need to