# REFLEX SYMPATHETIC DYSTROPHY IN CHILDREN : REVIEW OF A CLINICAL SERIES AND DESCRIPTION OF THE PARTICULARITIES IN CHILDREN

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**Few series on reflex sympathetic dystrophy syndrome (RSDS) have included children. The present series reviewed 10 affected children. The group consisted of 9 girls and one boy with an average age at onset of 11 years (5 years to 16 years). The diagnosis was based on the clinical findings of pain, dysesthesia and autonomic system dysfunction. All patients underwent x rays and bone scans. Their results showed great variation. Minor trauma was the most common trigger factor. The lower extremities were more often involved. The treatment consisted of pain relief and progressive mobilization. Less conventional treatments in children, such as calcitonin and bisphosphonate were also used. The severity and duration of the disease varied greatly among these children. Moderate pain and sympathetic dysfunction persisted often up to two years after onset. Reflex sympathetic dystrophy is more common in children than previously thought. There are differences with the adult form in presentation and clinical course : the diagnosis is often delayed, the lower extremities are more often involved, girls are affected more often and idiopathic forms are frequent. Significant emotional dysfunction is found in a majority of patients and they are best treated as inpatients by a multidisciplinary team.**

**Keywords** : reflex sympathetic dystrophy ; algodystrophy ; children ; emotional dysfunction ; calcitonin ; biphosphonates.
**Mots-clés** : dystrophie réflexe sympathique ; algodystrophie ; enfant ; dysfonction affective ; calcitonine ; biphosphonate.

## INTRODUCTION

Evaluation and management of chronic pain disorders in children is a frequent reason for visits to the pediatrician or orthopedic surgeon. Unfortunately, the task is difficult because the differential diagnosis of limb pain in childhood is long and includes a diverse collection of illnesses which may vary over a wide range of clinical expressions. Reflex Sympathetic Dystrophy Syndrome (RSDS) is one of these. The syndrome has been recognized to be underreported in children with a substantial number of cases undiagnosed or misdiagnosed (6, 12, 18, 19). There still lacks a clear concept of the disorder. Precise diagnostic criteria are ill-defined. A variety of terms are applied to the syndrome. Therapeutic modalities are not well proved and our understanding of the pathophysiology is still poor (10). In the pathogenesis of RSDS, two main etiologies are proposed : involvement of the sympathetic nervous system or an abnormal inflammatory tissue reaction (8). Two large series (18, 19) based the diagnosis on clinical signs of neuropathic pain with physical signs of autonomic dysfunction. There is controversy about radiographic and bone scan changes. Many papers report an association of the disease with significant underlying psychologic stress (17, 18), but whether the disorder is the cause or the consequence of those psychological problems is not clear (13). Methods of treatment vary widely. The present paper reports 10 well-documented cases treated at our institution.

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## PATIENTS AND METHODS

The charts of young patients (upper limit fixed at 17 years old) in whom a final diagnosis of RSDS was confirmed at Saint-Luc University Hospital between 1984 and 1994 were reviewed. Nine girls and one boy met these criteria. The median duration of follow-up was 6.3 years (2 to 11 years) after the initial visit. Table I reports the symptoms at the initial visit and places them in relation to the frequency of the symptoms in the largest series of RSDS in children ever reported (19). The mean age of the 10 patients was 11 years (5-16 years). Diagnosis and treatment were often delayed by a mean of 3.3 months (range 0.5 to 18 months) from the onset of symptoms to the diagnosis. Eight of the 10 patients were treated as inpatients for part of the course of the disease. In 7 cases a trigger factor was found : one aneurysmal cyst of the calcaneum, one fracture of the tibia and five minor sprains of a joint. Lower extremities were involved much more commonly than upper extremities : 6 children had episodes primarily involving the ankle region.

Table I. — Symptoms at the initial visit in this series, in relation to the frequency of these symptoms in the series of Wilder (19)

| Sign or symptom | Number in our 10 patients | % in Wilder (19) series |
|---|---|---|
| Pain | 10 | 100 |
| Mechanical allodynia | 8 | 86 |
| Edema | 6 | 77 |
| Cold extremity | 6 | 77 |
| Cyanosis | 7 | 73 |
| Mottling of the skin | 6 | 64 |
| Hyperalgesia to cold | 5 | 63 |
| Hyperhydrosis | 1 | 31 |

The following sites were involved once in one child each : wrist, hip, knee, leg. In the hip, pain aggravated by activity and associated with limp was the presenting feature. Passive range of hip movement was reduced. To exclude any other disease, a majority of the patients had a thorough workup. In addition to the clinical picture, an x ray with signs of demineralization in conjunction with a bone scan showing hyperfixation helped to confirm the diagnosis. These signs were particularly important when the clinical signs were less evident (for example in the patient with localization at the hip). Roentgenograms and 3-phase bone scans were performed during the course of the disease (between 15 days and 12 months after the onset of symptoms) in every child. Osteopenia (fig. 1) was noted on radiographs in 7 cases (in conjunction with a positive bone scan in the third phase — fig. 2 — in 6 cases). In the three cases without osteopenia on radiographs, two showed hyperfixation on scintigraphy and one, hypofixation during the three phases. Biochemical analysis was performed in 9 patients and never showed signs of a rheumatologic or inflammatory disease. Electromyography and vascular doppler sonography were performed in one patient each and did not show any anomalies. Significant underlying psychological stress was evident in most of our patients, and four required consultation with psychiatrists. The patients were usually managed initially with physical therapy. The treatment focused on desensitization to tactile stimuli and on the use of heat, followed by passive range-of-motion exercises and progressive weight-bearing for patients who had involvement of a lower extremity. RSDS was frequently characterized by demineralization as seen on x-ray and by accelerated bone turnover as seen on three-phase bone scan. These characteristics led to the indication of using calcitonin in 8 cases at a dose of 50 units per day, in one subcutaneous injection, for 20 days. We noted nausea with higher doses and therefore lowered them. When the effect of calcitonin seemed to be insufficient, we tried by analogy another more potent antiresorber, the second generation bisphosphonate pamidronate (APD). Three patients were treated for ten consecutive days with intravenous infusions of 0.5 mg/kg of the second generation bisphosphonate, pamidronate, in saline over 4 hours. These 3 patients had already been treated with calcitonin

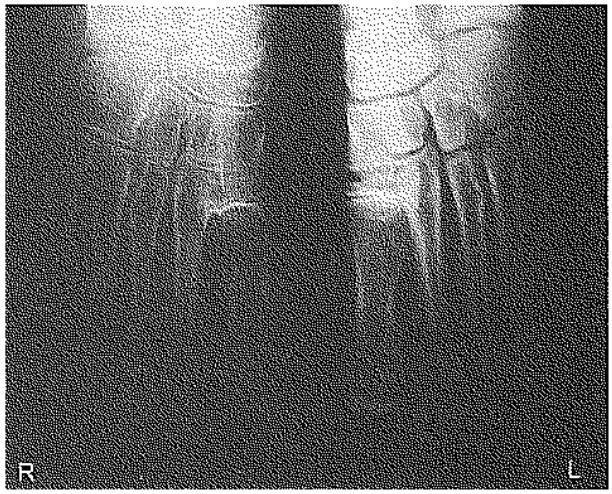
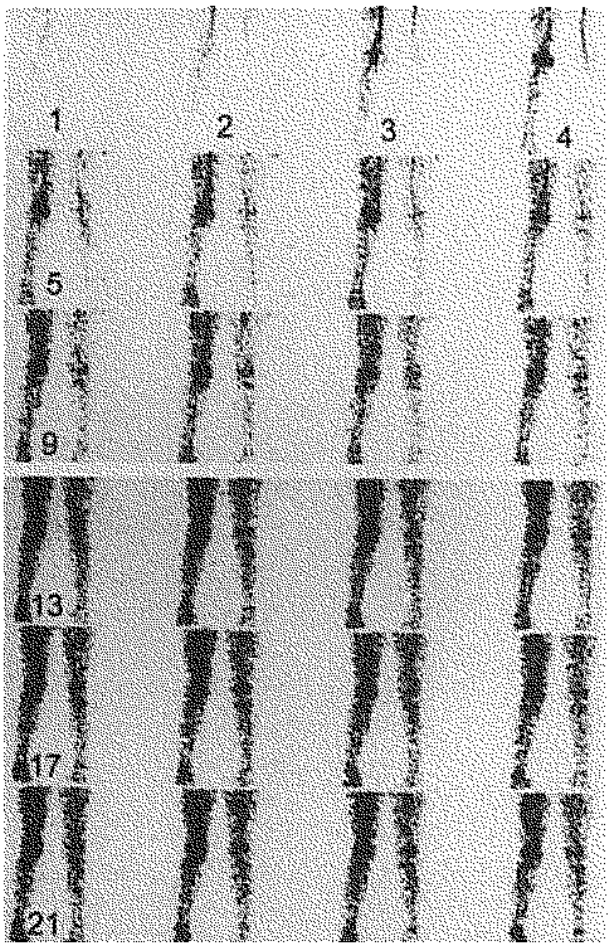



*Fig. 1.* — Fine-detail x-rays of the feet of a patient with RSDS, showing the normal left foot (L) and the demineralization in the affected right foot (R).

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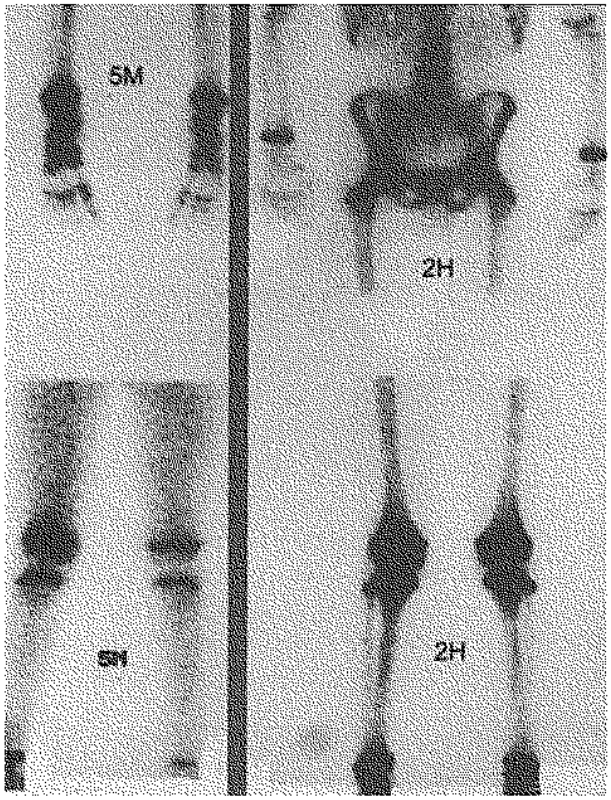


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*Fig. 2.* — Positive three-phase bone scan from a 5-year-old boy with RSDS of the right lower limb :
a) Rapid-sequence radionuclide (99mTc-MDP) flow studies of the lower limbs show asymmetrical flow.
b) Increased uptake in the right lower limb during the intermediate phase (blood pool), at 5 minutes.
c) Third-phase static scintigraph. The increased activity in the periarticular tissues of the affected right lower limb is evident.

and other means without success. In 2 cases, we noted benign secondary effects of this treatment : a self-limiting increase in temperature (less than 38°C) and transitory moderate lymphopenia. For those patients who presented with a swollen limb, nonsteroidal antiinflammatory drugs (NSAID's) were added. Although all the patients received psychological support by the physicians, only one received a well-defined psychologic treatment, including antidepressant drugs. The treatment of RSDS of the hip was only limitation of weight-bearing. None of the treatments used worsened the symptoms.

## RESULTS

Table II shows the various treatments and their reported effects. Calcitonin seemed to be effective in 5 out of 8 cases. The clinical symptoms improved favorably after the treatment with the second generation bisphosphonate, pamidronate, in all three cases. A regression of the symptoms, a real improvement in function and a nearly painless limb were noted after an average of 4.2 (1 to 12) months of treatment. We report the score

Table II. — Treatments applied to our 10 patients and their reported effects

| Treatment | Number of patients treated | Number of favorable effects |
|---|---|---|
| Physical therapy | 7 | 6 |
| Calcitonin | 8 | 5 |
| APD | 3 | 3 |
| NSAID'S | 5 | 1 |
| Psychotherapy | 1 | 1 |

for function at the latest follow-up in table III according to the classification of Wilder (19).

One patient showed recurrence of the disease in the same ankle one year after recovery from the initial symptoms. The initial treatment had been difficult. The recurrence was treated successfully with a second generation bisphosphonate. It seems that trophic changes can occur : we noted a difference between the diameters of the heads of the femur in a 13-year-old girl who presented with RSDS at the age of 7 years. The head of the right femur had a diameter of 50 mm and the left, which was involved with RSDS, a diameter of 54 mm (fig. 3).

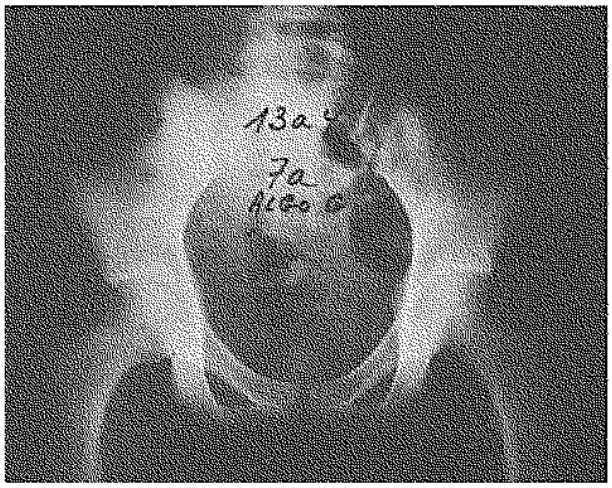

*Fig. 3.* — Anteroposterior radiograph of the hips of a 13-year-old girl, 7 years after the development of RSDS of the left hip. She developed a coxa magna on the left side.

## DISCUSSION

Until the late seventies, reflex sympathetic dystrophy was considered to be exceptional in children, and one finds mainly case reports (5). It is thus very difficult to estimate the real frequency of the disease because it is probably undiagnosed or misdiagnosed. The first larger series were published in the late seventies (2, 18, 19). These authors emphasize the clinical particularities in children and especially address the differences in presentation and clinical course with the adult form. Reflex sympathetic dystrophy in children is more often primary than in adults. About half the patients do not seem to have a trigger factor (2, 6). When a trigger factor is found, it is often minor trauma. This was the case in the present series. The delay in the diagnosis of RSDS can be from one week to up to one year. Often the child is first seen for minor trauma, and it can take a few visits until it becomes clear that the pain and symptoms are disproportionate to the causative event. The patient's background is also crucial : psychological evaluations reveal that up to 83% have some type of emotional dysfunction (18).

Table III. — Score for function in our 10 patients at the time of diagnosis and at latest follow-up according to the classification of Wilder (19)

| Score | Lower extremity | Upper extremity | Number of our patients | |
|---|---|---|---|---|
| | | | At diagnosis | Latest follow-up |
| 0 | Wheelchair | No movement | 3 | 0 |
| 1 | Crutches | Unable to eat or write | 4 | 0 |
| 2 | Cane | Can eat or write without difficulty | 3 | 0 |
| 3 | Unrestricted walking | Some atheletic restrictions | 0 | 2 |
| 4 | Athletic restrictions | No restrictions | 0 | 5 |
| 5 | No restrictions | No restrictions | 0 | 3 |

Problems at school, families having conflicts or being overprotective and abused children are noted psychosocial situations (17). The patient or the family is often reluctant to accept absence of a primary organic disease, and this complicates the diagnosis and handling of these patients. There is a significant predominance of girls. The peak age is 12 years. Lower extremity involvement predominates, and the foot and ankle are more often affected than the knee (19). The findings in the present series corroborate these facts. Hip involvement is rare and can lead to an enlarged femoral head and widened neck relative to the unaffected side (15). We attribute this difference to overgrowth of the involved hip due to temporary overvascularization (as confirmed by the blood-flow phase of scintigraphy) during the course of the RSDS. The most important clinical diagnostic finding is allodynia or pain provoked by stimuli not usually considered painful, such as light touch. Other common symptoms include pain rated as "severe", dysesthesias, or paresthesias. Pain may be the only symptom present at the beginning. This can also explain the difficulty of early diagnosis. Findings related to autonomic system dysfunction include skin color changes, swelling, cyanosis, abnormal hair growth (either too much or too little). One other quite frequent finding in children is coldness of the region as compared to the "normal" side. There can be a significant decrease in range of motion of the involved joint as well as muscle atrophy which may become irreversible if left untreated. These different symptoms are highly variable in their appearance as well as in the sequence of their presentation. Few patients will present all of these symptoms simultaneously. The present series confirmed these findings.

X-ray changes are found late in the course of the disease, even later than in adults. X-rays remain normal in half of the patients (2, 6, 18). Slight osteopenia is the most frequent finding but seems not to be a reliable criterion, since it cannot be differentiated from disuse osteopenia (10). Increased uptake, decreased uptake or a normal bone scan are reported (2, 7, 9, 11). This is a difference with the adult form where bone scan is specific, sensitive and a useful guide to therapy (10). In the present series a positive bone scan in the third phase was found in 9 out of 10 severely involved patients. Routine biochemical assays, hematology, bacteriology and serology are not relevant in algodystrophy (14). Other tests such as CT scan or MRI offer little information but are sometimes done in the workup of these patients where an organic cause had to be excluded (14). All these positive and negative findings allow elimination of other differential diagnoses (15).

All recent studies insist on the fact that the treatment is multidisciplinary (18, 19). The response of the patients to treatment is highly variable and very difficult to predict because the severity of the disease varies widely. A patient treated early in the course of the disease usually has a better response. Intensive and aggressive physical therapy brings relief in a few weeks for the less-involved patients, whereas multiple hospital stays and exhaustive rehabilitation programs are necessary for the more severely affected patients. Treatment modalities have proliferated because no single strategy provides remission in a majority of patients. They include : physical therapy, various types of immobilization, transcutaneous nerve stimulation, local anesthetic or steroid injections, intravenous or regional perfusion of steroids, oral corticosteroid, sympathetic blockade, subcutaneous injection of calcitonin and, in our series, also the use of intravenous injection of the second generation biphosphonate, pamidronate. The efficacy of these treatments varies widely : some authors (2) report excellent results with physical therapy, whereas others are less enthusiastic (18, 19). In the present series the treatment varied : 6 out of 7 patients responded well to physical therapy ; 5 out of 8 patients responded well to subcutaneous injection of calcitonin. Intravenous injection of diphosphonate was used in three patients where other treatment failed and was successful in all three. Striking relief of pain in RSDS following intravenous pamidronate was described in 1988 (4). Other reports confirmed that pain relief occurs in a lot of patients (1, 3). Pain relief can occur within 3 days of starting treatment (4) and may last for months (1, 3). Improvements within a few weeks in the function of the affected limb and in bone density have also been

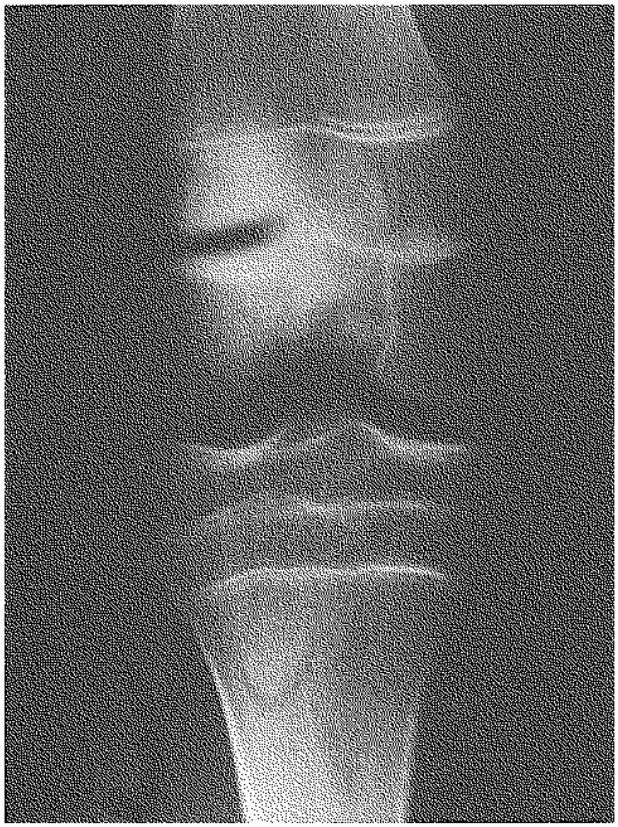

*Fig. 4.* — Anteroposterior radiograph of the right knee, previously affected by RSDS, of a 13-year-old girl. Note two bands of bone densification in the metaphysis of each long bone, due to two treatments with the bisphosphonate pamidronate 15 and 18 months earlier.

reported (1, 4). These drugs bind to bone and inhibit bone resorption by inhibition of osteoclasts (fig. 4), but processes that affect the structure of bone are not necessarily those responsible for the rapid pain relief (16).

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## SAMENVATTING

*O. BARBIER, N. ALLINGTON, J. J. ROMBOUTS. Reflex sympatische dystrofie bij kinderen : overzicht van een klinische reeks en beschrijving van de specifieke kenmerken bij het kind.*

Reflex sympatische dystrofie (RSD) bij kinderen wordt slechts zelden beschreven. Deze reeks bestaat uit 10 kinderen, 9 meisjes, één jongen met een gemiddelde leeftijd van 11 jaar (5 tot 16 jaar). De diagnose werd gesteld op de klinische bevindingen van pijn, dysesthesie en sympatische dysfunctie. Radiografieën en botscintigrafieën werden uitgevoerd met zeer wisselende uitkomst. Kleinere traumata waren meestal de oorzaak en het onderste lidmaat werd het meest getroffen. De behandeling bestond uit pijnstilling en progressieve mobilisatie. Andere minder conventionele therapieën zoals calcitonine en bifosfonaten werden eveneens gebruikt. De ernst en de duur van de RSD varieerde nogal bij deze kinderen met matige pijn en sympatische dysfunctie die tot 2 jaar na aanvang persisteerden.
RSD bij kinderen is waarschijnlijk meer voorkomend dan oorspronkelijk werd gedacht. De uiting en verloop zijn verschillend dan bij de volwassene : de diagnose wordt laattijdig gesteld, het onderste lidmaat meer getroffen dan het bovenste, meer bij meisjes en ideopatische vormen zijn frequent. Emotionele dysfunctie is significant aanwezig bij de meerderheid. De behandeling wordt best multidisciplinair en tijdens een hospitalisatie aangepakt.

## RÉSUMÉ

*O. BARBIER, N. ALLINGTON, J. J. ROMBOUTS. Dystrophie réflexe sympathique chez l'enfant : présentation d'une série clinique et description des particularités chez l'enfant.*

Seul un petit nombre de séries de cas d'algodystrophie sympathique réflexe inclut des enfants. La présente série analyse 10 cas d'atteinte chez l'enfant. Elle comprend 9 filles et 1 garçon âgés de 11 ans en moyenne (5 à 16 ans) au début de l'affection. Le diagnostic a été basé sur une symptomatologie clinique alliant douleurs, dysesthésies et dysfonctionnement du système nerveux autonome. Chez tous les patients, une investigation par radiographie et scintigraphie a été réalisée. Les résultats en sont variables. Le facteur déclenchant le plus habituel consiste en un traumatisme mineur. Il y a prépondérance d'atteintes aux membres inférieurs. Le traitement a été basé sur l'antalgie et la mobilisation progressive. Des traitements moins conventionnels chez l'enfant comme l'administration de calcitonine et de diphosphonate ont aussi été réalisés. D'importantes variations ont été notées dans le degré et l'importance de l'atteinte chez ces enfants. Des douleurs modérées et des troubles du système nerveux autonome ont souvent perduré jusqu'à 2 ans après le début des symptômes. L'algodystrophie sympathique réflexe est plus fréquente chez l'enfant que ce qui était habituellement reconnu. On peut noter des différences de présentation et d'évolution par rapport à l'adulte : le diagnostic est souvent tardif ; les membres inférieurs sont plus souvent atteints, l'atteinte est plus fréquente chez les filles et les formes idiopathiques sont fréquentes. Des troubles psychologiques sont notés chez la plupart des patients qui pourraient être traités au mieux, au cours d'une hospitalisation, par une équipe pluridisciplinaire.