

Treatment of Pediatric Localized Scleroderma: Results of a Survey of North American Pediatric Rheumatologists

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ABSTRACT. *Objective.* We surveyed pediatric rheumatologists (PR) in North America to learn how they treat pediatric localized scleroderma (LS), a disease associated with significant morbidity for the growing child.

Methods. A Web-based survey was sent to the 195 PR members of the pediatric rheumatology research alliance CARRA (Childhood Arthritis and Rheumatology Research Alliance). Members were asked which medications they use to treat LS and which factors modify their treatment strategies. Clinical vignettes were provided to learn the specific treatment regimens used.

Results. A total of 158 PR from over 70 clinical centers in the United States and Canada participated in the survey, representing 81% of the CARRA membership. These PR saw over 650 patients with LS in the prior year. Nearly all respondents treated LS with methotrexate (MTX) and corticosteroids; most of them intensify treatment for lesions located on the face or near a joint, and about half intensify treatment for recent disease onset (< 6 months). Most PR reserve topical medications for limited treatment situations. Clinical vignettes showed that PR use a broad range of treatment doses and durations for MTX and corticosteroids.

Conclusion. Most PR in North America treat localized scleroderma with a combination of MTX and corticosteroids. However, there is no consensus on specific treatment regimens. There is a need for controlled treatment trials to better determine optimal therapy for this potentially disabling disease. (First Release Nov 15 2009; J Rheumatol 2010;37:175–81; doi:10.3899/jrheum.090708)

Key Indexing Terms:

LOCALIZED SCLERODERMA PEDIATRICS DRUG THERAPY SURVEY

The optimal treatment for localized scleroderma (LS), a disease associated with significant morbidity for the growing child, is unknown. Because the disease often begins in early or mid-childhood and commonly affects deep tissue layers, children are at risk for major growth problems such as limb length discrepancy and hemiatrophy. About 20% of pedi-

atric patients have extracutaneous morbidity including arthritis, joint contractures, eye disease, and central nervous system involvement^{1,2}. Disability occurs frequently, with 25% of patients with linear scleroderma, the most common childhood LS subtype, reported to have mild or moderate disability at followup³.

Despite this potential for severe disease and adverse outcomes, no randomized controlled treatment trials have been carried out in pediatric LS patients. Case series report that methotrexate (MTX) appears effective for treating pediatric patients, but the published protocols vary greatly, particularly regarding dose, route, and frequency of concomitant corticosteroid therapy⁴⁻⁷. Improvement has also been reported with calcipotriol and topical medications such as imiquimod and tacrolimus⁸⁻¹⁰, but whether pediatric rheumatologists use such therapies is unknown.

To work toward developing a pediatric LS treatment trial, we carried out a survey to learn how pediatric rheumatologists (PR) in North America treat patients with LS. The survey included multiple-choice questions, open-ended options, and clinical vignettes. The survey followed the Padua Preliminary Classification Criteria of LS subtypes¹¹ with the exception that our interest was in the more serious forms of LS, so we excluded plaque morphea (circum-

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scribed superficial morphea) and asked about bullous morphea, which was not included in the Padua criteria.

MATERIALS AND METHODS

This survey was an effort of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Scleroderma Committee. CARRA is a North America pediatric rheumatology collaborative group. A Web-based survey (www.SurveyMonkey.com) was sent to all 195 pediatric rheumatology CARRA members in 2007. These 195 PR included 140 board-certified or senior PR (135 board-certified PR and 5 senior PR), 19 board-eligible PR, and 36 trainees (physicians in pediatric rheumatology fellowship programs). The majority of PR in North America are members of CARRA. In 2007, there were 249 North American members of the American College of Rheumatology who listed their specialty as pediatric rheumatology, including 10 clinicians who practiced both adult and pediatric rheumatology, 3 clinicians who practiced both allergy-immunology and rheumatology, and 50 trainees.

The aim of the survey was to learn how PR use systemic immunosuppressive medications to treat the more serious forms of LS; the survey therefore did not ask about circumscribed superficial morphea (plaque morphea). Definitions of the different LS subtypes were provided from the Padua Preliminary Classification Criteria¹¹: (1) circumscribed morphea (subtypes: superficial, deep), one or more oval or round lesions, with superficial lesions limited to epidermis and dermis, and deep lesions involving the subcutaneous tissue or panniculus; deep lesions often feeling taut and bound down; (2) linear scleroderma (subtypes: trunk/limbs, head), 1 or more linear lesions that can involve the underlying dermis, subcutaneous tissue, muscle, and bone; lesions on the head include *en coup de sabre* and Parry-Romberg syndrome; (3) generalized morphea, 4 or more large plaques (> 3 cm) that coalesce on at least 2 of 7 anatomic areas; the 7 areas are head/neck, right upper extremity, left upper extremity, right lower extremity, left lower extremity, anterior trunk, and posterior trunk; (4) pansclerotic morphea, deep generalized lesions that involve skin, subcutaneous tissue, muscle, and can involve bone; on extremities, there is circumferential involvement that spares fingertips and toes; no internal organ involvement for head or trunk lesions; and (5) mixed morphea, a combination of 2 or more of above subtypes. Bullous morphea was not included in the Padua proposed classification categories; this form involves formation of bullae, usually with ulceration of the skin, and extensive scarring and sclerodermatous changes.

Early exit points from the survey were provided for CARRA members who did not use systemic immunosuppressive medications, had limited experience treating these patients, or otherwise wished to exit the survey. The survey format consisted of multiple-choice questions and questions in which PR were asked to rank features. All questions provided an option to write in a response. Members were also provided with clinical vignettes and asked to describe their treatment strategy for the presented patients.

E-mail reminders were sent to obtain an overall response rate of at least 80% to ensure generalizability of the responses. When respondents listed a range of doses or durations, the average of the specified range was used. Descriptive statistics, including means, medians, and standard deviations, were calculated. For each disease feature a mean score was calculated by averaging the ranks.

RESULTS

Survey respondents. A total of 158 PR took the survey, representing 81% of the CARRA pediatric rheumatology membership. The respondents consisted of 114 board-certified or senior PR (81.4% of all CARRA board-certified/senior PR; 109 board-certified PR with average year of board certification 1995, median 1994; 5 senior PR), 15 board-eligible PR (79% of all CARRA board-eligible PR), and 29 fellows

(81% of all CARRA fellow members). The respondents came from a minimum of 71 different sites (18 responses were anonymous so that we could not identify responder's site), including all 28 pediatric rheumatology training programs in the United States and Canada; this represents 88% of the total 81 CARRA sites. There was a median of 2 respondents per site (range 1–6).

The respondents reported treating a total of 1041 patients with LS in the prior year, of whom 757 received systemic medications during the prior year. As these patient numbers may overestimate the LS population if patients are shared among the PR at a given site, we also calculated a “minimum” total patient number where we counted only 1 PR's patient count per site unless it was certain that duplication at a site did not exist. The patient numbers from the 18 anonymous survey respondents were excluded from this minimum count because their site affiliation was unknown. This yielded a minimum total of 666 patients with LS seen in the prior year, a median of 7.5 patients with LS at each site (range 0–86). The minimum number of patients with LS on systemic medications was 476 in the prior year, a median of 5 patients on systemic medications at each site (range 0–73).

A total of 33 respondents chose 1 of the 2 survey early exit points, either because they had never used systemic medications to treat LS (3 fellows, 1 board-eligible and 4 board-certified PR), because they did not treat patients with LS, or for other reasons. These 33 PR included 17 board-certified or senior PR, 4 board-eligible PR, and 12 fellows, and came from 19 sites (there were 3 anonymous respondents whose site we did not know). Overall, 125 PR continued with the survey.

The group that chose to exit the survey early had fewer experienced clinicians than the group that continued with the survey. Forty-eight percent of the early exit respondents had just finished training (board-eligible) or were still in fellowship, compared to 25% of those who continued with the survey. Moreover, the PR who chose to exit early saw fewer patients with LS in the prior year (median 2 patients) than those who continued with the survey (median 5 patients).

Treatment of different LS subtypes. PR were asked if they thought all patients with a specific LS subtype should be treated with systemic medications at some point during their disease course. The queried subtypes were circumscribed deep morphea, linear scleroderma of face or scalp, linear scleroderma of trunk or limb, generalized morphea, mixed morphea, pansclerotic morphea, and bullous morphea. Most PR thought patients with any of these subtypes should be treated with systemic medications, with a high level of agreement for linear scleroderma of face or scalp (92%), pansclerotic morphea (87%), linear scleroderma of trunk or limb (83%), and generalized morphea (77%). There was a lower level of agreement for treating mixed morphea, circumscribed deep morphea, and bullous morphea with systemic medications (68%, 66%, and 56%, respectively), with

15% and 29% of respondents choosing “do not know” for mixed morphea and bullous morphea treatment, respectively. *LS treatment medications.* When asked which systemic medications they use to treat LS, nearly all respondents use MTX administered subcutaneously (93.5%, 115/123 respondents) or orally (88.6%, 109/123). The majority of respondents also use oral corticosteroids (prednisone, 76.4%, 94/123) and intravenous methylprednisolone (IV MP, 68.3%, 84/123). A minority of respondents use oral cyclosporine (17.1%), oral tacrolimus (7.3%), hydroxychloroquine (7.3%), or mycophenolate mofetil (4.9%). Calcitriol, etanercept, intravenous gamma-globulin, D-penicillamine, azathioprine, imatinib, and pimecrolimus were each mentioned by no more than 2 respondents.

Most respondents use topical medications (64.5%, 78/121), with one-third willing to use topical therapy alone (33.1%, 40/121), and the others using them in conjunction with systemic therapy (31.4%, 38/121). The majority of those who were willing to use topical therapy alone specified that this treatment should be reserved for minimal disease, such as small, flat, and/or shallow lesions that were considered inactive or minimally active. Lesions on the face, head, near a joint, or in a cosmetically significant region were considered inappropriate sites for isolated topical treatment. The most commonly used topical treatments were corticosteroids (60.3%, 47/78), calcipotriene (42.3%, 33/78), tacrolimus 0.1% (41.0%, 32/78), pimecrolimus 1% (21.8%, 17/78), tacrolimus 0.03% (14%, 17/78), and imiquimod (9.1%, 7/78). Pimecrolimus 0.3% and sirolimus were infrequently used.

Factors that influence treatment. PR were asked whether specific disease characteristics altered their treatment strategy. Most respondents would treat lesions on the face (85.5%, 106/124) or near a limb joint (83%, 103/124) more aggressively (i.e., larger medication dose, longer duration of treatment, adding intravenous corticosteroids). About half the respondents treated scalp (51%, 63/124) and genital (44%, 55/124) lesions more aggressively. Few thought lesions on other body areas warranted more treatment.

About half the respondents (47%, 58/124) varied treatment according to disease duration, treating patients with recent onset (< 1 month 24%; 1–3 months 29%; 3–6 months 23%) more aggressively than those with longstanding disease. Most respondents did not modify treatment based on patient age (75%, 93/124). Those who did tended to treat younger patients more aggressively (age < 3 years 22%, 3–6 years 20%, 7–10 years 15%, 11–14 years 14%, > 15 years 1%). Similarly, the majority did not vary treatment in response to patient developmental stage (70%, 87/124); among the 30% who did, prepubertal (27%) or pubertal (20%) patients were treated more aggressively than those who were postpubertal.

Features of disease activity and remission. For these questions, we did not define disease activity or remission

because definitions for these terms do not currently exist for LS. Instead, we sought to elicit the characteristics that PR thought represent active and inactive disease, and how long the disease should appear inactive before the PR thinks the disease is in remission. PR were asked to rank features indicative of disease activity from 0 (irrelevant) to 5 (important indicator). Six features were rated as high activity features: new lesion, extension of an existing lesion, erythema, swelling or induration of lesion margin, violaceous color, and lesion edge warmth (mean scores 4.78, 4.62, 4.55, 4.40, 4.24, and 4.05, respectively). These features were significantly higher than distinct margin, subcutaneous atrophy, hyperpigmentation, dermal appendage atrophy, skin atrophy, or hypopigmentation (mean scores < 2.5). Additional high activity features listed by some PR were elevated acute-phase reactants, eosinophilia, discomfort, hidebound feel, and calcinosis.

PR were asked which features needed to be present before they would stop LS treatment. Most required the absence of features that they felt indicated activity, namely absence of new lesions (99%, 123/124), stable lesion size or shrinkage (98%, 121/124), lack of erythema (94%, 116/124), lack of violaceous coloration (87%, 108/124), and flat margins or resolution of marginal induration (77%, 96/124). The majority (60%, 74/124) also required resolution of laboratory indices of inflammation, while 22% (27/124) of respondents required completion of linear growth.

When asked the duration of time elapsed since the last indication of active disease before they would consider a patient in remission on medications, most specified 12 months (40%, 50/124) or 6 months (31%, 38/124). Complete remission required 12 months (54%, 67/124) or 24 months (28%, 35/124) of inactive disease off all medications. However, 8% said they did not know when complete remission was achieved.

Clinical vignettes. To learn if most PR follow similar treatment protocols, PR were asked to detail their treatment of clinical vignettes. PR were asked to assume that the presented vignettes were similar to average patients who fit the vignette history, and to assume that the vignette patients had an average response to treatment. All respondents were given the same vignette of a 4-year-old girl with a 2-month history of a linear LS lesion on her right lateral leg extending across her ankle. Her lesion was initially swollen, with an erythematous-violaceous border, and had warmth and subcutaneous tissue loss at the time of her visit. Her laboratory studies show an elevated erythrocyte sedimentation rate.

All respondents would treat this vignette patient with MTX, with most using the subcutaneous route (57%, 65/114; Table 1). The other respondents were equally divided between using oral MTX and not having a preference for route of administration. The majority of respondents calculated MTX dose based on body weight (mg/kg). For the 27% of respondents who calculated dose based on body sur-

Table 1. Methotrexate treatment regimen for linear scleroderma clinical vignette. The number of respondents (Resp) who specified a given initial methotrexate (MTX) dose and route of administration for the clinical vignette of a 4-year-old girl with linear scleroderma of her leg are shown. Initial MTX dose refers to the dose specified at the start of treatment, and is in milligrams per kilogram body weight per weekly dose (mg/kg). Doses that had been specified as milligrams per square meter of body surface area (mg/m²) were converted to mg/kg, assuming that the vignette patient was at the 50% for height and weight for a 4.5-year-old girl; this gave her a body surface area of 0.7 m². An MTX dose of 10 mg/m² became 0.41 mg/kg, 15 mg/m² became 0.62 mg/kg, 20 mg/m² became 1 mg/kg. Duration is expressed in months.

Initial MTX Dose	No. Resp (No. Ind)	No. SC	No. Oral	No. SC/Oral	Median Induction Duration (range)	Median Total Treatment Duration (range)	No. Did Not Specify
0.3	3 (2)	0	2	1	2 (1–3)	24 (15–25)	0
0.41	6 (3)	1	2	3	2 (1–6)	20.5 (13–30)	2
0.5	20 (15)	11	4	5	2.5 (1–12)	14 (6–36)	2
0.6–0.62	26 (13)	14	6	6	6 (2–24)	24 (12–48)	7
0.72–0.75	9 (2)	2	5	2	9 (6–12)	24 (12–30)	3
0.8–0.88	5 (3)	2	1	2	2 (1–3)	20.5 (15–24)	1
1.0	45 (23)	35	5	5	6 (1–24)	24 (3–48)	17
Overall: no. or duration (range)	114 (71)	65	25	24	6 (1–24)	24 (3–48)	32

Ind: number of respondents who specified separate induction and maintenance phases; SC: number of respondents who specified treating with the subcutaneous form of MTX; Oral: number of respondents who specified treating with the oral form of MTX; SC/Oral: number of respondents who would treat with either the subcutaneous or oral form of MTX; Did not specify: number of respondents who did not specify a treatment duration.

face area (mg/m²), the most frequently specified dose was 15 mg/m² (16.7%, 19/114). To simplify presentation of the MTX data, we converted the mg/m² doses into mg/kg dose by assuming that the vignette patient was a 4.5-year-old girl who was at the 50% for weight (17 kg) and height (104.3 cm), giving her a body surface area of 0.7 m² (weight and height values from the Centers for Disease Control girls 2–20 years growth chart, version 5/30/00, modified April 20, 2001, <http://www.cdc.gov/growthcharts>). The most commonly chosen MTX dose was 1 mg/kg weekly (39.5%), followed by 0.6 to 0.62 mg/kg (22.8%) and 0.5 mg/kg (18%) weekly.

About 60% (71/114) of respondents specified separate MTX induction and maintenance treatment phases. The median induction phase duration was longer for those who specified 0.72 to 0.75 mg/kg/dose (9 months), 1.0 mg/kg/dose (6 months), or 0.6–0.62 mg/kg/dose (6 months) compared to other doses (2 to 2.5 months). However, the significance of this is not clear, as many respondents did not change the MTX dose or route of administration for the 2 phases. Some respondents may have divided MTX dosing into 2 phases based on the corticosteroid-dosing regimen. The median specified total MTX treatment duration was 24 months, with a range of 3 to 48 months. About 30% (32/114) of the respondents did not specify a treatment duration, stating that duration would be determined by the patient's response to treatment.

Although nearly all respondents (96%, 110/114) would also treat this patient with corticosteroids, there was great variability in recommended regimens. Slightly more PR (40%) specified treatment with only intravenous corticosteroids or methylprednisolone 30 mg/kg/dose (IV MP) versus only oral corticosteroids or prednisone (30%), or a com-

bination of both oral and intravenous corticosteroid (combination corticosteroids, 27%; Table 2). Most of the respondents who specified combination corticosteroids or prednisone alone would follow an induction and maintenance regimen (90% and 65%, respectively), while only 38% of those using IV MP alone specified a separate maintenance regimen (data not shown).

The most commonly specified initial corticosteroid dosing regimens were IV MP given 3 consecutive days monthly (29%), prednisone 1 mg/kg/day (25%), IV MP given 3 days weekly (17%), and IV MP given once weekly (17%). Most of the respondents who would use IV MP 3 days/month did not combine it with prednisone, while the majority of those who would use IV MP 3 days/week or 1/week would also treat with prednisone. About one-third of the respondents who would initially treat with prednisone 1 mg/kg/day would also treat with IV MP.

The median duration of corticosteroid induction treatment was 2 months and median duration of total corticosteroid treatment was 4 months; 13% of respondents did not specify a duration for corticosteroid treatment (Tables 2 and 3). The total amount of corticosteroid given to this patient was calculated from each respondent's specified dose and treatment duration. The median total corticosteroid treatment amount was 270 mg/kg for respondents treating with IV MP or combination corticosteroid, and 120 mg/kg for respondents treating only with prednisone. Respondents differed enormously in treatment specifics, with the total amount of corticosteroid given to this patient ranging from 30 to 1080 mg/kg and the total duration of corticosteroid treatment ranging from 0.25 to 30 months.

Vignette variations and other clinical vignettes. Respondents were asked if they would alter treatment of this

Table 2. Initial corticosteroid (CS) treatment regimens for linear scleroderma clinical vignette. The number of respondents (Resp) who specified a given CS dosing regimen for the clinical vignette of a 4-year-old girl with linear scleroderma of her leg are shown. Treatment durations are in months. The listed initial prednisone doses represent milligrams per kilogram (mg/kg) body weight per day. Intravenous methylprednisone (IV MP) was dosed at 30 mg/kg/dose, at infusion frequencies of 1 infusion per month (1/mo), 3 consecutive daily infusions per month (3 days/mo), 1 infusion per week (1/wk), or 3 daily infusions per week (3 days/wk). All 31 respondents who specified combination CS treatment (Comb) would initially treat the patient with IV MP; 24 would also initially treat with prednisone, and the remaining 7 would use prednisone for maintenance treatment.

Initial CS Dose	No. Resp	No. Prednisone Only	No. IV MP Only	No. Comb	Median Induction Duration	Range of Induction Duration
No CS	4	NA	NA	NA	NA	NA
Prednisone						
0.5	11	6	NA	5	2.0	1–6
1	28	18	NA	10	1.0	1–6
2	18	10	NA	8	1.0	0.5–6
QOD	1	0	NA	1	2.0	1
IV MP						
1/mo	5	NA	4	1	6.0	1–6
3 days/mo	33	NA	28	5	3.0	1–6
1/wk	19	NA	8	11	1.0	1–2
3 days/wk	19	NA	4	15	0.25	0.25–3
Overall no., duration, or range	114	34	45	31	2.0	0.25–6

QOD: every other day dosing; No. Prednisone Only: number of respondents who specified only using the oral form of corticosteroid for treatment; No. IV MP Only: number of respondents who specified only using the intravenous form of corticosteroid for treatment; No. Comb: number of respondents who specified treating with both the intravenous and oral forms of corticosteroid; NA: not applicable.

Table 3. Duration and total amount of corticosteroid (CS) treatment for linear scleroderma clinical vignette. The number of respondents (Resp) who specified a given CS regimen, and number of respondents who did not specify treatment duration, for the clinical vignette of a 4-year-old girl with linear scleroderma of her leg are shown. The CS regimen refers to those specified for initial treatment (induction) or for overall treatment for respondents who did not have a separate induction and maintenance phase. Prednisone doses of 0.5, 1, and 2, represent milligrams per kilogram of patient body weight (mg/kg) per day, and intravenous methylprednisone (IV MP) was dosed at 30 mg/kg/dose, at infusion frequencies of 1 infusion per month (1/mo), 3 consecutive daily infusions per month (3 days/mo), 1 infusion per week (1/wk), or 3 daily infusions per week (3 days/wk). IV MP + prednisone refers to respondents who used both IV MP and prednisone. Total CS treatment duration (months) includes both induction and maintenance phases. Treatment amount is expressed as milligrams of CS per kilogram of patient body weight.

CS Regimen	No. Resp	Median Total CS Duration (range)	Median Total CS Amount (range)	No. Did Not Specify
None	4	NA	NA	NA
Prednisone only				
0.5	6	5.5 (2–8.5)	41 (30–90)	2
1	18	4.5 (1–13)	75 (30–240)	1
2	10	8.3 (3–30)	180 (100–552)	1
IV MP only				
1/mo	3	6.5 (1–18)	195 (30–540)	0
3 days/mo	28	3.0 (2–9)	270 (90–790)	6
1/wk	8	2.0 (1–14)	238 (30–630)	2
3 days/wk	5	3.1 (0.25–6.5)	675 (90–1080)	1
IV MP				
1/mo + prednisone	1	12 (12)	890 (890)	0
3 days/mo + prednisone	5	5.5 (4–9)	360 (233–615)	1
1/wk + prednisone	11	7.0 (4–15)	270 (135–765)	0
3 days/wk + prednisone	14	6.3 (2.25–9)	270 (165–791)	1
Overall no., duration, or amount (range)	114	4.0 (0.25–30)	240 (30–1080)	15

NA: not applicable.

vignette patient if the patient presented differently. Most (68.1%, 77/113) would treat less intensely (less or no corticosteroid, no treatment, no MTX, or shorter treatment dura-

tion) if the disease began 2 years before presentation to the pediatric rheumatologist, the lesion showed mild induration but no warmth or color change, and laboratory markers were

normal. Nearly 60% (66/113) would treat less intensely if the lesion was confined to mid-calf and did not cross a joint. Most would not alter treatment if the patient was 12 or 15 years old instead of 4 years [91.2% (103/113) and 85.8% (97/113), respectively].

Survey respondents were randomly assigned to receive 1 of 2 sets of 2 other clinical vignettes. These vignettes included circumscribed deep morphea of the forehead, linear scleroderma of the face, generalized morphea, and pansclerotic morphea. The majority of respondents would treat all of these patients with MTX [ranging from 91% (generalized morphea) to 100% (linear scleroderma of face and circumscribed deep morphea)] and corticosteroids [ranging from 84% (generalized morphea) to 97% (linear scleroderma of the face)]. Patient treatment appeared to be more influenced by the presenting features of the patient than by the patient's LS subtype. Treatment regimens for all vignettes showed a similar lack of consensus in medication dose, route of administration, and durations (data not shown).

DISCUSSION

This is the first study to examine treatment practices for pediatric localized scleroderma using a clinical vignette survey format. The 158 pediatric rheumatologists who participated in the survey included the majority of the pediatric rheumatology membership in CARRA, and represented over 70 institutions from across the United States and Canada. These physicians cared for between 666 and 1041 patients with LS in the year preceding the survey. Their responses should therefore reflect the general practice policies of pediatric rheumatologists in North America. The majority of survey respondents were experienced PR, with the average date of board certification 12 years prior to the survey. However, because 1992 was the first year of pediatric rheumatology board certification by the American Academy of Pediatrics, the board certification year does not adequately reflect the experience and years in practice for many of these PR.

The optimal treatment strategy for LS is unknown. The evidence base primarily consists of case series demonstrating response to therapies that range from topical creams to ultraviolet irradiation to systemic medications^{12,13}. Despite the lack of high quality evidence to support treatment decisions, we found substantial agreement among PR on the use of systemic medications to treat LS; only 5% of respondents did not use systemic medications to treat these patients. While adult rheumatology and dermatology studies commonly advocate topical treatments and phototherapy^{9,10,14-17}, most pediatric rheumatology respondents thought topical medications have a limited role, reserving them for use in conjunction with systemic treatment or for small, minimally active, inconspicuous lesions. This difference in treatment approach may reflect differences between pediatric and adult patients with LS, as pediatric patients

often have deep tissue involvement and have not completed their growth and development. In addition, there may be differences in the referred patient population as several PR said they typically saw only patients who had already failed topical treatment.

Early nonrandomized, open-label studies reported efficacy with MTX⁴ or oral corticosteroid as solo treatments for LS¹⁸. More recent studies have reported benefit from using combined MTX and corticosteroid treatment, with more reports employing intravenous than oral corticosteroids^{5-7,19}. Such combination strategy has acquired support with pediatric rheumatologists; over 90% of respondents used MTX to treat all the vignettes, with over 80% specifying concomitant corticosteroid treatment.

Although there was excellent agreement on choice of systemic medications for LS treatment, the clinical vignette responses showed that there was no clear consensus on dosing regimens. There was over a 3-fold range in MTX dose and over a 16-fold spread in MTX treatment duration for the first vignette patient. Respondents showed an even greater variation for corticosteroid treatment, with over a 30-fold range in total treatment amount, and over 100-fold difference in total treatment duration. The most commonly specified initial corticosteroid treatment dose was that from the first published IV MP dosing regimen for pediatric LS (30 mg/kg/dose, 3 consecutive days per month for 3 months)⁵. However, only about half the 29% of respondents who specified this dose strictly followed the published regimen. The others varied the duration of treatment, also treated with oral prednisone, or continued treatment with a different IV MP regimen. No one followed the combination oral and intravenous corticosteroid dosing regimen (IV MP 3 days/week for 2 weeks, prednisone given between and after the infusions) specified by Weibel, *et al*⁷.

Most respondents did not consider LS subtype (in this survey, that excluded consideration of circumscribed superficial morphea) to be a major factor in determining treatment. Instead, treatment was determined based upon signs of activity and specific patient features. Nearly all respondents favored more aggressive treatment of lesions located on the face or near a limb joint. Facial lesions are associated with an increased risk of ocular and central nervous system involvement^{2,11,20,21}, and lesions near a joint can result in contractures and functional disability¹¹. About half the respondents favored more aggressive treatment for recent disease onset (up to 6 months duration). This may reflect a belief in a "window of opportunity" for treatment, with newer lesions considered to be more "inflammatory" and more likely to respond to immunosuppressive medications. Uziel, *et al* reported earlier response to treatment in patients with more recent disease onset; however, Weibel, *et al* did not find any correlation between treatment response and disease duration^{5,7}.

Pediatric rheumatologists normally continue treatment

for a period of time after the disease appears to be inactive, before considering the disease to be in “remission on medications.” The most commonly chosen times were 6 and 12 months, while the time usually chosen for remission off medications was 12 and 24 months, similar to those proposed for juvenile arthritis²²⁻²⁴. However, many respondents expressed marked uncertainty about the duration of remission off medication. This likely reflects the difficulty of assessing disease activity in these patients and the significant rate of disease recurrences^{25,26}. Although active disease duration has been reported to be 2 to 5 years, this may not accurately reflect pediatric disease. In a study reviewing LS patient records for 33 years, 20% of patients with the most common childhood LS subtype, linear scleroderma, were still found to have active disease 20 years after disease onset³.

Our study is limited by its use of clinical vignettes that present incomplete information to the clinician compared to that available by direct clinical examination. However, clinical vignettes have been useful tools for assessing practice variation, and can provide better assessment than retrospective chart reviews²⁷. Many survey questions offered multiple-choice answers, which may have limited the responses. We tried to minimize this limitation by providing many choices and an open-ended option, as well as asking PR to rate all items for other questions. As with all questionnaires, some respondents may have found some questions ambiguous.

Our survey indicates that the majority of PR in North America use systemic medications to treat LS, with most employing a combination of MTX and corticosteroids in the initial approach to childhood LS. However, dosing and duration of therapy varied widely and highlight the need for treatment trials to better evaluate treatment efficacy. Better understanding of optimal treatment is vital to reduce the morbidity suffered by growing children with this disease.

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