American Experience With Low-Dose Thalidomide Therapy for Severe Cutaneous Lupus Erythematosus

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Background: There is a renewed interest in thalidomide therapy after its surprising effectiveness in treating erythema nodosum leprosum was first published. Thalidomide has subsequently been reported to be effective in treating a number of dermatoses, including cutaneous lupus erythematosus. We examined the efficacy and adverse effects of low-dose, long-term thalidomide monotherapy in 7 patients with various forms of cutaneous lupus erythematosus that were unresponsive to traditional systemic treatments.

Observations: Six of the 7 patients treated with thalidomide after discontinuation of other oral agents had complete or marked resolution of their previously treatment-resistant cutaneous lesions, with an average response time of 2.2 ± 0.8 months. Our cohort of 7 patients with cutaneous lupus erythematosus was treated with thalidomide therapy for an average of 2.4 ± 3.1 years (range, 1 month to 9 years). The most common adverse effects were sedation, constipation, and weight gain. Two patients reported experiencing intermittent shaking episodes, an adverse effect not previously reported in the literature. Four patients reported symptoms of paresthesia, but none was found to be caused by thalidomide-induced peripheral neuropathy.

Conclusions: A low starting dose of thalidomide as a monotherapy with continued sun avoidance is a safe and effective treatment for the various cutaneous manifestations of lupus erythematosus after traditional therapeutic options have failed to control disease. Our experience with low-dose, long-term thalidomide therapy suggests that peripheral neuropathy is not as common as suggested by other studies (up to 50% of patients treated with thalidomide in some series).

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HALIDOMIDE (α-N-phthalylglutamic-acid-imide), a glutamic acid derivative, was first synthesized in 1956 by Kunz and his coworkers in West Germany.1,2 Thalidomide became widely used as a sleeping aid but was removed from the market after teratogenic and neurologic effects were established.3-12 Subsequently, thalidomide became available only for experimental purposes. There was renewed interest in the clinical uses of thalidomide after Sheskin reported in 1965 the effectiveness of thalidomide in treating erythema nodosum leprosum. Sheskin, after giving thalidomide to patients with leprosy for sedative purposes, made a serendipitous discovery that the treatment resulted in immediate improvement in symptoms, and that the patients’ cutaneous erythematos lesions resolved in as little as 3 days. His findings were confirmed by other reports13-16 and by his follow-up study.17

Recently, thalidomide therapy has been approved by the Food and Drug Administration for the treatment of erythema nodosum leprosum. However, it remains an experimental treatment for a variety of inflammatory skin disorders.18 Among those reported included actinic prurigo,19,20 orogenital ulcerations,21-23 Weber-Christian disease,24 graft-vs-host disease,25-28 and chronic cutaneous lupus erythematosus (CCLE).29,30

Many European studies have documented that thalidomide is an effective treatment for various inflammatory dermatoses, such as cutaneous lupus erythematosus (CLE), that are unresponsive to standard therapy. Knop et al31 in a study of 60 cases of CCLE, reported that 90% of the patients had a complete or marked response to treatment with thalidomide, 400 mg/d, and that 71% had relapses when thalidomide was withdrawn. Stevens et al32 had similar findings with thalidomide, 50 to 100 mg/d, with various adjustments, if any, in the doses of other oral medications already being used to treat CLE. Improvements were observed within 2 weeks of treatment, and maximum benefits were
PATIENTS AND METHODS

We reviewed the medical records of 7 women with disfiguring CLE who were treated with thalidomide in a 100-mg/d starting dose after exhausting the other therapeutic options, including glucocorticosteroids, antimalarials, immunosuppressants, dapsone, clofazimine, and retinoids. These patients continue to receive thalidomide therapy. Candidates for thalidomide therapy were selected by the presence of severe CLE that had previously been treated with first- and second-line therapies. This treatment was offered on a compassionate basis by the Department of Dermatology, University of Rochester, Rochester, NY, for patients who had been referred by community dermatologists. Table 1 lists their conditions and Table 2 describes the therapeutic modalities that failed. Candidates were further selected by their ability to understand the risks and benefits of thalidomide therapy. Further requirements included a willingness to comply with the monitoring requirements, and to sign an informed consent (reviewed and approved by the University of Rochester Research Subjects Review Board). After a candidate for thalidomide therapy was identified, a single-patient investigational new drug application was submitted to the Food and Drug Administration. After this application was submitted and approved (usually 3-6 months after submission), the Food and Drug Administration issued an investigational new drug number (see Table 3). Contraception was initiated in women of childbearing age. A prescription with payment and IND number were mailed to the supplier of thalidomide. This drug was then mailed to the prescribing physician, who dispensed the thalidomide to the patient. All 7 patients were treated according to the published guidelines for thalidomide use. All other systemic medications for controlling CLE were discontinued. The patients returned every 3 months for follow-up, and the efficacy and adverse effects of their thalidomide treatment were documented. Nerve conduction studies, complete blood cell counts, 12-factor automated blood chemistry studies, and thyroid studies (free thyroxine, thyrotropin) were done every 6 months or sooner as needed for baseline comparison. Any change in blood cell count or results of serum chemistry studies was followed up closely to determine if it was thalidomide related. All patients were examined at baseline with a complete neurologic examination, with a focus on clinical assessment of touch, scratch, vibratory, and position sensations. These examinations were repeated at 6-month intervals during thalidomide therapy. Nerve conduction studies were done in all patients at baseline and at 6-month intervals to detect evidence of drug-induced sensory or motor loss in the extremities. The nerve conduction studies included unilateral examination of the arm and leg. Standard techniques of percutaneous stimulation and surface recording were used. Motor conduction velocity, distal motor latency, and the amplitude of the compound muscle action potential were measured from the common peroneal, tibial, ulnar, and/or median motor nerves. Sensory conduction velocity, sensory distal latency, and the amplitude (baseline to negative peak) of the sensory nerve action potential (SNAP) were obtained from the sural, superficial peroneal, ulnar, and/or median sensory nerves. The patients understood that they must stop taking thalidomide should they begin to experience paresthesia. All patients continued sun avoidance and use of sunscreen.

Table 1. Patient Histories*

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>Duration of Cutaneous LE, y</th>
<th>Lesion Sites</th>
<th>Diagnosis</th>
<th>1982 ARA Criteria for SLE</th>
<th>Autoantibodies</th>
<th>Contraception</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/46</td>
<td>25</td>
<td>Scalp</td>
<td>CCLE</td>
<td>ANA</td>
<td>ANA</td>
<td>Tubal ligation</td>
</tr>
<tr>
<td>2/F/48</td>
<td>7</td>
<td>Scalp, face, trunk, extremities</td>
<td>CCLE, SLE</td>
<td>Malar rash, discoid rash, photosensitivity, ANA</td>
<td>Malar rash, discoid rash, photosensitivity, ANA</td>
<td>Tubal ligation</td>
</tr>
<tr>
<td>3/F/49</td>
<td>33</td>
<td>Face, trunk, extremities</td>
<td>SCLE, SLE</td>
<td>ND</td>
<td>ANA, anti-La</td>
<td>Tubal ligation</td>
</tr>
<tr>
<td>4/F/28</td>
<td>11</td>
<td>Scalp, face,</td>
<td>CCLE</td>
<td>ND</td>
<td>Malar rash, discoid rash, photosensitivity, ANA</td>
<td>ANA, anti-RNP, anti-Ro</td>
</tr>
<tr>
<td>5/F/28</td>
<td>9</td>
<td>Scalp, face, trunk, extremities</td>
<td>CCLE, SLE</td>
<td>ND</td>
<td>ANA, anti-RNP, anti-Ro</td>
<td>Oral, barrier</td>
</tr>
<tr>
<td>6/F/64</td>
<td>18</td>
<td>Face, mouth, trunk, extremities</td>
<td>Scleroderma with LE, LP overlap</td>
<td>ANA</td>
<td>ANA, anti-Ro</td>
<td>None (postmenopausal)</td>
</tr>
<tr>
<td>7/F/43</td>
<td>28</td>
<td>Face, mouth</td>
<td>CCLE</td>
<td>ND</td>
<td>ND</td>
<td>Hysterectomy</td>
</tr>
</tbody>
</table>

*LE indicates lupus erythematosus; ARA, American Rheumatism Association; SLE, systemic lupus erythematosus; CCLE, chronic cutaneous lupus erythematosus; SCLE, subacute cutaneous lupus erythematosus; LP, lichen planus; ANA, antinuclear antibody; ND, not determined; anti-La, Sjögren syndrome B antigen; anti-RNP, antiribonuclear proteins; and anti-Ro, Sjögren syndrome A antigen.

achieved within 16 weeks. Another study involving 11 patients reported that a maintenance dose of 25 to 50 mg every night or every other night was necessary to prevent relapse. Other studies were also published confirming the effectiveness of thalidomide, 100 to 400 mg/d, in the cutaneous treatment of various forms of lupus erythematosus (LE). The reported adverse effects in these studies included paresthesia, drowsiness, abdominal disturbances, dry mouth, urticaria, rash, mood changes, circulatory changes, amenorrhea, and edema. Of these, par-
Table 2. Previous Unsuccessful Therapies for Cutaneous LE

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Glucocorticosteroids</th>
<th>Antimalarials</th>
<th>Dapsone</th>
<th>Clofazimine</th>
<th>Isotretinoin</th>
<th>Immunosuppressants</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Class I topical and intralesional injections for 20 y; repeated tapering courses of oral treatment at 0.5 mg/kg per day over 2 y</td>
<td>Hydroxychloroquine, 200 mg po BID alone or in combination with quinacrine hydrochloride, 100 mg/d for 5 y</td>
<td>50 mg/d for 8 wk; discontinued because of lack of efficacy</td>
<td>NU</td>
<td>1.0 mg/kg per day; discontinued because of lack of efficacy</td>
<td>Azathioprine, 150 mg po BID for 6 mo; discontinued because of lack of efficacy</td>
</tr>
<tr>
<td>2</td>
<td>Class I topical administration over 5 y; repeated tapering courses of oral treatment at 0.5 mg/kg per day over 5 y</td>
<td>Hydroxychloroquine, 200 mg/d po for 2 mo; discontinued because of severe pruritus; chloroquine, 500 mg/d po for 4 wk, also caused pruritus</td>
<td>NU</td>
<td>NU</td>
<td>NU</td>
<td>Azathioprine, 50 mg/d po for 3 mo; discontinued because of lack of efficacy</td>
</tr>
<tr>
<td>3</td>
<td>Class I-III topical treatment during 20 y; repeated tapering courses of oral drugs at 0.5-1.0 mg/kg per day over 3 y</td>
<td>Hydroxychloroquine, 200 mg po BID for 3 mo; quinacrine hydrochloride, 100 mg/d for 4 mo; discontinued because of lack of efficacy</td>
<td>NU</td>
<td>NU</td>
<td>NU</td>
<td>Azathioprine, 75 mg po BID for 3 mo; discontinued because of lack of efficacy</td>
</tr>
<tr>
<td>4</td>
<td>Class I-III topical drugs and intrallesional injections over 18 y; repeated tapering courses of oral drugs at 0.5-1.0 mg/kg per day over 4 mo</td>
<td>Hydroxychloroquine, 200 mg po BID for 3 y; quinacrine hydrochloride, 100 mg/d po over 4 y intermittently; chloroquine, 500 mg twice a week po for 4 mo; discontinued because of lack of efficacy</td>
<td>NU</td>
<td>100 mg/d po for 4 mo; discontinued because of lack of efficacy and nausea</td>
<td>NU</td>
<td>Azathioprine, 100 mg po BID for 5 mo; discontinued because of lack of efficacy and nausea</td>
</tr>
<tr>
<td>5</td>
<td>Class I-III topical drugs; repeated tapering courses of oral drugs, 0.5-1.0 mg/kg per day over 6 y</td>
<td>Hydroxychloroquine, 200 mg po BID for 2 y; chloroquine, 500 mg/d po for 4 mo; quinacrine hydrochloride, 100 mg/d for 7 mo; discontinued because of lack of efficacy</td>
<td>NU</td>
<td>NU</td>
<td>1 mg/kg per day po for 4 wk; discontinued because of pancreatitis</td>
<td>Azathioprine, 75 mg po BID for 5 mo; methotrexate, 20 mg/wk for 4 mo; cyclophosphamide, 50 mg/d po; discontinued because of lack of efficacy</td>
</tr>
<tr>
<td>6</td>
<td>Class I-II topical drugs; repeated tapering courses of oral drugs, 0.5-1.0 mg/kg per day over 14 y</td>
<td>Hydroxychloroquine, 200 mg po BID; quinacrine hydrochloride, 100 mg/d po alone and in combination for 2 y; discontinued because of lack of efficacy</td>
<td>NU</td>
<td>NU</td>
<td>1 mg/kg per day po for 4 mo; discontinued because of lack of efficacy</td>
<td>Azathioprine, 50 mg po BID for 2 mo; discontinued because of increase in liver enzyme levels; cyclophosphamide, 50 mg po BID for 1 mo; discontinued because of leukopenia</td>
</tr>
<tr>
<td>7</td>
<td>Class I topical treatment for 6 y; repeated intralesional injections of triamcinolone acetonide, 10 mg/mL; patient refused oral glucocorticosteroids</td>
<td>Hydroxychloroquine, 200 mg po BID; quinacrine hydrochloride, 100 mg/d po alone and in combination for 5 y</td>
<td>NU</td>
<td>NU</td>
<td>1 mg/kg per day po for 8 wk; discontinued because of lack of efficacy</td>
<td>Azathioprine, 50 mg/d po for 2 wk; cyclophosphamide, 50 mg/d po for 4 wk (both caused leukopenia)</td>
</tr>
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</table>

*LE indicates lupus erythematosus; po, orally; BID, twice daily; and NU, not used.

Esthesia, sedation, and constipation were the most common.

Although thalidomide is well recognized as an effective agent for CLE through the studies done mainly in Europe, it is rarely used to treat this disorder in the United States because of its risks and because it is difficult to obtain. For these reasons, there are no randomized trials that have proved the efficacy of thalidomide as a second-line drug in CLE. Herein, we report our experience in treating 7 patients with CLE during 9 years. Our experience confirms its remarkable efficacy and surprising safety as monotherapy.
RESULTS

Table 3 summarizes the course of each patient's treatments; Table 4 describes their reported adverse effects. Six of the 7 patients responded to thalidomide treatment. One patient dropped out after 1 month of thalidomide treatment with concerns about the possible adverse effect of neuropathy (this patient had not experienced any adverse effects at the time of discontinuing thalidomide). Of the 6 patients who responded to treatment, 2 had complete resolution of their cutaneous lesions by the end of the first year of treatment. The other 4 showed marked (80%) improvement in their skin, with scarring and hypopigmentation remaining in the scalp or chest. One patient had hair regrowth after 2 months of treatment, and this regrowth reached a plateau by the sixth month of treatment. Figure 1 summarizes the effects of thalidomide therapy on the cutaneous lesions in patients 3 through 6. Figure 2 depicts the effects of thalidomide therapy on the histological changes of CCLE in patient 5.

Table 4 lists the adverse effects reported to us by the patients. The most common adverse effects reported were paresthesia, sedation, constipation, and weight gain. Sedation and constipation were for the most part well tolerated by the patients. Most became accustomed to the drug's sedative effect, and 2 patients reported insomnia when not taking thalidomide. Constipation was tolerable after dietary changes and taking laxatives as needed. No treatment was recommended for weight gain, since this adverse effect was transient and not distressing to any of the patients. There were no complaints of decreased libido.

Nerve conduction studies did not demonstrate abnormalities that specifically related to treatment with thalidomide. The motor nerve conduction data were all within the normal range for distal motor latency (peroneal, <5.8 milliseconds; tibial, <6.2 milliseconds; ulnar, <4.0 milliseconds; median, <4.2 milliseconds), for compound muscle action potential amplitudes (peroneal, >2.2 mV; tibial, >6.0 mV; ulnar, >4.0 mV; median, >6.0 mV), and for motor conduction velocities (peroneal, >40 m/s; tibial, >38 m/s; ulnar, >52 m/s; median, >50 m/s). Sensory nerve conduction was also within the normal range with the exception of 1 patient. This pa-

<table>
<thead>
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<th>Table 3. Efficacy of Thalidomide Therapy*</th>
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<tr>
<td><strong>Patient No.</strong></td>
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<tr>
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<tr>
<td>1</td>
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<tr>
<td>2</td>
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<td>3</td>
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<td>4</td>
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<td>5</td>
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<td>6</td>
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<td>7</td>
</tr>
</tbody>
</table>

* FDA indicates Food and Drug Administration; IND, investigational new drug; and NA, not applicable. For all patients, thalidomide was given at a dose of 100 mg/d.
† Average, 2.4 ± 3.1 years.
‡ Average, 2.2 ± 0.8 months.
§ Ongoing treatment.
¶ Source of thalidomide: GWL Hansen’s Disease Center, Baton Rouge, La.
# Source of thalidomide: Pediatric Pharmaceuticals, Iselin, NJ.
** Dropped out of treatment. It was not possible to determine whether this patient responded to thalidomide.

<table>
<thead>
<tr>
<th>Table 4. Patient-Reported Adverse Effects</th>
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</thead>
<tbody>
<tr>
<td><strong>Adverse Effect</strong></td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Neurologic symptoms</td>
</tr>
<tr>
<td>Sedation</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Weight gain</td>
</tr>
<tr>
<td>Weakness</td>
</tr>
<tr>
<td>Muscle cramps</td>
</tr>
<tr>
<td>Mood changes</td>
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<tr>
<td>Shakes</td>
</tr>
</tbody>
</table>

* Neurologic evaluation and nerve conduction studies did not show thalidomide as cause of symptoms.
† Laboratory testing did not disclose a hematological, biochemical, endocrinological, or neurological basis for these symptoms (data not shown).
A patient developed a decline and loss of the SNAP signals from her left sural and left superficial peroneal nerves in association with clinical and imaging findings of a compressive left L5-S1 radiculopathy. Otherwise, the sensory nerve conduction data for the patients were within the normal ranges for the amplitudes of SNAPs (sural, >6 µV; superficial peroneal, >6 µV; ulnar, >17 µV; median, >20 µV) and for the sensory conduction veloci-

Figure 1. Clinical responses to thalidomide therapy. Patient 3 (subacute cutaneous lupus erythematosus) before thalidomide therapy (A) and after 8 weeks of thalidomide therapy at 100 mg/d (B). There was marked flattening of lesions and decrease in the severity of the erythema. Patient 4 (chronic cutaneous lupus erythematosus of scalp) before thalidomide therapy (C) and after 16 weeks of thalidomide therapy (D), which caused complete resolution of the associated erythema. Patient 5 (widespread chronic cutaneous lupus erythematosus) before therapy (E) and after 8 weeks of thalidomide therapy (F). Patient 6 (scleroderma with lupus erythematosus–lichen planus overlap syndrome) 8 weeks after temporarily discontinuing thalidomide therapy (G), resulting in a relapse of the inflammatory skin lesions (October 1996), and during thalidomide therapy, 100 mg/d (April 1997) (H).
ties (sural, >40 m/s; superficial peroneal, >40 m/s; ulnar, >49 m/s; median, >48 m/s). Amplitudes of the SNAPs varied in the same nerve on different studies, but there was no consistent trend in the values to indicate a significant decline in amplitudes. Coexisting clinical conditions rather than the treatment with thalidomide caused neurologic symptoms.

Four patients reported experiencing paresthesia, but sensory nerve conduction studies did not disclose any drug-induced abnormalities. None of the 4 cases could be linked to thalidomide by neurologic evaluation and nerve conduction studies (see Table 4). In 1 patient, perioral paresthesia resolved when thalidomide treatment was withdrawn for 2 weeks and did not recur when treatment was restarted. The second patient had improvement in neurologic symptoms while still receiving thalidomide; nerve conduction studies showed abnormalities consistent with her underlying connective tissue disease but not with thalidomide neuropathy. The third patient was found to have paresthesia caused by a C6 compression of a nerve root. The last patient recently developed paresthesia after 9 years of thalidomide treatment. Nerve conduction studies did not show a thalidomide neuropathy.

It is of interest that 2 patients reported similar adverse effects of intermittent “shaking” episodes since starting thalidomide treatment. These shaking episodes were described as being similar to tremors and chills. They were preceded by thoughts of impending shakes by the whole body. These symptoms initially occurred in the mornings, progressed to occur all day, and then gradually resolved. No hematologic, biochemical, or nerve conduction abnormalities were found that could explain this phenomenon. There were no abnormalities in body temperature associated with these shaking episodes. In 1 patient, this symptom resolved while the patient was still receiving thalidomide. Since complete neurologic examinations did not show any abnormalities, magnetic resonance imaging of the brain was not performed.

No significant changes in blood cell count were noted in any of the patients after initiation of thalidomide treatment. One patient had a history of slightly depressed white blood cell count that did not change after thalidomide was started. No electrolyte disturbances were noted, and the serum urea nitrogen and serum creatinine levels in the patients with systemic LE remained stable at baseline. None of these patients developed abnormalities in thyroid function tests (data not shown).

In patients who had circulating autoantibodies at baseline (patients 1, 3, 5, and 6), thalidomide therapy did not decrease these circulating antibodies, despite its beneficial effects on their dermatologic disease (data not shown). This suggests that the thalidomide may be working by an anti-inflammatory mechanism, rather than the immunomodulation of a pathogenic immune response.

**COMMENT**

Cutaneous lesions secondary to systemic LE, subacute CLE, or CACLE in the 6 patients who took thalidomide, 100 mg/d, for more than 1 month all showed marked improvement. The average response time was 2.2 ± 0.8 months. The patients’ conditions remained stable even after discontinuing other treatment modalities, including oral, injected, or topical glucocorticosteroids, and other immunosuppressive or modulating pharmacologic agents (Table 2). In addition to the resolution of the clinical signs and symptoms associated with CLE (Figure 1), thalidomide also resulted in the resolution of the histological changes associated with CLE (Figure 2). The patients with

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**Figure 2. Effect of thalidomide therapy on the histological changes of chronic cutaneous lupus erythematosus. A, Skin biopsy specimens were obtained from patient 5 before thalidomide therapy, which corresponds to the clinical lesions depicted in Figure 1, E. There was an inflammatory infiltrate and an active interface dermatitis around hair follicles and dermoepidermal junction (hematoxylin-eosin, original magnification ×20). B, After 8 weeks of thalidomide therapy, which corresponds to the clinical lesions depicted in Figure 1, F, there was resolution of the interface dermatitis, and the intensity of the inflammatory infiltrate had diminished considerably. There was considerable pigment incontinence (hematoxylin-eosin, original magnification ×20).**
systemic LE have not shown signs of their systemic disease since starting thalidomide and discontinuing other treatments. The use of sunscreens and sun avoidance remains a must, since most of these patients have histories of photosensitivity.

There is a general lack of agreement on the effective starting dose and treatment schedule of thalidomide. In our experience, 100 mg daily in the evening is an adequate starting dose. We have been successful in tapering the dose of thalidomide in 3 patients (patients 1, 5, and 6) (from daily dosing to alternate-day or every-third-day dosing with 100 mg of thalidomide). In the other patients (patients 2 through 4), our attempt to taper the dose of thalidomide resulted in a prompt exacerbation of their condition, which necessitated the continuation of a daily dosing regimen.

Complete discontinuation of thalidomide therapy has not been possible in any of our patients, because of relapses in their dermatologic disease. This is in contrast to what has been suggested by other clinicians, that the dose be gradually decreased until treatment can be discontinued altogether. The induction of long-term remission by thalidomide has not been reported, and this has been our experience as well. This suggests that a maintenance dose is necessary for long-term control of disease.

One of the patients with CCLE (patient 1) was initially treated with thalidomide provided by a Hansen disease treatment center (Table 3). This source of thalidomide was interrupted because of a drug shortage, which necessitated obtaining thalidomide from a different supplier (Pediatric Pharmaceuticals, Iselin, NJ). Although we have no information about the relative bioavailabilities of thalidomide from the 2 suppliers, this patient maintained an excellent clinical response to thalidomide provided by a different supplier. There are 3 American pharmaceutical companies that manufacture and distribute thalidomide, but relative bioavailabilities of thalidomide from these sources is not known. This is a potentially important issue that warrants study.

The mechanism of action of thalidomide remains unknown, but the drug is known to possess certain anti-inflammatory and immunomodulatory properties. The actions of thalidomide include the inhibition of monocyte tumor necrosis factor α production, inhibition of polymorphonuclear leukocyte chemotaxis and phagocytosis, inhibition of lymphocyte proliferation in response to mitogenic or allogenic stimulation, inhibition of helper T-cell type 1 cytokine production while enhancing helper T-cell type 2 cytokine production, and inhibition of angiogenesis. One or more of these mechanisms may explain thalidomide’s effectiveness in controlling the cutaneous manifestations of LE.

The most serious adverse effects of thalidomide treatment are teratogenicity and neuropathy. Therefore, strict contraceptive measures and close monitoring of neurologic symptoms are necessary. In our patients, no serious adverse effects have been observed, even in those treated for longer than 1 year, and discontinuation of treat-
Nerve conduction testing is a useful adjunct to the means to detect the early development of neuropathy. Receiving thalidomide provides the single most effective

Table 5. Guidelines for Prescribing Thalidomide

For Female Patients
1. Establish appropriateness of thalidomide therapy vs therapeutic alternatives
2. Provide comprehensive counseling on risks and benefits of thalidomide therapy
3. Determine if patient has childbearing potential
   - Two forms of contraception, beginning at least 4 wk before therapy, all during therapy, and at least 4 wk after stopping therapy with thalidomide
   - Contraceptive methods must include at least 1 highly effective method (eg, intrauterine device [IUD], hormonal [birth control pills, injections, or implants], tubal ligation, or partner's vasectomy) and 1 additional effective method (eg, latex condom, diaphragm, or cervical cap)
4. Continue selected birth control options for at least 4 wk before initiating thalidomide therapy
5. Initiating therapy
   - Repeat patient counseling
   - Perform pregnancy test, even if continuous abstinence is the chosen method of birth control
   - Administer thalidomide patient quiz
   - Complete informed consent form
   - Complete mandatory and confidential survey enrollment form
   - Provide prescription
6. Patient monitoring during first 4 wk of therapy
   - Repeat patient counseling
   - Perform pregnancy tests every week for first 4 wk of therapy
   - If pregnancy test is negative, provide prescription for 1-wk supply of thalidomide
7. Subsequent patient visits (after first 4-wk period)
   - Repeat patient counseling
   - Perform pregnancy tests every 2 wk if patient's menstrual cycles are regular, every 2 wk if cycles are irregular
   - Complete follow-up survey form
   - If pregnancy test is negative, provide prescription for 4-wk supply of thalidomide

For Male Patients
1. Establish appropriateness of thalidomide therapy
2. Provide comprehensive counseling on risks and benefits of thalidomide therapy
3. Provide contraceptive counseling, including counseling on emergency contraception
   - Male patients must be instructed to use a latex condom every time they have sexual intercourse with a woman, even if they have had vasectomy
   - Use patient education materials
4. Administer thalidomide patient quiz
5. Complete informed consent
6. Complete mandatory and confidential survey enrollment form
7. Provide prescription
8. Subsequent visits
   - Repeat patient counseling
   - Complete follow-up survey
   - Provide prescription for 4-wk supply


The minor adverse effects have been tolerable to the patients. We continue to monitor the symptom of shaking. This phenomenon has not been previously reported, and we have not been able to link it to thalidomide-induced biochemical, hematological, or neurologic abnormalities. This symptom has not been a dose-limiting toxic effect. In one patient, the symptom has resolved without interrupting treatment; in the other patient, this symptom has persisted but has not been dose limiting.

Overall, the patients who have shown improvement have been pleased with the results of thalidomide therapy. The patients have perceived a benefit in arresting the progression of their chronic, previously unrelenting dermatologic disease. The minor adverse effects of thalidomide have been tolerable in all patients, since all of them have been afflicted with their dermatoses for many years (Table 1).

Various studies, mainly in Europe, have reported the safety and effectiveness of various doses of thalidomide in the treatment of the CLE. In our experience, a low starting dose of thalidomide has been a safe and effective monotherapy for CLE after traditional therapeutic options have been exhausted. Minor adverse effects are common but tolerable. The dispensing of thalidomide is tightly regulated in the United States, given the drug’s infamous history. Even so, thalidomide is a promising treatment option for clinicians to consider, but caution and familiarity with the prescribing guidelines cannot be overemphasized (Table 5).

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