Livedo Reticularis with Ulcerations

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Idiopathic livedo reticularis may be associated with ulcerations of the lower extremities beginning primarily during the warmer or summer months, as well as the more usual occurrence of winter ulcerations. Summer ulceration apparently is a new and rare entity which has many clinical and histopathologic features similar to winter ulcerations. Hypertension, Raynaud’s phenomena, acrocyanosis and thrombosis of digital arteries were noted only in patients with winter ulcerations, while edema of the legs and feet was a more prominent feature in patients with summer ulcerations. Medical treatment, including rest in bed, elastic supportive bandages and a trial of hexamethonium (bistrium bromide) injections, seemed to be the treatment of choice. Lumbar sympathectomy did not seem to be of great permanent value.

Although idiopathic livedo reticularis* may occasionally be associated with ulcerations, a thorough clinical and histopathologic study of this condition has seldom been reported. It has been assumed that the effect of cold on the blood vessels of the skin accounted for the predominance of the symptoms and the occurrence of the ulcerations during the winter months. However, in reviewing the records of more than 400 patients seen in the Mayo Clinic in the past 10 years with a diagnosis of livedo reticularis and pernio,† we have been able to define a group of patients with a new entity in that idiopathic livedo reticularis is associated with ulcers starting only or primarily during the warm months of the year, especially during the summer.¹

The first part of this report will briefly summarize some of the medical literature concerning livedo reticularis, and the second part will contain the data on winter and summer ulcerations in livedo reticularis.

1. Review of the Medical Literature Concerning Livedo Reticularis

Definitions

Livedo reticularis is a condition of the skin characterized by a reddish blue, mottled, reticular or blotchy discoloration. It persists with a variation of degree regardless of the skin temperature, and has also been described as a marbling or a fish-net discoloration. Synonyms in the medical literature for this condition have been “generalized telangiectasia,” “livedo racemosa,” “livedo annularis” and “asphyxia reticularis.”

“Cutis marmorata” is a term generally used for a transient reticular discoloration which appears on exposure to cold, as in livedo reticularis, but is not permanent and disappears with warmth. The term has been used interchangeably with “livedo reticularis” in the medical literature.

The word “livedo” is derived from the Latin word, “liveo,” meaning to be black, blue or livid. The term was used by Hebra in 1868.²

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* Unless otherwise designated, the term “livedo reticularis,” when mentioned in this report, applies to idiopathic livedo reticularis, not to symptomatic livedo reticularis as a result of such diseases as periarteritis nodosa or which has been described with tuberculosis or syphilis.

† Pernio, when mentioned in this report, refers to the disease known as “perniones” (erythema pernio, chronic chilblains, frostbeulen and frostbites) resulting from exposure to cold. It is not used in the sense of “lupus pernio” (Besnier), which is a manifestation of sarcoid, or “lupus pernio” (chilblain lupus, Hutchinson), which represents the cutaneous manifestations of disseminated lupus erythematosus.
The local coloration, he believed, was the result of idiopathic passive hyperemia and he proposed the term "livor cutis, livedo (Blauung)." Kaposi stated that the discoloration was due to an excessive amount of blood in the most superficial layer of the corium and that it was due solely to "the injection of the finest vessels, the capillaries and the finest arteries and veins." Unna, Ebert, Lewis and Williams and Goodman discussed the pathologic physiology of livedo reticularis. Rothman has presented a review of the recent concepts of vascular anatomy and physiology of the skin. He implied that cutis marmorata is due to a developmental anomaly of the cutaneous vascular system and is not connected with any particular disease, but that livedo reticularis, in contrast, is a consequence of arteriolar disease. The reticular areas seemed to be more vulnerable to inflammatory stimuli than the pale areas, possibly because there were more open vessels in the reticulum.

To summarize, a possible concept of the physiopathologic mechanism of livedo reticularis could be as follows: Blood supply to the skin is from central arterioles which pierce the skin from below and the central zone capillary arborizations have a slightly greater tone and faster blood flow than in peripheral capillaries. Then, either through organic changes or through vasosppasm of arteries or arterioles of the skin, capillary atony and slowing of blood in peripheral capillaries is further increased, which results in a livedo reticularis pattern in annular rings about central paler areas. Cold causes increased vasoconstriction of arteries and arterioles, resulting in an intensification of the livedo. Peripheral capillaries, if temporarily atonic and dilated, would result in a transient cutis marmorata or, if permanently dilated, would result in a permanent discoloration. On elevation of the affected part, the livedo might decrease if the venules draining the capillaries were not obstructed and could dilate and drain the stagnant blood from the capillaries. Warmth and sympathectomy could reduce the vasospasm of the arteries and arterioles and also result in less discoloration.

**Clinical Types of Livedo**

Livedo reticularis is best classified after Williams and Goodman with some modifications.

1. **Cutis Marmorata.** This is a transitory mottling with exposure to cold. There is probably no pathologic alteration in the peripheral circulation, but it is only the result of a vasomotor phenomenon. It is frequent in infants and may disappear as they grow older. Aldao reported that cutis marmorata of 24 to 48 hours' duration may be the only cutaneous manifestation, or one of the cutaneous manifestations, of compressed-air illness. The cause was considered to be an obstruction of the vessels of the skin with air emboli resulting in ischemic areas and also areas of passive congestion.

2. **Idiopathic Livedo Reticularis.** This is manifested by a relatively permanent motting which persists in a variation of degree, amount and arrangement regardless of temperature changes. This group includes cases in which no definite local or systemic disease is discovered as an explanation for the livedo. Williams and Goodman expressed the belief that this is an anomaly of the blood vessels, possibly congenital. There may be minimal or no organic changes in the vessels except increased number and dilatation of the capillaries in the livid areas, although more severe organic changes have been noted in the blood vessels. Such cases have been reported by several authors. Brain has reported data on two children, 9 weeks and 13 years of age respectively, who have had "naevus vascularis reticularis" present since birth.

3. **Symptomatic Livedo Reticularis.** This group could be divided into three subdivisions.

**A. Questionable Factors in Livedo Reticularis**

The literature of livedo reticularis contains many reports of livedo reticularis in patients with various diseases, such as in children with rickets, mongolism, various endocrine dysfunctions, such as hyperthyroidism, hypothyroidism, pituitary disorders, such as Cushing's disease, malnutrition, varicose veins and
other vascular diseases such as arteriosclerosis, infectious diseases (typhus) and toxic conditions (arsphenamine intoxication), congenital vascular defects and ectodermal abnormalities, cirrhosis of the liver and other visceral diseases. Nerve injuries may result in livedo reticularis and a patient believed to have perniones and livedo of a poliomyelitic limb was presented at a dermatologic meeting by Senear.\textsuperscript{14} Local livedo racemosa only about the site of an intramuscular injection of bismuth has been noted.\textsuperscript{15} It was believed to be due to an unintentional intra-arterial injection of bismuth with subsequent embolus and occlusion of smaller vessels in the vicinity resulting in a livedo reticularis pattern.

The influence of some of these diseases on the pattern of livedo reticularis is unknown; perhaps in some of these conditions the livedo reticularis and the disease are coincidental.

Lutz and Picard\textsuperscript{16} described a patient who had a livid eruption, clinically similar to livedo racemosa, which was worse in the winter and better during the summer, but there were areas of cutaneous atrophy which suggested anetoderma. There were no ulcerations.

\textbf{B. Probable Factors in Livedo Reticularis}

(1) Hypertension has been noted to occur in 30 per cent of a group of patients with livedo reticularis on whom data have been reported by Barker, Hines and Craig,\textsuperscript{11} and there have been several isolated reports of hypertension in patients with livedo.\textsuperscript{5-12} It is interesting to note that arteriolar spasm is a feature in patients with hypertension and also is a major factor in the etiology of livedo reticularis.

(2) Nervousness and emotional instability were noted in about 50 per cent of patients in one series of livedo reticularis and arsenic or lead poisoning was considered a possible etiologic factor in several patients reported by the same investigators.\textsuperscript{11}

\textbf{C. Purported Causes of Livedo Reticularis}

The term “inflammatory livedo” might be applied to this group, since a specific histologic picture may be found.

(1) Tuberculosis. Adamson\textsuperscript{17} in 1916 reported data on a group of girls from 11 to 15 years of age with “chilblain circulation,” generalized livedo annularis, nodules of the legs and lymphadenopathy; several had enlargement of the spleen. In two of his cases the Wassermann reaction was positive. He believed these cases to have manifestations of tuberculosis and erythema induratum with a livedolike distribution. Other scattered cases in the medical literature in which tuberculosis was considered an etiologic factor were found by Ebert\textsuperscript{3} and Becker.\textsuperscript{12}

An evaluation of the cases cited in the previous paragraph reveals that the evidence for tuberculosis, especially active tuberculosis, is meager. Histologic examination of a cutaneous specimen for biopsy from one of Adamson’s patients was not diagnostic, and ulceration of the lower extremities cannot be assumed to be of tuberculous origin because of the clinical appearance. Although some patients with pulmonary or other systemic types of tuberculosis may have livedo reticularis and ulcerations which suggest erythema induratum, a tuberculous histopathologic picture or cultural and animal inoculation studies which reveal the organism are necessary before the ulceration can be assumed to be erythema induratum, since ulceration could be the result merely of the livedo reticularis.

(2) Syphilis. Ehrmann\textsuperscript{18} in 1907 reported data on nine patients who had “livedo racemosa syphilitica.” He believed that in patients with cutis marmorata a large macular syphilitic could develop after Treponema pallidum settled in an area of sluggish capillary circulation. The discoloration was described as raised without ulceration and assumed a treelike distribution with branching. Histopathologic studies in two cases revealed constriction and some obliteration of dermal and subcutaneous arteries without any venous changes.

Since the initial reports by Ehrmann on livedo reticularis due to syphilis, the evidence for syphilis being a significant factor in the etiology of livedo has been scant and the presence of a positive serologic reaction for syphilis or a history of a latent infection is not sufficient to enable one to conclude that a patient with livedo has “livedo racemosa syphilitica.”
(3) Some cases of periarteritis nodosa have been shown by Ketron and Bernstein to cause livedo reticularis and ulceration, especially in the lower extremities. Histopathologic studies revealed thrombosis with or without inflammation of vessels and occasional necrosis of small vessel walls, but larger and deeper subcutaneous vessels showed more classic changes.

Ruiter has reported on a group of patients having a basically similar clinical and histopathologic picture of a hematogenous, allergic, disseminated eruption ("allergic cutaneous vasculitis"). He included periarteritis nodosa which involved the medium-sized vessels of the cutaneous-subcutaneous border and distinguished it from "arteriolitis allergica," which has a similar histopathologic involvement of the smaller vessels of the corium with insignificant or no involvement of the larger arteries. Such features as superficial hemorrhage and necrosis, urticarial lesions and telangiectasia were often manifestations of allergic arteriolitis. Although livedo reticularis was not described, the clinical and histologic features of telangiectasia in allergic arteriolitis might be considered as analogues to the livedo in typical periarteritis nodosa.

Gougerot and Duperrat have expressed the belief that the condition described by Ruiter is similar to "the nodular dermal allergides of Gougerot."

Histopathology

The histopathology of the skin from areas of lividness in cases with nonulcerative idiopathic livedo reticularis has shown a varying type and degree of changes such as dilatation and increase in number of capillaries in the upper corium, endarteritis and endophlebitis of the smaller vessels, at times with occlusion, periarteritis and periphlebitis and occasionally thickening of the walls of arterioles in the dermis and subcutaneous tissue. Mogensen reported the case of a man 48 years of age who clinically had a generalized livedo reticularis without ulceration of 20 years' duration. Histopathologic studies from an area of livedo revealed an inflammatory infiltrate of lymphocytes and plasma cells and a moderate increase of mast cells, but not as great as usually occurs in urticaria pigmentosa. The condition resembled in some respects telangiectasia macularis eruptiva (urticaria pigmentosa) and a connection with that disease was supposed.

The histopathologic changes in idiopathic livedo reticularis with ulceration have been recorded by several authors. Ebert described the case of a woman 33 years of age with ulcers of the legs for seven years, which started as subcutaneous nodules, most frequent and recurring during the summer. Persistent livedo reticularis had been present for four years. Histologic examination of a cutaneous specimen for biopsy from a nonulcerative livid area on a buttock revealed in the upper corium a peri-vascular round cell infiltrate with dilatation of the small vessels and lymphatics and thrombosis of veins draining the sweat glands. At the junction of the cutis and subcutis there was perivascular infiltration of a large artery and vein and proliferative changes in the walls of both vessels with thrombosis of the vein. Microscopic examination of a specimen for biopsy from a recently ulcerated nodule of the external malleolus revealed infiltration in the corium extending into the subcutaneous fat and occurring especially about vessels, sweat glands and ducts. The infiltrate consisted of leukocytes, plasma cells, lymphocytes and epithelioid cells. There were degeneration and destruction of the elastic tissue. The nutrient arteries of the subcutis and corium were hypertrophied and there was some marked proliferative change. Ebert thought that the ulceration was most probably tuberculoid, although there was no clinical or laboratory evidence of tuberculosis. This case could represent a case of livedo reticularis with summer ulceration.

Barker and Baker reported extensive histologic studies of a man, aged 34 years, with livedo reticularis, ulceration of a leg and thrombosis of the great toe. Microscopic examination of a specimen for biopsy from an ulcer revealed moderate fibrosis and nonspecific inflammation. No acid-fast bacilli were seen. Lumbar and cervical sympathectomies were performed but later the patient insisted on amputation of his left leg because of recurrent ulceration and pain. Pathologic examination of the removed limb revealed that the smaller blood vessels (arterioles and venules and the vasa vaso-rum) had proliferative and occlusive intimitis (endarteritis and endophlebitis), and thickening of the walls of arterioles also was noted but was thought to be a secondary feature. There was evidence of an ischemic neuritis with perineural and intraneural fibrosis and patchy loss of myelin sheaths. The long and short saphenous veins revealed some proliferation of the intima and some inflammation of their walls as in a venous stasis picture. The large arteries, such as the posterior tibial, showed only slight intimal proliferation without occlusion and some inflammation of their walls.

Barker, Hines and Craig reported four cases with livedo reticularis and ulceration. In one case
histopathologic examination of a specimen of tissue from an ulcer revealed that the arterioles, 75 microns or less in diameter, were surrounded by lymphocytes and there was some reduction in size of the lumen associated with thickening of the vessel wall, but no definite intimal proliferation was described.

**Diagnosis**

The first stage in the diagnosis of livedo reticularis is made by noting a mottled, reticular, blue-red discoloration which has persisted to some degree in spite of temperature changes. Then it must be determined whether the eruption is idiopathic or symptomatic, by obtaining a thorough history, general physical examination and various laboratory examinations including chest roentgenogram, serologic tests for syphilis, sedimentation rate and in some cases a cutaneous biopsy.

If there is no ulceration, then the differential diagnosis might include acrocyanosis,\(^{25, 26}\) which causes a diffuse blue color affecting the hands or occasionally the feet, which is permanent, asymptomatic, does not change with warmth and does not result in ulceration or necrosis. Histopathologic studies have revealed hypertrophy of the media of cutaneous arterioles, which could be secondary to spasm, and dilatation and new formation of cutaneous capillaries. Raynaud’s disease causes intermittent symptoms classically having a triple color change of white, blue and red. It occurs in young women in 70 per cent of cases\(^{25}\) and involves primarily the fingers or toes, rarely the nose and ears. There is slight, limited or no ulceration or necrosis, confined to the portions of the body involved in the color changes.

The ulceration in livedo reticularis is clinically not specific and several conditions with similar vascular changes, such as chronic pernio, hypertensive ischemic ulcer and hemolytic anemias, may result in a similar-appearing ulcer. Pernio\(^{27}\) or perniones occur particularly in young women and result in localized blue-red areas without motting, becoming redder with warmth or vasodilatation, not changing with posture, occurring only with exposure to cold and sometimes resulting in ulceration.

Histopathologic examination, as reported by McGovern, Wright and Kruger,\(^{27}\) revealed a pathologic picture, most characteristically revealing angitis of the smaller cutaneous vessels, fat necrosis and some giant cells. They stated that this picture was not morphologically specific, since a number of vascular conditions involved similar histologic changes and represented a chronic irritative process, either primary or secondary, in the subepidermal tissues. The subcutaneous ulcerated nodules in extremities affected by anterior poliomyelitis or erythrocyanosis of Telford\(^{28}\) probably represent perniones disease. Hypertensive ischemic ulcers\(^{29}\) result occasionally in individuals who usually have had hypertension for a long time. The ulcer is indolent, small and painful, responds poorly to treatment and has an ischemic appearance. Histopathologic examination of an ulcer reveals no significant changes except in the arterioles, which reveal an increase in thickness of the arteriolar walls and decrease in the diameter of the lumen. Other changes in the arterioles include hyaline degeneration of the media, intimal proliferation and periarteritis.

Nodular vasculitis\(^{30-35}\) may cause ulcerative lesions of the lower extremities and is manifested by chronic, persistent or recurrent nodules, chiefly on the legs, which are not of tuberculous origin. Ulceration occurs occasionally, especially in women past 30 years of age, although it can affect either sex at any age. Hypertension has been associated occasionally.\(^{36}\)

The lesions of nodular vasculitis have the same distribution as erythema induratum but are more painful, usually of shorter duration and may clear with rest in bed and elevation of the legs. However, the clinical distinction between nodular vasculitis, erythema nodosum and the nodose type of erythema induratum is often difficult. Histopathologic examination of the lesions of nodular vasculitis reveals vasculitis with varying degree of thickening and obliterative changes in both veins and arteries, a varying degree of fibrosis of the subcutaneous tissue with collections of foreign-body giant cells and atrophy of the fat but without definite tubercle formation.
Ulceration of the lower extremities could also result from conditions such as those of factitial origin, ulceration secondary to varicose veins and venous insufficiency, arteriosclerosis obliterans, thromboangitis obliterans and various blood dyscrasias including hemolytic anemias. But in these cases, livedo reticularis is not noted and concomitant clinical, laboratory and histopathologic studies would aid in establishing the diagnosis.

_Treatment_

Treatment of idiopathic livedo involves surgical and nonsurgical methods.

(1) Nonsurgical treatment includes protection from the cold, vasodilating drugs such as priscoline or hexamethonium drugs, elastic bandages for the lower extremities if edema occurs, especially with ulceration, hospitalization and rest in bed if ulceration or thrombosis occurs, and mild antiseptic dressings for the ulcerations. Typhoid vaccine has been used intravenously. 11, 21

(2) Surgical treatment includes sympathectomy or injection of alcohol to produce sympathetic block.

Barker, Hines and Craig11 in 1941 reported three cases in which livedo reticularis was treated with lumbar sympathectomy. Two patients with gangrene had no recurrence of gangrene after 1 and 3 years respectively and the livedo and symptoms improved. One patient reported by Barker and Baker21 had ulceration of the legs and thrombosis of toe arteries which occurred after lumbar sympathectomy. Finally the patient insisted on amputation.

Barker, Hines and Craig expressed the belief that sympathectomy is a justifiable procedure in cases of severe livedo when no definite etiologic factor is found or when extensive gangrene is present.

Shumaker22 reported data on a patient with livedo reticularis and coldness and numbness of the feet who improved after bilateral lumbar sympathectomy. The feet became warm and dry, there was no discomfort and only a faint dependent mottling persisted.

If the patient has tuberculosis, syphilis or periarteritis nodosa and it is believed that these diseases are factors in the etiology of the livedo, treatment should be directed toward them.

2. DATA OF THE PRESENT STUDY

_A. Livedo Reticularis with Winter Ulcerations_  

Idiopathic livedo reticularis is not uncommonly associated with ulcerations, usually starting during the winter months. The ulcers usually occur on the normally exposed aero parts of the body, especially the lower extremities. The legs, ankles and feet are especially frequent sites of ulceration. Digital arterial occlusion of the toes occurring with livedo reticularis may result in ulceration occurring on the toes.

A brief summary of the findings in 18 patients with livedo reticularis and primarily winter ulcerations is presented in table 1 and a brief summary of the histories of two patients follows:

_Report of Cases (Patients 1 and 2, Table 1)_

_Case 1._ A white, divorced, female clerk, aged 24 years, from Chicago, Ill., was seen in Nov. 1952. She stated that four years previously an asymptomatic, bluish, mottled discoloration of the legs had developed, which quickly spread to involve the entire lower extremities and arms. The motting was worse with cold weather but warmth caused no particular change. In the past three years edema and painful “blood blisters” had developed, which progressed to ulcerations involving the feet, ankles and legs. The initial episode of ulceration occurred during the winter and the ulcers recurred most frequently and severely during the cold months, so that she was advised to move to a warmer climate. The edema of the legs and feet would subside on elevation but a variety of prior treatments for the ulcerations, including oral and local antibiotics, roentgen treatment, cortisone, elastic bandages, elastic-paste boots and several weeks of rest in bed had resulted in little benefit.

She had had the best relief from pain and ulceration while lying a great deal in the sun for six months in 1952, but then a severe exacerbation of ulceration and edema developed and subsequently five lumbar sympathetic ganglion blocks with procaine hydrochloride had been of decreasing benefit.

Approximately one year previously, paresthesias had developed in the lower extremities and for three days she had had temporary “paralysis” of the right leg. Since then she had had some intermittent subjective numbness in both lower extremities. With exposure to cold she had noted numbness and
**Table 1.—Livedo Reticularis with Winter Ulcerations**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, sex</th>
<th>Duration of livedo</th>
<th>Duration of ulceration</th>
<th>Location and description of ulcerations</th>
<th>Microscopic examination</th>
<th>Bilateral lumbar sympathectomy</th>
<th>Miscellaneous</th>
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<tbody>
<tr>
<td>1</td>
<td>24 F</td>
<td>4 years</td>
<td>3½ years</td>
<td>Small, superficial, irregular ulcer of ankles. Scars at sites of former ulcers over feet and legs (fig. 1a)</td>
<td>L. foot: Arterioles in dermal thickened walls and thrombi occluding lumen. Vein at dermo-subcutaneous junction showed thickened wall, perivascular infiltrate and occlusion of lumen by thrombus (fig. 1b, c, d and e)</td>
<td>Hexamethonium (bistrium bromide) treatment during and after hospitalization seemed to be of benefit in more rapid healing of ulcerations</td>
<td></td>
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<tr>
<td>2</td>
<td>42 F</td>
<td>4 years</td>
<td>2½ years</td>
<td>Ischemic ulcer of left fourth toe</td>
<td></td>
<td>Two right lumbar ganglia and three left lumbar ganglia and respective intervening chains</td>
<td></td>
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<tr>
<td>3</td>
<td>45 F</td>
<td>5 years</td>
<td>2 years</td>
<td>Toes cyanotic and cold with crusted ulcers on tips of toes (fig. 2a)</td>
<td>R. leg: Arteriole in subcutaneous tissue revealed hyalinization of wall and thrombosis with obliteration of lumen</td>
<td>Raynaud’s. B.P. 158/108</td>
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<tr>
<td>4</td>
<td>30 F</td>
<td>7 years</td>
<td>Same</td>
<td>15-20 scars of prior ulcerations on ankles</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>5</td>
<td>22 F</td>
<td>All life</td>
<td>6 years</td>
<td>Scars of prior ulcerations on legs</td>
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<td></td>
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<tr>
<td>6</td>
<td>35 M</td>
<td>8 years</td>
<td>2 years</td>
<td>Cyanosis of several right and left toes. Superficial ulceration of right leg</td>
<td></td>
<td>Acrocyanosis. Cold feet and hands</td>
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<tr>
<td>7</td>
<td>37 F</td>
<td>11 years</td>
<td>Several yr.</td>
<td>Scars of prior ulcers on both feet</td>
<td>Right: Greater and lesser splanchnic-nerve resection with removal of portion of celiac ganglia and L2-L3 ganglia and intervening chain. Left: Similar splanchnic and celiac-ganglia resection and L1-L2 ganglia and intervening chain</td>
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<tr>
<td>8</td>
<td>36 F</td>
<td>All life</td>
<td>8 years</td>
<td>Ulcer 4 x 2 cm. on left leg (fig. 2b)</td>
<td>L. thigh normal. L. leg: Many small arterioles with completely or partially obliterated lumina</td>
<td>Right: Two ganglia and intervening chain in region L1. Left: Three ganglia and intervening chain in region L1</td>
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Raynaud’s
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<tr>
<td>9</td>
<td>45 F</td>
<td>Since childhood</td>
<td>20 years</td>
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<td>10</td>
<td>48 F</td>
<td>1 week</td>
<td>2 years</td>
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<td>11</td>
<td>50 M</td>
<td>3 months</td>
<td>Same</td>
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<td>12</td>
<td>26 F</td>
<td>8 years</td>
<td>1 year</td>
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<td>13</td>
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<td>10 years</td>
<td>3½ months</td>
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<td>4 days</td>
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<td>6 months</td>
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<td>14</td>
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<td>15</td>
<td>54 M</td>
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Fig. 1 (case 1, table 1). Case of livedo reticularis with winter ulcerations (figures have been reduced from stated magnification).

a. Note livedo reticularis, ischemic infarctive ulcerations and depigmented and pigmented scars.

b. Left ankle, lower dermis. Small arteriole shows some thickening of the wall and occlusion of the lumen by a thrombus (elastin H; X625).

c. Left ankle, edge of ulcer. Dilatation of capillaries and lymphatics under the base of the ulceration. Occlusion of several vessels in the mid and lower dermis and occlusion of a large vein at the dermal-subcutaneous junction (hematoxylin and eosin; X35).

d and e. Higher magnifications of dermal subcutaneous vessels shown in c, d. Note arterioles at X which reveal occlusion of the lumina by thrombi and similar occlusion of vein at Y (hematoxylin and eosin; X100). e. Thickening of venous wall, thrombosis of the lumen and moderate nonspecific perivascular infiltrate (hematoxylin and eosin; X300).
some color changes of her hands and feet but no definite Raynaud's phenomena.

The past history and family history were not significant. She smoked one-half package of cigarettes daily.

Examination revealed a blood pressure of 130 mm. of mercury systolic and 80 diastolic. Livedo reticularis involved the entire lower extremities, buttocks and forearms. The feet were warm and there were numerous ulcerations and slight edema of both ankles. Pigmented scars of the feet and legs remained at sites of prior ulceration (fig. 1a). There were no varicose veins or evidence of venous insufficiency, and the arterial pulsations in the lower extremities were normal. The results of the remainder of the examination, including the neurologic examination were not unusual.

Laboratory examination revealed a normal or negative urinalysis, erythrocyte, leukocyte and leukocyte differential blood counts, hemoglobin, sedimentation rate (Westergren), serologic test for syphilis and chest roentgenogram. A basal metabolic rate was −5 per cent. Skin temperature studies revealed very little or no change in a cold room, but normal increase of skin temperature in a hot room. Two trials of 25 mg. of hexamethonium (bistrium bromide) by subcutaneous injection on two occasions revealed little or no rise in the skin temperature. Microscopic examination of a specimen for biopsy at the edge of an ulcer of the left lateral ankle revealed a large vein at the dermal-subcutaneous junction which had thickened walls, slight perivascular infiltrate and thrombosis of the lumen. In the dermis were several vessels, especially some arterioles, which revealed thrombosis (fig. 1b, c, d and e).

The patient entered a hospital on Dec. 2, 1952, and was treated with elevation of the lower extremities, local antiseptic wet dressings and rest in bed. From December 8 until December 13 she received 25 mg. of bistrium bromide subcutaneously every eight hours. When she was dismissed on Dec. 13, 1952, the ulcerations were 90 per cent healed. She was advised to use elastic supportive bandages for the lower extremities and continue with bistrium injections at home.

In January, 1953 (one month later), the patient wrote that the previous ulcers had healed, no new ulcers had developed and there was no edema or pain. She continued to use the elastic bandages and bistrium injections. In February, 1953, she discontinued the bistrium and, although there was an increase in perspiration, no ulcerations occurred. During the summer and fall of 1953, several ulcers developed on the feet and legs, but the addition of bistrium bromide injections, 25 mg. every eight hours for one week, seemed to result in rapid healing of the ulcers. Her last letter in October, 1953, stated that she had no ulceration, edema or pain and she continued to use elastic supportive bandages.

**Case 2.** A white, married housewife, aged 42 years, from Kentucky was seen in June, 1954. She stated that during February and March, 1950, she had had one episode of pain and discoloration of the right third toe which subsided spontaneously in a few days. During May, 1950, she had the sudden onset of pain and purple discoloration in the same toe which became progressively worse and in June, 1950, she underwent right lumbar sympathetic ganglion block with procaine hydrochloride continuously for 36 hours. The pain was relieved and the normal color of the toe was restored. She was advised to use Priscoline orally and had no recurrence until February, 1951, when a progressive discoloration was noted to involve all the toes, both feet and the right ankle. The discoloration was worse during the winter and on exposure to cold weather. During the past two winters ulcers had developed on the right great and left fourth toes. The ulcers would start during the winter and had persisted into the summer, but never had started in the summer months. During the prior winter she had noted occasional burning and redness of the tips of the fingers with exposure to cold but no definite Raynaud's phenomena.

There was no history of claudication in the lower extremities on walking, edema of the legs or thrombophlebitis.

The past history and family history were not significant except that five years previously she had been told that she had hypertension and for eight years she had had irritable colon which responded well to treatment. Roentgenographic examinations of the intestinal tract and proctoscopic examination had been normal. She had smoked one-half package of cigarettes daily until stopping four years previously.

Examination revealed a blood pressure of 170 mm. of mercury systolic and 100 diastolic. Funduscopic examination revealed narrowing and sclerosis, grade 1, of the retinal arterioles. A faint precordial systolic murmur, grade 1, was audible. There was a mottled, bluish discoloration of both feet, intense over the toes and less marked over the right ankle. The toes of both feet felt cold to touch. The left fourth toe was entirely blue and had an ischemic ulcer. All arterial pulsations in the lower extremities were good. There were no signs of varicose veins or venous insufficiency.

Laboratory examination revealed negative or normal erythrocyte, leukocyte and leukocyte differential counts, roentgenograms of the chest and colon (barium enema), sedimentation rate (Westergren), fasting blood sugar, blood urea and cholesterol determinations. A roentgenogram of the thighs and a simple roentgenogram of the abdomen revealed no vascular calcification in the thighs or abdominal aorta. The basal metabolic rate was −5 per cent.

The patient entered a hospital on July 4, 1954. A trial of 25 mg. of hexamethonium (bistrium bromide) seemed clinically to result in less marked livedo and
in warming of the toes, but skin-temperature studies did not show a significant rise in temperature. The ingestion of an alcohol test dose and hot-room testing revealed a normal rise of skin temperature. The patient did not wish to continue with a therapeutic trial of hexamethonium injections but preferred sympathectomy. She did not desire to have the more extensive subdiaphragmatic sympathectomy used in the treatment of hypertension as well.

On July 10, 1954, bilateral lumbar sympathetic ganglionectomy and trunk resection was performed with removal of three left lumbar ganglia and intervening chain and two right lumbar ganglia and intervening chain. Postoperative examination revealed the feet to be warmer and the livedo much improved. However, cyanosis of the left third and fourth toes still remained. No information about this patient has been received since her dismissal after the operation.

Livedo reticularis and winter ulcerations associated with it are illustrated in figures 1 and 2.

**Analysis of Clinical and Laboratory Data**

There were 18 patients with livedo reticularis and primarily winter ulcerations, of whom 12 were women and six were men. All were of the white race. Of the seven married women all had one or more children. Thirteen (72 per cent) of the 18 patients were between the ages of 20 and 49 years, inclusive. The youngest patient was 18 years old and the oldest was 55 years old.

When first seen at the clinic because of ulceration, three patients were living in Canada, three in Minnesota, two in Michigan, two each

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**Fig. 2.** Cases of livedo reticularis with winter ulcerations (figures have been reduced from stated magnification).

*a* (case 3, table 1). Note prominent livedo reticularis, especially of the lower extremities, and ulceration of the distal portions of the toes.

*b* (case 8, table 1). Left calf: Irregular, indolent, "punched-out" ulceration which clinically appears not unlike ulcers suspected to be of factitial origin or erythema induratum.
also in Iowa and Illinois and the others were one each from Arizona, Kentucky, South Dakota, Texas, Wisconsin and Wyoming.

Seven of the women were full-time housewives; the other women had occupations in which they were not exposed to unusual degrees of heat or cold. The six male patients had a variety of occupations, none of which seemed related to excessive exposure to heat or cold. Approximately two-thirds of the patients smoked an average of one package of cigarettes daily; the remainder were nonsmokers. The past history in this group of patients was relatively noncontributory. No pertinent history of illnesses such as tuberculosis, syphilis and so forth was elicited concerning the patient or the patient's family. Raynaud's phenomena had been noted in 6 of the 18 patients (one third) and in another third there was a history of sensitivity to cold such as "cold feet" during the winter or paresthesias of the extremities with cold weather. In the remaining third of the patients, symptoms or signs of intolerance to cold were not recorded. Several patients had noted prominent hyperhidrosis, especially of the palms and soles. There was no history of lead or arsenic intoxication.

The present history of these patients was similar to the history from patients with livedo reticularis and summer ulcerations except for the seasonal difference, and a typical sequence of events comprising the present history is included in the part of the report dealing with summer ulcerations. The results of physical examination in this group of patients were similar to those in the summer group of ulcerations except for four findings. Several patients with winter ulcerations had acrocyanosis in addition to the livedo reticularis, and digital arterial occlusion with associated ulcerations of the toes was noted in seven patients, of whom three had Raynaud's phenomena. Hypertension was noted in several patients with winter ulcerations, as recorded in table 1. In several of these patients hypertension would not be unusual considering the age of the patient, but several relatively young patients had severe hypertension (for example, patients 2 and 6). Several patients in this group had unilateral or bilateral absence or marked diminution of pulsation of the dorsalis pedis or posterior tibial arteries. This usually occurred in patients with arterial occlusion of the toes.

Laboratory examinations, as in the summer group of ulcerated livedo reticularis subsequently described, revealed essentially negative or normal results of urinalysis, erythrocyte and leukocyte counts and hemoglobin. The sedimentation rate (Westergren) was usually normal. A basal metabolic rate was within normal limits in three patients. Chest roentgenograms were essentially normal in all of the patients. Cryoglobulin and lupus erythematosus blood test in one instance were negative. Cultures for bacteria and fungi from the chronic ulcerations in one patient revealed normal bacterial flora and no fungi. Histopathologic examinations of cutaneous specimens for biopsy, usually from ulcer sites, are recorded in table 1 and a comparison of the histopathologic features of winter and summer ulcers is presented in part 3. The findings were essentially similar to those recorded for summer ulcerations. No fungous elements were noted.

Cutaneous-temperature studies in several patients revealed findings similar to those in the summer group of ulcerations, in that there was generally a normal initial cutaneous temperature of the fingers and toes with a normal rise of cutaneous temperature after ingestion of alcohol, hot-room exposure and lumbar sympathectomy. Hexamethonium (bismuthium bromide) treatment of several patients did not seem to result in a rise of cutaneous temperature by measurable means, but clinically the livedo seemed less marked afterward, the feet seemed warmer and the ulcers seemed to heal more rapidly.

**Treatment**

Of the 18 patients with winter ulcerations associated with livedo, five patients underwent bilateral lumbar sympathectomy (the sympathectomy in case 13 was not done at the clinic), 11 patients were treated with or advised to have rest in bed, elastic supportive bandages for the lower extremities, local antiseptic and
**TABLE 2.—Summary of Some Findings in Twelve Patients with Summer Ulcerations**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, years</th>
<th>Duration of Livedo</th>
<th>Duration of Ulceration</th>
<th>Location and Description of Ulcers</th>
<th>Microscopic Examination</th>
<th>Bilateral Lumbar Sympathectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1†</td>
<td>31</td>
<td>7 years</td>
<td>Same</td>
<td>1946: Scars on anterior legs, ankles and plantar surface foot. 1948: About 1 year after sympathectomy; ulcer 2 x 2 cm. on medial malleolus. Ischemic and infected</td>
<td>1946: Thigh: Arteriole at dermal - subcutaneous junction thickened and lumen thrombosed. Calf: Similar findings</td>
<td>I.2-L3. Recurrence of ulcers 4–5 months after operation and in late summer for 6 years. Ulcers fewer, more superficial and less persistent after operation</td>
</tr>
<tr>
<td>2†</td>
<td>40</td>
<td>Not stated</td>
<td>15 years</td>
<td>Scars and hemorrhagic spots on both legs. Ulcers on dorsa of both feet and ankles</td>
<td>Leg: Arterioles in dermis revealed thickening of wall with narrowed or obliterated lumina. Subcutaneous vein had thickened wall, intimal proliferation and obliteration of lumen</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>47</td>
<td>7–8 years</td>
<td>Same</td>
<td>Crusted infected ulcers on ankles</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>1½ years</td>
<td>About 16 months</td>
<td>1942: Small focal hemorrhagic ulcers about ankles. 1951: Pigmentation and scars on feet, ankles and lower legs</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>31</td>
<td>Not stated</td>
<td>13 years</td>
<td>Thickening, scaling, crusting and hemorrhagic spots over dorsa of feet and anterior aspect of legs</td>
<td>Leg: Arterioles in dermis and subcutaneous tissue showed slight thickening of walls. Large vein in subcutaneous tissue had thickening of wall and obliteration of lumen</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>54</td>
<td>7 years</td>
<td>4 years</td>
<td>Tiny ulcer on lateral aspect of lower leg</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>27</td>
<td>4½ years</td>
<td>4 years</td>
<td>Scars on dorsa of feet and ankles; atrophy of skin about ankles; 1–2 cm. punched-out ulcers with necrotic bases on plantar surfaces of feet</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>34</td>
<td>7 years</td>
<td>Same</td>
<td>Scars on feet and ankles. Irregular ulcers with necrotic bases on dorsum of foot and sole</td>
<td>Ankle: Several arterioles in dermis had thickening of walls, intimal proliferation and occlusion of lumen</td>
<td>I.2-L4. Recurrence of ulcers after 1 month and for subsequent 2 years. Patient believed operation was not beneficial</td>
</tr>
<tr>
<td>9‡</td>
<td>36</td>
<td>23 years</td>
<td>Same</td>
<td>Scars, purpuric spots and crusted ulcers about ankles</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>I.1-L5. Ulcers recurred after 7 months during subsequent spring and summer months</td>
<td></td>
</tr>
</tbody>
</table>
red-blood-cell paste to the ulcers and occasionally typhoid vaccine, and in addition, two patients received hexamethonium injections. We have been unable to learn the results of the patients treated medically without hexamethonium. Little is known of the eventual results of the patients treated with sympathectomy. One patient (number 13) with digital artery thrombosis and ulceration of the toes, seemed to have no permanent benefit, since ulcers continued to recur after the operation. Both patients treated with hexamethonium seemed to have some benefit and it has been our impression that the use of this drug in other patients with livedo reticularis and ulcerations, not included in this report, was worth while.

**B. Livedo Reticularis with Summer Ulcerations**

Several patients have been at the clinic who had ulcerations similar to those seen in livedo reticularis and chronic pernio but beginning only or primarily during the warm months of the year. From the approximately 400 records of patients with livedo reticularis and pernio which were reviewed, 12 patients with this entity were found.

A report of the findings in one patient is presented, and table 2 summarizes some of the findings in all 12 patients. An initial report of this new syndrome was published previously by us.1

**Report of Case (Patient 11, Table 2)**

A white housewife and bookkeeper, aged 35 years, from Detroit, Mich., was seen in July, 1952. For
many years she had noted an asymptomatic, bluish red discoloration of the arms and legs when exposed to cold weather, but in the summer of 1940 a similar confluent eruption developed, which was confined to the lower extremities from knees to ankles followed by residual brownish hyperpigmentation. Two weeks afterward, there developed a burning sensation of the ankles, swelling of both feet and small red spots over the lateral malleoli of the ankles which subsequently became “blisters” and ulcers with drainage of serosanguineous fluid, crusting and finally healing. The entire episode from appearance of hemorrhagic spots to healing covered four to six weeks.

From 1940 to 1944 the patient was never free of ulcerations for more than four weeks and the painful ulcerations started predominantly during the summer months. After 1944 further ulcers did not develop until September, 1950, when necrotic ulcers of the ankles again developed, which only cleared temporarily with elevation and local treatment.

In 1951 and 1952 paresthesias developed with pain and burning in the left foot and several toes, and afterward the patient had a permanent subjective hypalgesia in these areas. About six times in the prior two years she had noted cramps in the right calf on first waking in the morning but these disappeared on further exercise.

The family history revealed that two siblings and a distant nephew had tuberculosis, another sibling had rheumatic heart disease, the patient’s mother had gallbladder and heart disease while her father had hypertension. She smoked one package of cigarettes daily.

Examination revealed a blood pressure of 104 mm of mercury systolic and 60 diastolic. There was a faint livedo reticularis of the arms which was of variable intensity. From knees to ankles there were hyperpigmented areas, and on the sides of the ankles and dorsa of the feet were several ulcers, in areas of livedo reticularis, some crusted, with surrounding inflammation and edema (fig. 3a). There were scarring and pigmentation at sites of former ulcers and a few dilated superficial venules were evident over the legs but no large varicose veins. Arterial pulsations were all good.

Complete neurologic examination revealed only a subjective decrease of pain, touch and temperature in several left toes and medial aspect of the left foot which was thought to be a mononeuritic multiplex type involvement seen in occlusive arterial disease affecting the vasa vasorum.

Laboratory examination revealed flocculation re-
action for syphilis, chest roentgenogram, platelet count, bleeding and clotting time to be negative or normal. Cultures of the ulcers revealed pseudomonas organisms. Microscopic examination of a cutaneous specimen for biopsy from the right ankle revealed increased number, dilatation and tortuosity of subepidermal capillaries and intimal proliferation and occlusion of the lumina of dermal arterioles by bland amorphous thrombi. There were thickening, hyalinization and nonspecific cellular infiltration of some arteriolar walls. A large vein at the dermal-subcutaneous junction had fibrosis and thickening of the walls with obliteration of the lumen (fig. 3b). The results of other pertinent laboratory examinations were not remarkable.

On Aug. 1, 1952, the patient underwent left lumbar block with absolute alcohol performed at L-2. The pain of the ulcers of the left lower extremity was relieved and the extremity became warm and comfortable. Elevation of the legs and mild local treatment were advised.

A right lumbar block was not performed, and on Aug. 18, 1952, the ulcers were healed. The patient was dismissed and 1 month later, although pain in the left foot had recurred, no ulcers were present.

A letter in May, 1953, from a dermatologist reported that he had seen the patient and that she had no active ulcers, only residual pigmentation and scars.

**Analysis of Clinical and Laboratory Data**

All patients who had summer ulcerations were white women. Four were single and eight were married. All the patients but three were in the age group of 21 through 40 years. The oldest patient was aged 54 years, and the youngest was aged 17 years.

All the patients lived within 500 miles of the clinic; four patients were living in Illinois, two resided in Michigan, and the others were one each from Kentucky, Iowa, Wyoming, Kansas, Minnesota and Ontario, Canada.

None of the patients were employed in an occupation which exposed her to excessive heat or cold; eight were housewives, two were employed in clerical office work, one was employed as an assembly worker and one patient was a student.

Four patients were nonsmokers, while seven patients were mild to moderate smokers of about one package of cigarettes or less daily. A history of smoking was not recorded in one case.

The past history in the patients as a whole was noncontributory. A history of a relative or relatives having had tuberculosis was present in three cases but none of the patients had had tuberculosis. A vague history of frostbite as a child was reported by one patient.

Several patients believed that they were "nervous," and hyperhidrosis of the palms or soles was noted by a few patients. In no case was a history of syphilis or Raynaud's phenomena reported. There was no history of intoxication by lead or arsenic.

The present history of each patient was remarkably similar. Other than the seasonal occurrence, the history in patients with summer and winter ulcerations is essentially similar.

A typical sequence of events was, in a patient with summer ulcerations, as follows: A variable amount of livedo reticularis over the body, especially of the lower extremities was noted for several weeks, months or years before onset of the ulcerations. The livedo was usually more prominent in the winter than in the summer. During the spring, or summer, edema of the feet and ankles developed which was most severe at the end of the day and less in the morning after rest. Shortly after the development of edema there occurred red to bluish infarctive areas over the legs, ankles, dorsa of the feet and soles which would either disappear spontaneously, or ulcerations would occur at these sites after several weeks. The infarctive lesions and ulcerations would appear spontaneously and no prior insect bite or trauma could be definitely incriminated. Healing would result in an atrophic, pigmented or depigmented scar. These ulcers would be very painful and resistant to most medical forms of treatment, both local and systemic. The entire course from onset of infarcts to ulceration and healing would be usually one and one half to three months. New ulcerations would continually develop during the summer, but with cold weather the ulcers would tend to heal and not recur, so that during the winter the patient would be free of ulcerations or markedly better. In the patients with winter ulcerations, of course, the reverse was true, in that the ulcerations would primarily occur during the winter and tend to heal in the
summer months. Occasionally a summer ulceration would persist throughout the winter and occasionally an ulcer would start during the winter months, but this was the exception in the patients with primarily summer ulcerations.

The results of examination of the patients, other than the ulcerations and presence of livedo reticularis, were essentially normal in every instance of summer ulcerations. No unusual body habitus or undue obesity was noted. The blood pressure was essentially normotensive in all of the patients. Active ulcerations or scars of previous ulcerations were present mostly about the ankles, dorsa and soles of the feet and on the lower part of the legs. No ulcers were present above the knees, on the upper extremities, or any other part of the body, regardless of the distribution of the livedo. The initial lesion would appear as a painful, red to bluish infarctive or hemorrhagic area. The ulcers were generally irregular in shape and of various sizes from 0.5 cm. to 1 or 2 cm. in diameter and were deep or superficial, discrete or confluent. Many were infected and had purulent drainage. The ulcerations clinically at times suggested ulcers of factitial origin or erythema induratum. Edema of the feet and ankles was usually present to some degree. In no patient were there noted significant varicose veins or evidence of chronic venous insufficiency. Arterial pulsations were normal in the lower extremities in all patients except one (patient 7) who had a diminished right dorsalis pedis pulsation. Occlusive arterial disease was not suspected or demonstrated in any patient. There was no history or evidence of digital arterial thrombosis or superficial phlebitis in any patient.

Laboratory examinations revealed an essentially normal urinalysis, erythrocyte and leukocyte counts and hemoglobin. Sedimentation rate by the Westergren method usually revealed normal results. The serologic reaction for syphilis was negative in every case. The chest roentgenogram was essentially normal in all of the patients.

Although none of these patients was suspected of having hyperthyroidism, hypothyroidism or myxedema, basal metabolic rate determination in two patients revealed results of +12 and −14 per cent. Bacteriologic culture from an ulcer in one patient revealed pseudomonas organisms.

Treatment

Of the 12 patients in the summer group of ulcerations with livedo reticularis, six were advised to have rest in bed, elastic supportive bandages for the lower extremities and mild local therapy to the ulcerations, and one patient, in addition, used hexamethonium therapy; four patients underwent bilateral lumbar sympathectomy and one patient underwent unilateral lumbar alcohol block. No information has been received as to the results in the patients treated medically without hexamethonium. The patient with the unilateral lumbar alcohol block seemed to have more rapid healing of the ulcerations, and she had only healed scars 10 months afterward when she was seen by a dermatologist elsewhere. The results of lumbar sympathectomy are noted in table 2. Usually little permanent benefit was gained from sympathectomy.

Patient 2, table 2, seemed to gain considerable benefit from hexamethonium treatment and it has been our impression that other patients with livedo reticularis and primarily winter ulcerations (table 1) seemed to benefit from hexamethonium.

3. Comparison of Histopathologic Features of Winter and Summer Ulcers

Histopathologic Examination

Histopathologic examination was done usually from biopsies at the sites of ulcers in five patients with winter ulcerations and seven patients with summer ulcerations.

Of these patients with ulcerations the following was noted: The epidermis usually revealed acanthosis and proliferation of the rete pegs about the site of the ulcer. In several cases histopathologic examination revealed granulation tissue, edema and nonspecific cellular infiltrate with little or very slight intimal proliferation and thickening of small arterioles. Dilated subepidermal capillaries, lymphatics and venules were noted in the majority of the
cases. In four of the five patients with winter ulcers and four of the seven patients with summer ulcers on whom microscopic examination was performed, there were thickening of the wall of the arterioles of the cutis and subcutaneous tissue and occlusion of these vessels, and of these, in two cases each, of both the summer and the winter group, the arterioles revealed occlusion by a thrombus. In the biopsies of one patient with winter ulcers and three patients with summer ulcers, there were veins evident in the subcutis which showed thickening of the walls and obliteration of the lumen of the vein. There was usually a mild to moderate nonspecific infiltrate in the cutis which was usually perivascular, with some infiltration of the occluded arterioles and veins. There was relatively little panniculitis or fibrosis of the subcutaneous fat and no giant cells were evident in any section. Elastic-tissue stains generally revealed that the internal elastic limiting membrane of the intima of the arterioles was undamaged. Fragmentation of the elastic fibers in the corium was noted in several specimens. Iron stains for hemosiderin were positive in more than 50 per cent of the cases. However, in all these cases the specimen for biopsy was removed from the lower extremities, where some hemosiderin can be demonstrated in persons without peripheral vascular disease or clinical evidence of venous insufficiency.

Hotchkiss-McManus or periodic acid-Schiff stain revealed that several of the thickened arteriolar walls in various sections were stained intensely with this stain. No fungal elements were noted. Maresch modification of the Bielschowsky stain for reticulum fibers and Bodian silver stain for nerve fibers revealed no increase in any case. Stains for amyloid did not reveal presence of amyloid in any case and the Giemsa stain did not reveal an abnormal number of mast cells. There was no histopathologic evidence for periarteritis nodosa or syphilis in any section.

**Histopathologic Differential Diagnosis**

There are several diseases which resemble to a varying degree the histologic picture in livedo reticularis. Pernio, nodular vasculitis, venous insufficiency and sometimes erythema induratum may be especially difficult or impossible to differentiate by histopathologic examination. Pernio can have a similar angitis, but may have a good degree of panniculitis and giant cells. Nodular vasculitis may show a vasculitis of both arteries and veins with varying degrees of thickening and oblitative change; however, fibrosis and atrophy of the subcutaneous tissue and foreign-body giant cells may be more prominent. In chronic venous insufficiency of the lower extremities, both arterioles and veins may reveal intimal proliferation and thickening of the walls as in cases of livedo reticularis. Erythema induratum classically shows typical tubercles but in about 30 per cent of cutaneous biopsies, examination shows a nonspecific granuloma and vasculitis which is not diagnostic. Hypertensive ischemic ulcers reveal only involvement of the arterioles with such changes as thickening of the walls, decrease of the size of the lumen and some periarteritis.

Superficial thrombophlebitis, erythema nodosum and panniculitis of Weber-Christian do not usually cause ulceration, but might be considered in the biopsy of a nonulcerated lesion. Thrombophlebitis involves only the veins with occlusion of the lumen, inflammatory infiltrate of the wall of the vein and varying amounts of periphlebitis. Erythema nodosum may show an acute inflammatory reaction in the corium and subcutaneous tissue with polymorphonuclear leukocytes, fat-replacement atrophy and Miescher granuloma formation, but thrombosis of the vessels and proliferative changes of the walls are not unusual. Secondary thrombophlebitis and a tuberculoid reaction may be found in erythema nodosum. Panniculitis of Weber-Christian generally reveals an inflammation primarily of the fat, and minimal changes, usually in the vessels.

In summary, the histopathologic picture of summer ulcerations or winter ulcerations with livedo reticularis reveals no essential difference in the type or degree of vessel involvement. Arterioles generally showed thickened walls, intimal proliferation and occlusion of the lumen, sometimes by a thrombus. Several
veins in the summer group and one in the winter group showed thickening and infiltration of the wall with obliteration of the lumen.

**Comment**

We have studied a group of patients who have idiopathic livedo reticularis and ulcerations of the legs or feet beginning both during the winter and summer months of the year. The patients had noted the livedo reticularis for several weeks or years before the onset of the ulcerations. Although the livedo was usually worse during the winter, in one group the ulcerations were primarily during the warm months and healed after the onset of cool weather. Edema of the feet or ankles was associated with and usually preceded the hemorrhagic, infarctive lesions in both winter and summer ulcerations. However, it was our impression that the edema was a more prominent feature in those patients with summer ulcerations than in those with winter ulcerations. Painful ulcers subsequently developed at these sites, which might heal after several months, but new ulcers recurred during the summer or warmer months of the year in the summer group of ulcerations in contrast to the healing of the ulcers during the summer in the usual instance of winter ulcerations. Occasionally a patient with primarily winter ulcerations would develop ulcerations during the summer months, such as was reported by patient 1 in the winter group. The summer ulcerations generally seemed to be more resistant to treatment than the winter ulcerations. The associated edema and increased vasodilatation during the summer may be a factor in the increased frequency of ulcerations during the summer months in certain individuals. However, the ulcers did not have the features of typical stasis ulcers. It is possible that pressure from edema of the skin might increase the localized ischemia of the skin and further the development of ulceration.

A review of the literature concerning livedo has revealed that the occurrence of livedo reticularis and ulcerations during the warm months of the year has not been a recognized syndrome. Ebert described the findings in a woman, aged 33 years, which seems to be the only similar recorded case. Some of the pertinent features in this patient are noted in the histopathologic portion of part 1 in this report. Ebert expressed the belief that the ulcerations were most probably tuberculoid, although there was no clinical or laboratory evidence of tuberculosis. Ebert's patient could represent a case of livedo reticularis with summer ulcerations similar to the cases in the group that we are reporting.

Histopathologic studies from biopsies at ulcer sites in the patients with summer ulcerations often revealed occlusion of the arterioles and veins, but these findings were not unique for the cases with summer ulcerations, since similar histopathologic findings were seen from biopsies of winter ulcerations with livedo. The edema preceding the onset of the ulcers would seem to indicate a stasis factor and the biopsies revealed involvement of veins as well as arterioles. Kulwin and Hines reported pathologic changes in the cutaneous arterioles and veins not too dissimilar from our findings in patients with chronic venous insufficiency with edema even in areas of normal-appearing skin of the lower extremities.

Treatment of these patients with winter and summer ulcerations by sympathectomy did not seem of permanent value according to the follow-up information which we possess. Medical treatment employing local antiseptic dressings, powdered red blood cells, rest in bed with elevation of the extremities, elastic supportive bandages, and a trial of the hexamethonium drugs seems to be the best therapy. Typhoid vaccine treatment seemed to be beneficial in several of these patients with livedo reticularis and ulceration, especially in patient 13, table 1.

**Summary and Conclusions**

A brief summary of the medical literature concerning livedo reticularis is presented, especially in reference to the occurrence of ulcerations. In reviewing the records of approximately 400 patients with livedo reticularis and pernio seen at the Mayo Clinic in the past 10 years, 18 patients with winter ulcerations and 12 patients with primarily summer ulcerations and livedo reticularis were found. The
clinical and histopathologic data in these patients form the basis of this report.

The clinical and histopathologic findings in these two groups of patients are very similar. All of the patients in the summer group and two thirds of the winter group were women. Hypertension, Raynaud’s phenomena, acrocyanosis, digital artery thrombosis and occasional absence of dorsalis pedis and posterior tibial arterial pulsations were noted only in the patients with winter ulcerations. There was no difference in the appearance or location of the ulcerations occurring on the legs, ankles or feet other than the ulcerations secondary to occlusion of digital arteries in the winter group. Edema of the legs and feet was often an associated feature in this group with livedo and ulcerations. The edema was a more prominent feature in the patients with summer ulcerations than in those with winter ulcerations.

Histopathologic studies revealed similar changes of occlusion in the arterioles and veins which were not diagnostic. No evidence of tuberculosis, syphilis or periarthritis nodosa was discovered as a causal feature in any case.

Therapy stressing rest in bed, elastic supportive bandages to prevent edema, and hexamethonium was the treatment of choice. Sympathectomy seemed of little permanent value in the majority of patients.

ADDENDUM

Since this paper was written it has been brought to our attention that Yorke and Klaber have reported a case not unlike those with summer ulcerations discussed here (Yorke, G. A. [for Dr. Robert Klaber]: Asphyxia reticularis multiplex [Unna]. Proc. Roy. Soc. Med. 37: 640, 1944).

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Livedo Reticularis with Ulcerations
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