BLIND EVALUATION OF THE DIAGNOSTIC SPECIFICITY OF NAILFOLD CAPILLARY MICROSCOPY IN THE CONNECTIVE TISSUE DISEASES

JAY G. KENIK, HILDEGARD R. MARICQ, and GILES G. BOLE

Twenty-four patients with connective tissue diseases and 5 control subjects were studied by "wide-field" photography. A total of 44 photographs of the nailfold were sent to the second author (HRM) for "blind" diagnostic interpretation. The scleroderma-dermatomyositis pattern was identified in 17 of 18 photographs of 11 scleroderma patients, and 5 of 5 photographs of 2 dermatomyositis patients. Six of 8 photographs of 5 patients with systemic lupus erythematosus were correctly identified, as were 7 of 7 photographs of 5 control subjects. These results demonstrate that characteristic patterns of nailfold capillary abnormalities can be identified and correlated blindly with the clinical diagnosis in several connective tissue diseases.

Characteristic patterns of nailfold capillaries have been described for certain connective tissue diseases (1–10). These consist of dilated capillaries frequently bordering avascular areas in both scleroderma and dermatomyositis as well as overlap syndromes when scleroderma is a component (Figures 1 through 5). In systemic lupus erythematosus (SLE) a tortuous or "meandering" pattern, though not specific or universally noted, is characteristic for this disorder (Figures 6 and 7). Although scleroderma and dermatomyositis are frequently indistinguishable by capillary morphology, occasionally a "bushy" pattern is recognized which has been seen more often with dermatomyositis (Figure 5) (11).

In the present study, "wide-field" photomicrography was performed on a group of patients with a variety of connective tissue diseases and also on control subjects. To assess the specificity and challenge the diagnostic potential of capillary microscopy, these photographs were coded without diagnosis and sent to the second author (HRM) at a separate institution for evaluation and diagnostic interpretation.

MATERIALS AND METHODS

Subjects. Twenty-four patients with connective tissue diseases and 5 control subjects were studied at the University of Michigan Medical Center (UMMC). The following diagnostic groups were included: 1) scleroderma: 11 patients; 2) dermatomyositis: 2 patients; 3) polymyositis: 2 patients; 4) systemic lupus erythematosus: 5 patients; 5) scleroderma-polymyositis overlap: 2 patients; 6) Raynaud's syndrome: 2 patients; 7) normal subjects: 5.

The age of the patients were as follows: scleroderma: range 9–68, mean 43 years; dermatomyositis: 49 years and 54 years; polymyositis: 31 years and 39 years; systemic lupus erythematosus: range 25–52, mean 35 years; scleroderma-polymyositis overlap: 48 years and 58 years; Raynaud's syndrome: 29 years and 48 years; controls: range 25–42, mean 30 years.

The diagnosis of scleroderma was made clinically by observation of the presence of thickened skin proximal to the metacarpophalangeal joints. Each diagnosis was agreed upon by at least 2 rheumatologists at the University of Michigan Medical Center.

Dermatomyositis was diagnosed by the presence of myositis characterized by muscle weakness, elevated creatine

Supported by Training Grant AM 07080 and the University of Michigan Multipurpose Arthritis Center Grant AM 20557 from the National Institutes of Health.

Jay G. Kenik, MD: Fellow in Rheumatology, Arthritis Division and Rackham Arthritis Research Unit, University of Michigan Medical School, Ann Arbor; Hildegard R. Maricq, MD: Associate Professor of Research Medicine, Rheumatology Division, Medical University of South Carolina, Charleston; Giles G. Bole, MD: Professor of Medicine and Chief Arthritis Division and Rackham Arthritis Research Unit, University of Michigan Medical School, Ann Arbor.

Address reprint requests to Jay G. Kenik, MD, Rheumatology Division, Creighton University School of Medicine, 601 North 30th Street, Omaha, Nebraska 68181.

Submitted for publication June 23, 1980; accepted in revised form February 2, 1981.

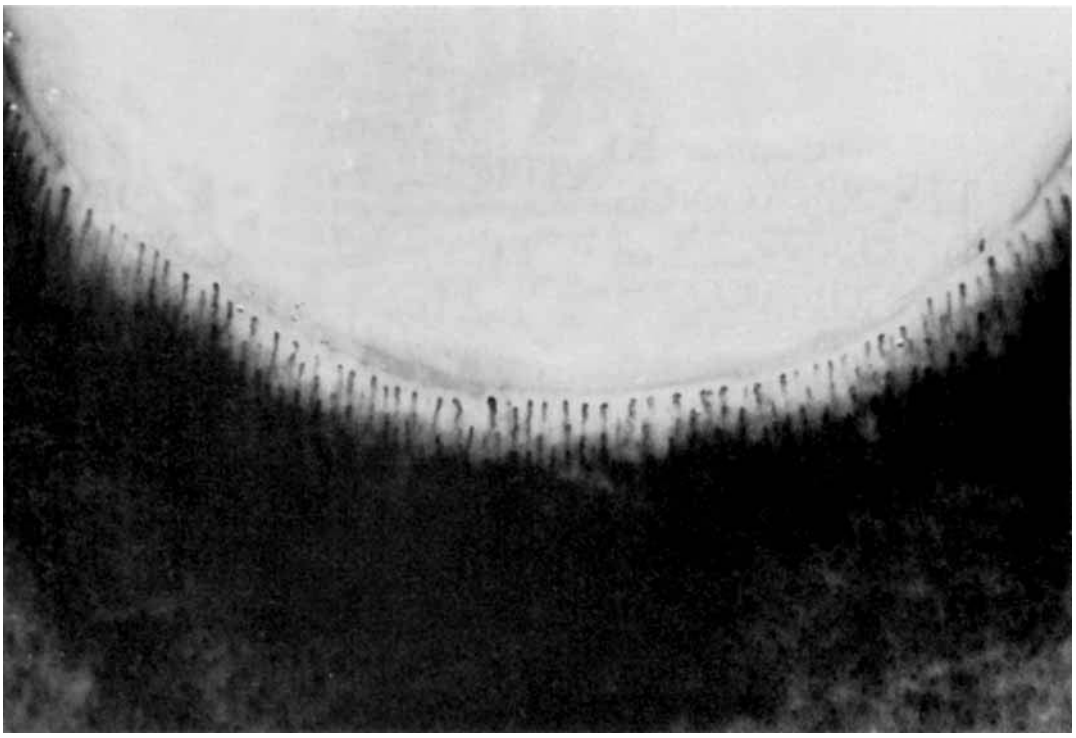

Figure 1. Normal nailfold capillary pattern in a control subject.

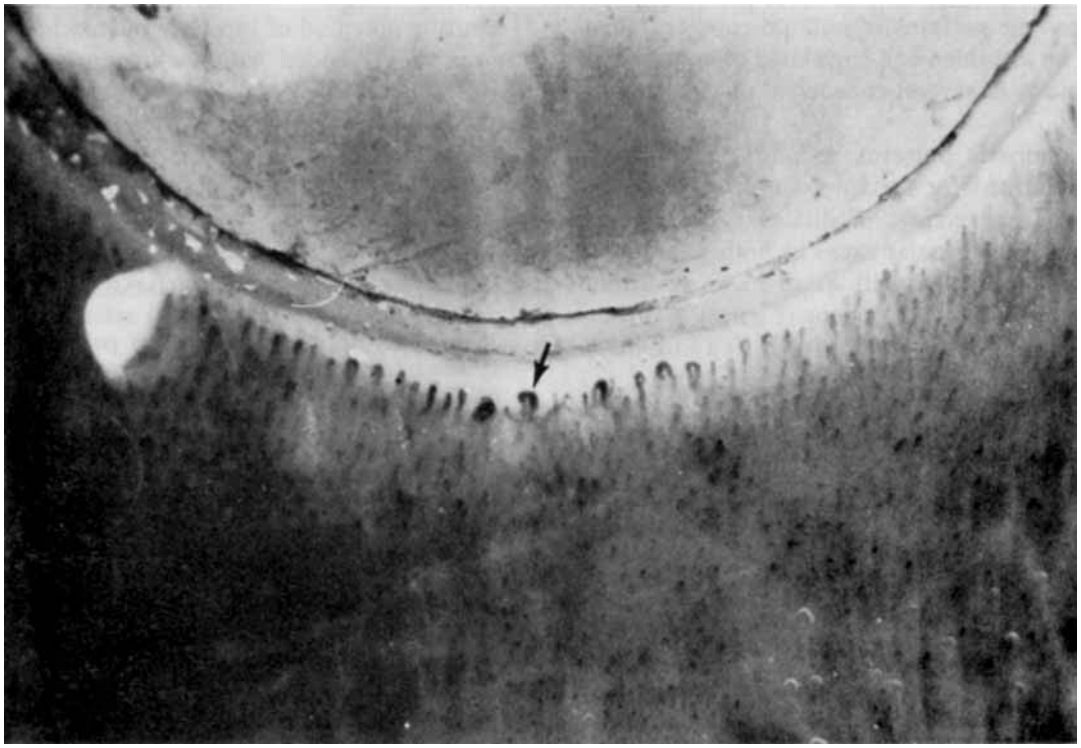

Figure 2. Early capillary changes in a scleroderma patient (**arrow**) (early scleroderma-dermatomyositis pattern).

Figure 3. More advanced capillary changes in a scleroderma patient (scleroderma-dermatomyositis pattern).

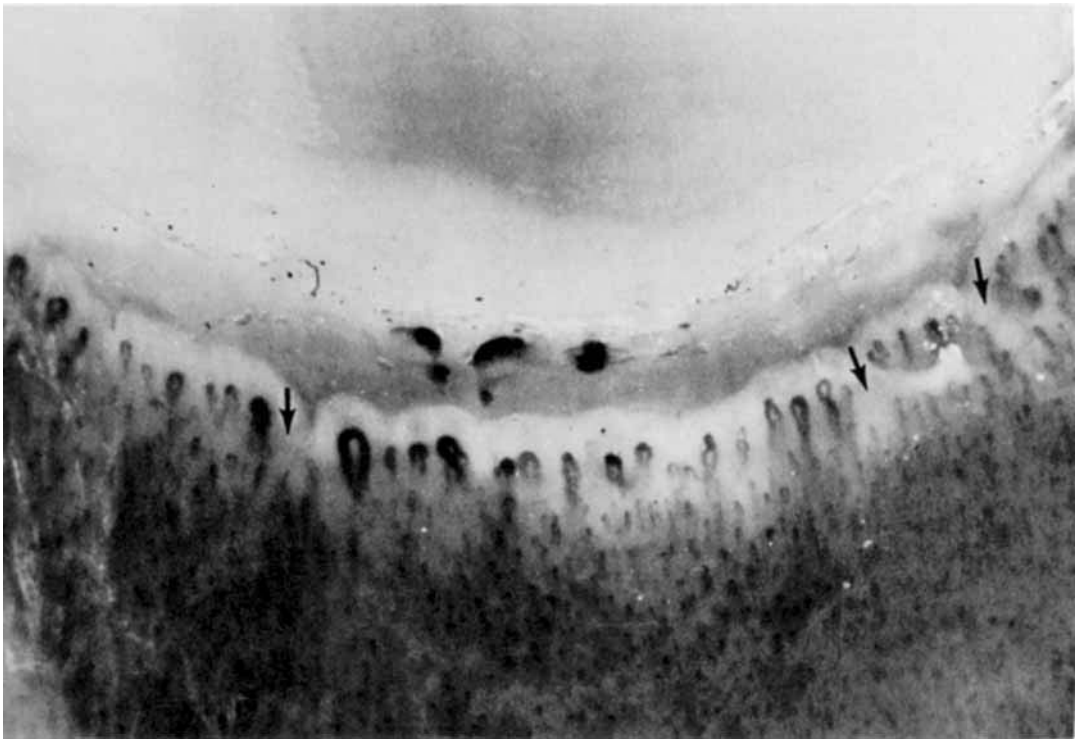

Figure 4. Dilated capillaries with avascular areas (**arrows**).

Figure 5. Dilated capillaries with extensive avascular areas in a patient with dermatomyositis. "Bushy" capillary pattern is evident in some regions (**arrows**) (scleroderma-dermatomyositis pattern).

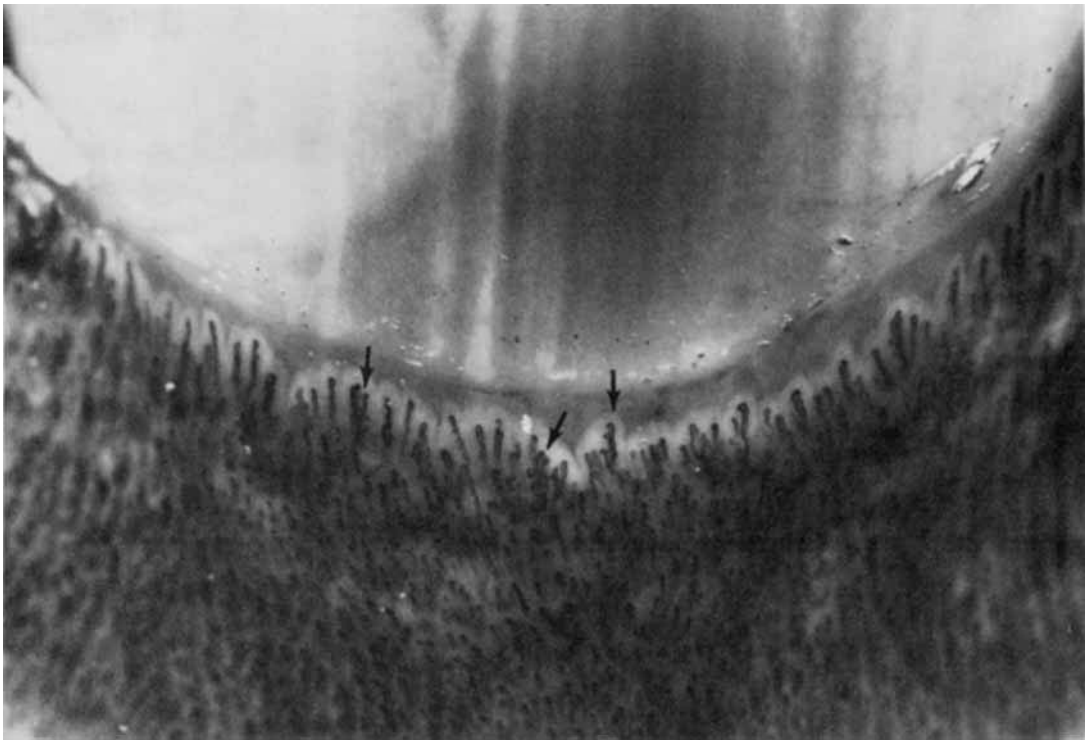

Figure 6. Tortuous or "meandering" capillaries (**arrows**) in a patient with systemic lupus erythematosus.

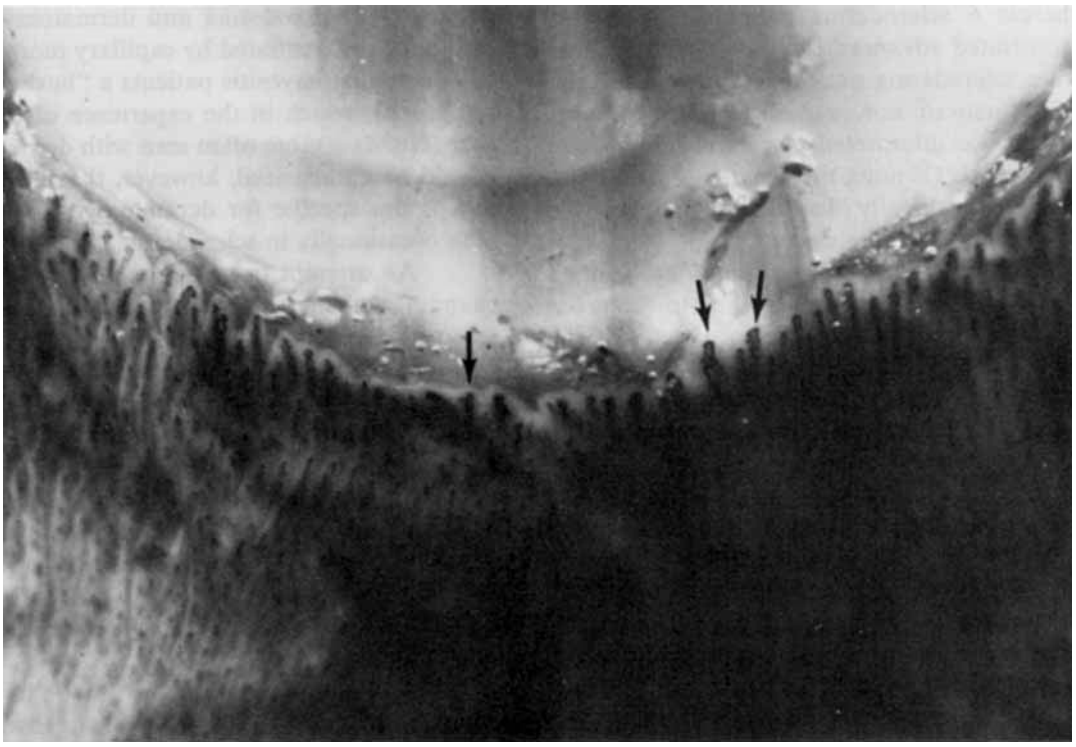

Figure 7. Tortuous or "meandering" capillaries (**arrows**) in another patient with systemic lupus erythematosus.

phosphokinase (CPK) levels, and abnormal electromyograms demonstrating a myopathic pattern. In addition, both patients had diagnostic muscle biopsies as well as the characteristic skin rash involving the hands and face. Polymyositis was diagnosed by the same myopathic findings as dermatomyositis, including elevated CPK levels, abnormal electromyograms, and muscle biopsy, with neither patient having cutaneous lesions.

All patients with systemic lupus erythematosus fulfilled at least 4 ARA criteria in addition to having elevated levels of antibody to native DNA during at least one period in their clinical course.

The scleroderma-polymyositis overlap patients both had evidence of sclerodactyly, cutaneous telangiectasias, positive speckled pattern antinuclear antibodies, and myositis characterized by weakness, elevated CPK levels, and characteristic biopsy.

Raynaud's syndrome was diagnosed by physician observation of at least a biphasic (pallor followed by either cyanosis or erythema or both) color change on exposure of the hands to cold. Both of these patients have been followed with these symptoms for over 5 years with no other clinical or laboratory evidence to support a diagnosis of a connective tissue disease.

Normal controls were selected from members and students of the Arthritis Division. None of the normal controls reported symptoms at the time of the examination.

Technique. After gentle washing, the nailfold areas of all 10 fingers were examined under a StereoZoom 7 dissecting microscope at 30–70x (Bausch and Lomb, Rochester, New York). Before each finger was examined, a drop of type B immersion oil was applied to the nailfold area to facilitate visualization of the capillaries. A standard Bausch and Lomb Nicholas illuminator provided the external light source. Photographic records of representative patterns were made on Kodak 5069 high contrast copy film (Eastman Kodak, Rochester, New York) using a single lens reflex camera fitted with a Topcon 58 mm macro lens and bellows (Tokyo Optical Co., Tokyo, Japan). A Bowens macrolight (Bogen Photo Corp., Englewood, New Jersey) provided both the modeling light source and flash necessary for photography. Final magnification was 2½ times on the negative.

A total of 44 photographs of the nailfolds were submitted for analysis. Photographs of more than one digit in the same subject were used in certain cases and in some of the controls. The totals for each group were: scleroderma: 18 (11 patients); dermatomyositis: 5 (2 patients); polymyositis: 2 (2 patients); systemic lupus erythematosus: 8 (5 patients); scleroderma-polymyositis overlap: 2 (2 patients); Raynaud's syndrome: 2 (2 patients); controls: 7 (5 subjects).

RESULTS

A scleroderma-dermatomyositis pattern was identified by the second author who was unaware of the clinical diagnosis or the patient's status in 17 of 18 photographs of the scleroderma patients and 5 of 5 of the dermatomyositis patients. Five scleroderma patients (6 photographs) demonstrated only modest capillary

changes, whereas 6 scleroderma patients (11 photographs) demonstrated advanced capillary changes. One nailfold from a scleroderma patient was interpreted as having a normal pattern; however, a second digit from that same patient was interpreted as a scleroderma-dermatomyositis pattern. Of note, the 5 patients with dermatomyositis were specifically identified by the "bushy" pattern evident in these examples (Figure 5).

Of the patients with systemic lupus erythematosis, 6 of 8 were correctly identified by their tortuous or "meandering" capillary pattern. This tortuous pattern though not specific or universally noted in lupus tends to favor this diagnosis when a connective tissue disease is being considered. One of the lupus patients was interpreted as having a normal pattern and one as having a scleroderma-dermatomyositis pattern (this last SLE patient has subsequently developed early sclerodactyly and may indeed represent an early SLE-scleroderma overlap syndrome).

The 2 patients with Raynaud's syndrome were interpreted as having normal capillary patterns as were both patients with polymyositis. One patient with polymyositis-scleroderma overlap was interpreted as having a scleroderma-dermatomyositis pattern and the other as being consistent with systemic lupus. All 7 photographs of the controls were recognized as having normal nailfold capillary patterns. All the results are tabulated in Table 1.

DISCUSSION

These results demonstrate that characteristic patterns of nailfold capillaries can be recognized from coded photographs and correlated with the clinical diagnosis. In a recent study, 41 of 50 patients with scleroderma had the morphologic pattern characteristic for this disorder, a prevalence of 82% (12). In another report, 7 of 8 patients with dermatomyositis also had this pattern (1). Scleroderma and dermatomyositis usually cannot be differentiated by capillary morphology alone. In our dermatomyositis patients a "bushy" pattern was recognized, which in the experience of the second author (HRM) is more often seen with dermatomyositis. It should be emphasized, however, that the "bushy" pattern is not specific for dermatomyositis and has been seen occasionally in scleroderma.

An attempt to compare the degree of capillary changes with the extent of cutaneous disease failed to show a correlation. Of the 5 patients with only modest capillary changes, 3 were in advanced stages of their cutaneous disease. Conversely, 3 patients with advanced capillary changes of scleroderma were in the early stages of their cutaneous disease, emphasizing the diagnostic utility of capillary microscopy. To underscore the importance of examination of all the digits in each patient, one should note the case where one digit had a normal pattern while a second digit from that same patient had the characteristic scleroderma-dermatomyositis pattern.

Although no attempt was made in this study to compare the degree of capillary changes with the extent of visceral disease, a positive correlation was found in an earlier study (13). Capillaroscopic findings were correlated with Raynaud's phenomena as part of a multicenter study on 120 patients (46 scleroderma, 37 SLE, 26 mixed connective tissue disease, 11 Raynaud's disease). Other than those in the scleroderma group, dilated capillaries were noted in 14 patients with mixed connective tissue disease and one patient each in the lupus and Raynaud groups (12). This tends to support the specificity of this pattern for scleroderma, dermatomyositis, and overlap disorders when scleroderma is a component.

In the experiences of the authors, certain cases of scleroderma have had capillary changes precede full clinical expression of this disease. In such cases capilla-

Table 1. Blind interpretation of nailfold patterns in several connective tissue diseases

	Scleroderma-dermatomyositis	Tortuous "meandering"	Normal	Total photographs
Scleroderma	17		1	18
Dermatomyositis	5			5
Systemic lupus erythematosus	1	6	1	8
Raynaud's syndrome			2	2
Polymyositis			2	2
Scleroderma-polymyositis overlap	1	1		2
Normal controls			7	7

roscopy may be useful in predicting which patients with Raynaud's phenomenon could proceed to a diagnosis of scleroderma. This hypothesis is supported by preliminary results from a study on the predictive value of capillary microscopy in patients with Raynaud's phenomena (14).

The tortuous or "meandering" pattern seen in systemic lupus erythematosus is neither specific nor universal. In the multicenter study this pattern was seen in 25 of 60 SLE patients, a prevalence of 42%. Of note, 17 of 60 SLE patients (28%) showed no capillary abnormalities (12). In the same study 4 of 11 (36%) of the patients with Raynaud's disease had this pattern. However, as demonstrated by our study, the tortuous or "meandering" pattern can be identified and, when correlated with other clinical and laboratory parameters, can be an additional useful diagnostic finding.

In the mixed connective tissue disease syndrome, both the scleroderma-dermatomyositis and tortuous pattern have observed prevalences of 54% (14 of 26) and 12% (3 of 26) respectively (12). In the experience of the authors and as demonstrated in the 2 examples in this study, polymyositis unlike dermatomyositis does not display consistent or characteristic patterns of capillary abnormalities. This observation may have diagnostic significance in those patients with myositis who manifest only subtle cutaneous features or have been partially treated when first seen by the consultant. In addition, this finding may also have pathogenic significance in the further dissection of subsets of inflammatory muscle disease.

We conclude that capillary microscopy, a simple noninvasive technique, when performed by a trained observer can be of considerable value in assisting with the differential diagnoses of several of the major forms of connective tissue disease. It again emphasizes that pathologic changes in the capillary beds are important and in certain instances may be primary lesions in several of the connective tissue diseases.

REFERENCES

1. Maricq HR, LeRoy EC: Patterns of finger capillary abnormalities in connective tissue disease by "wide-field" microscopy. Arthritis Rheum 16:619–628, 1973
2. Maricq HR, Blume RS, LeRoy EC: Wide-field study of nailfold capillary bed in disorders of connective tissue. Sixth European Conference on Microcirculation. Aalborg, 1970–1971, pp 116–122
3. Maricq HR, LeRoy EC: Progressive systemic sclerosis: disorders of the microcirculation. Clin Rheum Dis 5:81–101, 1979
4. Redisch W, Messina EJ, Hughes G, McEwan C: Capillaroscopic observations in rheumatic diseases. Ann Rheum Dis 29:244–253, 1970
5. Gilje O, Kierland R, Baldes EJ: Capillary microscopy in the diagnosis of dermatologic diseases. J Invest Dermatol 22:199–206, 1954
6. Brown GE, O'Leary PA: Skin capillaries in scleroderma. Arch Intern Med 36:73–88, 1926
7. Buchanan IS, Humpston DJ: Nailfold capillaries in connective tissue disorders. Lancet 1:845–847, 1968
8. Ross JB: Nailfold capillaroscopy—a useful aid in the diagnosis of collagen vascular diseases. J Invest Dermatol 47:282–285, 1966
9. Fukushiro R: Capillary microscopic examination in various skin diseases. Jpn J Dermatol (Series B) 75:486–502, 1965
10. Kawashima Y: Capillary microscopic examination in collagen disease. Jpn J Dermatol (Series B) 76:23–31, 1966
11. Maricq HR: Unpublished observations
12. Maricq HR, LeRoy EC, D'Angelo WA, Medsger TA, Rodnan GP, Sharp GC, Wolfe JF: Diagnostic potential of in-vivo capillary microscopy in scleroderma (systemic sclerosis) and related disorders. Arthritis Rheum 23:183–189, 1980
13. Maricq HR, Spencer-Green G, LeRoy EC: Skin capillary abnormalities as indicators of organ involvement in scleroderma (systemic sclerosis), Raynaud's syndrome and dermatomyositis. Am J Med 61:862–870, 1976
14. Maricq HR, Weinberger AB, LeRoy EC: Predictive value of capillary microscopy in patients with Raynaud's phenomenon (abstract). Arthritis Rheum 23:716, 1980