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Quantification of the Nail Fold Capillary Abnormalities in Systemic Sclerosis and Raynaud's Syndrome*

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Measurements were made of capillary luminal diameters and capillary numbers in four groups: 19 normal controls 10 patients with 'idiopathic' Raynaud's disease, 12 patients with Raynaud's phenomenon with an underlying connective tissue disease other than systemic sclerosis, and 18 patients with systemic sclerosis. There was a significant reduction of capillary numbers in all three patient groups compared with the normal controls. Both the afferent and efferent luminal diameters were also increased in each patient group. Patients with Raynaud's phenomenon, either on its own or associated with connective tissue disease, gave results intermediate between normal controls and patients with systemic sclerosis. There were no significant correlations between either the reduction in capillary numbers or increase in luminal diameter with disease severity or duration in systemic sclerosis. It is unlikely that capillary microscopy will provide useful prognostic information for an individual patient with systemic sclerosis; its predictive value in Raynaud's disease must await the outcome of long term follow-up studies. *Key words: Capillaries; Raynaud's.* (Received June 18, 1985.)

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Morpholoical changes of the nail fold capillaries have been described for many years in a variety of conditions, including systemic sclerosis. Maricq et al (1) described a "scleroderma pattern" of abnormality, which is present in 95% of cases of systemic sclerosis (SS) and a similar proportion of case of dermatomyositis. This pattern consists of definite, and sometimes gross, enlargement of many nailfold capillaries surrounded by patchy avascular areas. These changes were not observed in normal subjects and were very infrequently seen in systemic lupus erythematosus. However, 50% of patients with mixed connective tissue disease and 15% of cases of apparently idiopathic Raynaud's disease (RD) show this abnormality, a finding which has led to speculation that these individuals may be destined to the later development of systemic sclerosis. A subjective grading of the degree of capillary loss and enlargement in systemic sclerosis (2) showed a significant correlation between these changes and the disease severity as indicated by the number of organ systems affected by SS; in a later study a significant correlation was found between the disease severity and the pattern of antinuclear antibody (ANA) fluorescence which also correlated with the capillary morphology (3). However, Lee et al. (4) in a semi-quantitative study of the capillary loss and enlargement in systemic sclerosis showed a weak correlation ($p<0.05$) between the extent of avascular lesions and the disease duration, but no correlation with the number of organ systems involved by SS; nor was there a correlation between either of these factors and the degree of capillary enlargement.

The present study was designed to accurately quantify the capillary numbers and

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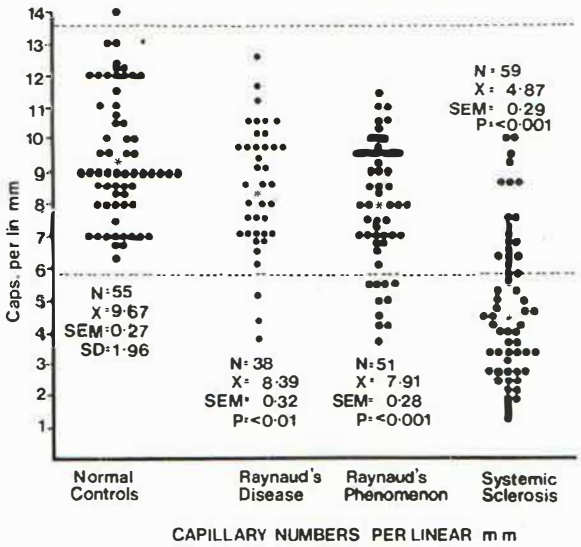

Fig. 1. Capillary numbers per linear mm. ●, mean numbers per digit, *, group mean, ---, ± 2 standard deviations for normal controls.

luminal in SS and to compare the results with other groups: normal controls, patients with RD and patients with Raynaud's Phenomenon (RP) secondary to a connective tissue disease other than systemic sclerosis.

PATIENTS AND METHODS

The following groups were studied: 19 normal controls drawn from hospital staff and patients' visitors, none of whom had any symptoms of RD or collagen vascular disorder; 10 patients with RD of at least three years duration without clinical evidence of an underlying connective tissue disease (ANA were uniformly negative in this patient group); 12 patients with RP secondary to underlying diseases (systemic lupus erythematosus: 9 patients, polyarteritis nodosa: 1 patient, mixed connective tissue disease: 2 patients); and 18 patients with SS as defined by the criteria of the American Rheumatism Association (5).

All examinations were performed in a standardized manner with the subject seated in a warm room (ambient temperature 20–23°C). After acclimatizing for 20 min the 2nd, 3rd and 4th digits on both hands were examined via a binocular microscope with the digit secured to a microscope stage for fine adjustment of position. A drop of immersion oil was placed on the nail fold to enhance the visibility of the underlying capillaries. Photomicrographs were taken, from each digit, at ×10 and ×40 magnifications for enumeration of capillaries and mesurement of capillary luminal diameters respectively. All photomicrographs were coded for subsequent blind evalution. Photomicrographs taken at ×10 magnification were projected at a final magnification of ×260 and the presence of a scleroderma pattern of abnormality (as defined by Maricq et al (1)) was noted. At this magnification, capillary

Table I. *Age and sex distributions of groups studied*

	Systemic sclerosis	'Idiopathic' Raynaud's	Secondary Raynaud's	Normals
Males	2	0	4	7
Females	14	12	8	12
Mean age (years)	48	37	45	41
SEM	3.58	3.88	3.43	3.94

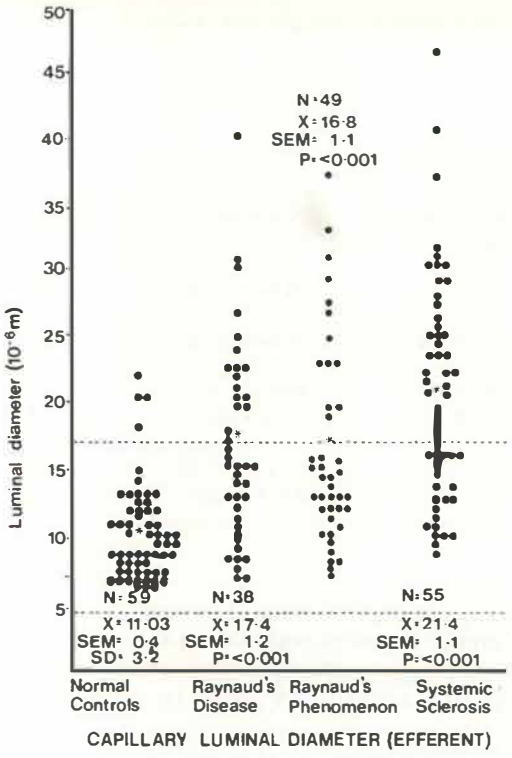

Fig. 2. Efferent luminal diameters. ●, mean diameters per digit, *, group mean, ---, ± 2 standard deviations for normal controls.

numbers were counted: firstly, per linear mm, counting only those capillaries in the distal row of the nailfold, and secondly in 0.5 mm ×1.0 mm strips along the distal edge of the nail fold. Photomicrographs at ×40 magnification were projected at a final magnification of ×1000 and the diameter of the red cell columns (equivalent to the diameter of the capillary lumen—the vessel wall is not visible in vivo) of the afferent and efferent limb of each capillary was measured. Measurements were made perpendicular to the diretion of flow at two points for each afferent and efferent lumen immediately proximal and distal to the curved apical portion of the capillary loop. The mean of these two values was recorded. Only those capillaries in clear focus were measured.

Each patient with SS was assigned a system score for the extent of organ involvement (6), one point being awarded for cutaneous sclerosis in each of the following: the face, hands, trunk, and three points for documented evidence of involvement in each internal organ system.

The Student's *t*-test was used for inter-group differences for capillary numbers and diameters. Rank correlation (Kendall's method) was used to test for correlations with disease duration and system score.

RESULTS

The age and sex distributions of the four groups are shown in Table I.

The scleroderma pattern of morphological change was present in 16 out of 18 subjects with SS. It was also seen in two patients with RD and in two patients in the RP group, one of whom had mixed connective tissue disease with features of systemic sclerosis, and another who had systemic lupus erythematosus with cutaneous vasculitis. None of the normal controls showed any significant abnormality of capillary morphology.

A mean of 8.4 linear mm and a mean of 8.4 strips 0.5 mm × 1.0 mm were counted per subject studied and a total of 1520 measurements of luminal diameters giving a mean of 23.0 measurements for each subject.

Table II. *Published values for capillary luminal diameters in normal controls and ystemic sclerosis*

Authors		Normal controls	Systemic sclerosis
Redisch et al. 1970	Mean diameter (Afferent)	10 μm SEM—not given	Not given
	Range	5–20 μm	
Rouen et al. 1972	Afferent diameter (range)	11.7–17.3 μm	20.6–71.2 μm
	Efferent diameter (range)	14.5–21.1 μm	25.0–99.0 μm
Statham and Rowell (present study)	Afferent diameter Mean (SEM)	8.5 μm (0.33)	16.1 μm (0.7)
	Range	5–17.5 μm	7.5–30 μm
	Efferent diameter Mean (SEM)	11.0 μm (0.4)	21.4 μm (1.1)
	Range	6.0–22.0 μm	8.0–46.0 μm

There was a statistically significant reduction in capillary numbers, as counted by both methods in both the RD and RP groups and in the SS group, compared with the normal control population. The greatest reduction was found in the SS group. (Per linear mm: see Fig. 1; per 0.5 mm × 1.0 mm: normal 16.7±0.6, RD 13.5±0.7, RP 12.3±0.5, SS 7.7±0.5 (mean ± SEM).)

All three patient groups studied show a significantly greater diameter for both afferent and efferent limbs in comparison with the normal control population, the greatest diameter being found in the SS group. (Efferent diameters: see Fig. 2; afferent diameters 10^{-6} m. Normal 8.5±0.3, RD 13.3±0.8, RP 12.7±0.8, SS 16.1±0.7 (mean ± SEM).)

There were no significant correlations between the capillary numbers or diameters and the system score or disease duration for the SS group.

DISCUSSION

It is difficult to make a valid comparison between the capillary luminal diameters found in this study and those reported in previous studies (7, 8) which have expressed their results differently. Table II summarizes the data from these studies. The mean diameter and range in the normal population in this study is very similar to those reported by Redisch et al. (7) in 1970.

It has long been recognized that capillary enlargement occurs in RD (9); our study documents the degree of this change for the first time. The reduction in capillary numbers observed in the present series has not been previously reported; this finding is contrary to a study of Houtman et al. (20) who found no significant reduction in capillary numbers in a group with RD. To exclude the possibility that the two patients with RD, who showed a scleroderma pattern of morphological change, may have biased the values in this group, the *t*-test was recalculated, having excluded these two sets of results. The result was still significant. The reason for the discrepancy between Houtman's study and our own is unclear.

The aetiology of the reduced capillary numbers in SS is not known. It seems likely, however, to be related to the frequent capillary thromboses which are observed in the nail fold in this condition. Such thromboses in turn give rise to micro-infarcts that heal by

scarring, the clinical counterpart to these changes being the ragged cuticles observed in this group of disorders. Why the reduction of capillary numbers should be most severe in SS remains to be explained.

Unlike the study by Maricq et al. (2) we found no correlation between disease severity or duration and the severity of the capillary changes in SS. A number of factors may be responsible for this discrepancy: Maricq's grading system (2) took no account of the degree of capillary loss and was influenced by capillary changes in sites other than the nail fold. Also, our patient populations may have differed in terms of disease severity; in her later study (3) the pattern of ANA fluorescence was found to correlate with the disease severity. Our findings are more in keeping with those of Lee et al. (4), who found only a weak correlation between the degree of capillary loss and disease duration in SS.

In individual patients there is often a striking discrepancy between the severity of the capillary changes and the severity of SS. Occasional patients are seen with advanced disease but normal capillary morphology and the converse situation is also encountered; this makes it unlikely that capillary microscopy would provide useful prognostic information on an individual basis.

Three prospective studies (11, 12, 13) have now shown that a small proportion of patients with RD, who demonstrate a scleroderma pattern of capillary abnormality, will progress to SS or other connective tissue diseases. However, the number of patients showing this progression of disease in each study is small, and further prolonged follow-up studies will be needed to accurately evaluate the predictive value of capillary microscopy in these circumstances.

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