Blood Vessels of the Skin in Chronic Venous Insufficiency

By Myron H. Kulwin, M.D., and Edgar A. Hines, Jr., M.D.

This study concerns an evaluation of the anatomicopathologic changes found in blood vessels of the skin in areas of venous insufficiency in the lower legs. These changes have been compared with the vascular structure in comparable areas of skin in normal persons. Apparently evidence of arteriolar damage is more a concomitant finding in the clinical picture of chronic venous insufficiency than are venular changes. This is demonstrated in a study of 30 patients. The vascular changes show no correlation with the condition of the skin at the site from which the biopsy material was taken.

The basic problem which was studied in this investigation may be stated as follows: In patients who show clinical evidence of chronic venous insufficiency, do the blood vessels of the skin in areas of venous insufficiency differ from those in comparable areas of skin in normal persons and, if so, what is the qualitative nature of the changes?

Specimens of skin were obtained from the lower part of the leg in a group of patients in whom a diagnosis of chronic venous insufficiency had been made. Specimens of skin from comparable areas in apparently normal persons (that is, normal from the standpoint of there being no evidence of any peripheral vascular disease) were then obtained for comparison. The group of patients with "chronic venous insufficiency" was carefully screened to exclude all persons who did not present very definite clinical evidence of venous insufficiency, such as varicose veins, edema following thrombophlebitis, or brawny induration.

The material for study was obtained from specimens for biopsy from patients in the Section on Dermatology and Syphilology and from sections of skin taken at the site of incision (in the region of the ankle) in patients who underwent operation for treatment of varicose veins.

Control material was obtained in cases in which necropsy was performed and in which there was no history of peripheral vascular disease or arterial hypertension. These specimens were obtained from comparable sites to those of the cases of chronic venous insufficiency and from persons in approximately the same age range.

A detailed clinical analysis of the patients included in this study is being given elsewhere and will be but briefly mentioned here. Sixteen control specimens of skin were obtained, 10 of which were from men and 6 from women. The oldest patient was 85 and the youngest 16 years of age.

Thirty-one specimens of skin were obtained from 30 patients for whom a clinical diagnosis of chronic venous insufficiency had been made. Of these, 14 were men and 16 women. The oldest was 76 and the youngest 24 years of age.

Histopathologic Studies

The epidermal and dermal changes (other than those involving the blood vessels) will not be reported in detail, inasmuch as they have been well described by Gans. Other than this description by Gans and a study of a single tissue specimen from a varicose ulcer reported by Golden, no description of the cutaneous vascular changes associated with chronic venous insufficiency has been found in a search of the literature. It is assumed, therefore, that this investigation represents the first detailed description of the changes in the arterioles and venules of the skin in this condition.
Method

The tissue specimens were fixed in formalin and blocked in paraffin. Three stains were used on the specimens—hematoxylin and eosin, elastin H, and Verhoeff's elastic tissue stain. These stains were counterstained with van Gieson's connective tissue stain, hereinafter referred to as the ELVG stain. The problem of whether vascular structures are altered in size during the fixing processes has been raised, but, inasmuch as the control specimens were processed in an identical manner, any such phenomenon is a constant factor and as such can be discounted. It has been shown that physiologic constriction or dilatation of the vessels is not rendered permanent by fixation of tissue.

Since at least six to eight sections of each specimen were studied for evidence of vascular changes, it is felt that the possibility of having missed changes which were present is slight.

In this investigation, attention was concentrated on the vessels at the dermosubdermal junction, first, to establish a degree of uniformity in the size of the vessels studied, and second, because blood vessels smaller than those found at this level could not always be definitely identified as arterioles or venules.

Pathologic Findings

Control Group. Of the 16 control specimens, abnormal vessels were found in only one, which was taken from skin on the leg of a man 63 years of age, who had died of carcinoma of a kidney and metastatic growths. The arterioles in this section showed marked intimal proliferation. In the other 15 control specimens, the appearance of the arterioles and venules con-
patients had no evidence of cardiovascular disease, one had mild arterial hypertension (150 mm. of mercury systolic and 90 diastolic), and in one patient no blood pressure determination was made.

The 25 specimens which showed arteriolar pathologic change were considered from the standpoint of changes in the intima, the internal elastic membrane, the endothelium, and the media, in that order. No single specimen in this group showed pathologic changes in all of these structures.

Intimal proliferation was seen in 16 of the 25 specimens which showed arteriolar changes, in 2 of which elasticization of the intima was also seen, and no intimal change was seen in 9. Two of the specimens without intimal changes were from hypertensive patients and 4 of the specimens with intimal changes were from patients with definite arterial hypertension. Of the 16 specimens which showed intimal damage, 8 were from areas of ulceration, 6 from areas of dermatitis, and only 2 were from normal skin.

The internal elastic membrane appeared normal in 22 specimens of 29 in which this structure was examined, and showed evidence of fragmentation or reduplication or both in 7. In all 6 patients in this group of 25 (with arteriolar changes) who had arterial hypertension (in addition to chronic venous insufficiency), the internal elastic membrane appeared normal. Of the seven specimens which showed evidence of damage to the internal elastic mem-

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**Fig. 3 (left).**—Cutaneous arteriole from leg of a woman aged 75 years who had had induration and edema of both legs for approximately fifty-five years. Blood pressure 160 mm. of mercury systolic and 80 diastolic. Note the intimal proliferation and elasticization as well as thickening of the medial layer of the vessel wall (elastin H stain, X200).

**Fig. 4 (right).**—Cutaneous arteriole from leg of a man aged 24 years who had had thrombophlebitis of the left iliofemoral vein following an operation three years previously. Subsequently, varicose veins developed on the left leg. Blood pressure 114 mm. of mercury systolic and 80 diastolic. This section shows intimal proliferation, a normal internal elastic membrane, and hypertrophy of the medial coat (elastin H stain, X285).
brane, three were from areas of ulceration, and two each from areas of dermatitis and of normal-appearing skin.

Endothelial hyperplasia was seen in 4 specimens, two of which were from hypertensive patients; of these 4 specimens, two were from ulcerated sites, and one each from normal skin and from areas of dermatitis.

The medial coat of the arterioles was thickened in twenty-one specimens of the twenty-nine in which this coat could be observed and normal in eight. Five of the hypertensive patients showed this change and one did not. The condition of the skin in these twenty-one biopsy specimens was as follows: seven ulcerated, 6 dermatitis, and 8 normal.

Complete obliteration of the arterioles was seen in 3 specimens, all of which were from ulcerated areas. None of these patients was hypertensive.

Fig. 5 (left).—Arteriole in skin from leg of a man aged 31 years who had had episodes of induration and edema of both legs for one and a half years without a definite antecedent history of thromboflebitis. Blood pressure 126 mm. of mercury systolic and 86 diastolic. Intimal proliferation, reduplication of the internal elastic membrane and medial hypertrophy are seen in this section (elastin H stain, X95).

Fig. 6 (right).—Cutaneous venule from leg of a man aged 36 years. This patient had had a crushing injury to the left leg six years previously, and postpneumonic thrombophlebitis of the left iliofemoral vein nine months previously; immediately after the latter episode bilateral varicosities developed. Blood pressure 125 mm. of mercury systolic and 74 diastolic. This section shows endothelial hyperplasia and a very pronounced degree of medial hypertrophy with a laminated appearance of the media (ELVG stain, X75).

Changes in the venules were classified as intimal, endothelial and medial. Only one specimen showed changes in all three structures.

(2) Venular Changes: Of 30 specimens in which the structure of the venules was studied, 15 were normal. Eight of these specimens were taken from areas of dermatitis, 3 from ulcerations and 4 from normal-appearing skin.
Six specimens showed intimal proliferation, 3 showed endothelial hyperplasia, and 13 showed broadening of the medial layer. Of the 15 sections which showed venular changes, 4 were from areas of dermatitis, 6 from ulcers and 5 from sites of normal skin. Three specimens showed complete venular occlusion; these were all from ulcerated areas.

Figures 3 to 5 illustrate representative arteriolar changes which were seen in this study, and figure 6 illustrates typical venular changes.

**Comment**

The fact that of the 25 specimens that showed arteriolar changes, 8 were from areas of normal-appearing skin indicates that the arteriolar changes are not necessarily secondary to inflammatory changes in the skin and subcutaneous tissue. Also, of the 8 patients in this series with chronic venous insufficiency and normal skin, only one showed no evidence of vascular pathologic changes.

The thickening of the medial arteriolar coat found in 21 specimens (only 5 of which were from patients with arterial hypertension) is not too dissimilar from that seen in hypertensive arteriolar disease.

Of 16 specimens which showed intimal hyperplasia of the arterioles, 14 were from areas of cutaneous changes (dermatitis or ulceration or both) and only 2 were from normal cutaneous sites. It appears that this finding might bespeak the role played by cutaneous lesions in the production of intimal vascular pathologic changes, as has been suggested.\textsuperscript{7,8}

Since venular changes were found in only 15 of 30 specimens studied, it would seem that no definite conclusions can be drawn as to their significance.

Detailed studies of capillary structures were not included in this investigation. It was noticed, however, in the process of reviewing these sections of skin, that a large number of specimens showed evidence of capillary dilatation and proliferation, particularly in the upper portion of the cutis in lesions of long duration.

**Summary and Conclusions**

The anatomicopathologic features of the blood vessels of the skin in 31 biopsy specimens from 30 cases of chronic venous insufficiency of the lower extremities have been studied.

Twenty-five specimens, 8 of which were of normal-appearing skin, showed evidence of arteriolar damage in the form of intimal proliferation, fragmentation or reduplication, or both, of the internal elastic membrane, endothelial hyperplasia, medial hypertrophy, or some combination thereof.

Fifteen specimens showed evidence of venular pathologic changes in the form of intimal proliferation, endothelial proliferation and hyperplasia, medial hypertrophy, or some combination thereof. Five of these specimens were of normal-appearing skin.

Pathologic changes in the arterioles of the skin are a usual concomitant finding in areas of chronic venous insufficiency of the lower extremities. Changes in the venules exist in about one-half of the cases. The causal relationship of these changes to cutaneous manifestations of chronic venous insufficiency has not been determined.

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**References**


\textsuperscript{5} **Mallory, F. B.:** Quoted by Romeis,\textsuperscript{4} p. 170.


\textsuperscript{7} **Homans, John:** The late results of femoral thrombophlebitis and their treatment. New England J. Med. 225: 249, 1946.

\textsuperscript{8} **Thompson, K. W.:** Studies on relationship of dermatomyositis to ulceration and gangrene of extremities. Yale J. Biol. & Med. 16: 665, 1944.
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