limits before and after feeding. The diet, with one minor exception, was constant. The daily rations consisted of 200 grams of beef heart supplemented with cod-liver oil, yeast and bone ash. This recovery from the previous diabetic state has been maintained to the termination of the experiment, a period of more than three months in several of the animals. The cats continued to gain weight throughout this period.

Biopsy specimens of the pancreas of permanently diabetic cats taken *before* treatment with insulin show marked hydropic degeneration of the islands of Langerhans. In cats exhibiting functional recovery *following* insulin therapy the islands are histologically normal. Some animals did not show "permanent" recovery with insulin treatment. These instances were associated with infections, poor control of the diabetes by insulin or institution of insulin treatment after more than five months of diabetes.

In dogs made diabetic by removal of about nine tenths of the pancreas hydropic degeneration of the islands is present for the first few months.[3] Using such dogs, Copp and Barclay[4] have observed morphological restoration of the islands *during* periods of insulin therapy. Despite the morphological improvement it was necessary to continue the administration of insulin. Since the diabetes had been produced by partial pancreatectomy alone, it was not to be expected that morphological restoration of the remaining islands would maintain functional recovery. We have failed to obtain morphological (or functional) recovery in dogs made permanently diabetic with anterior pituitary extract. This we attribute to the early development of atrophy of the islands of Langerhans in our dogs, in contrast to the hydropic degeneration found in the experiments of Copp and Barclay and in our cats. However, it has recently been demonstrated in dogs that the concurrent administration of insulin may hinder the fall in the insulin content of the pancreas and the hydropic degeneration of the islands which occurs during the period of injection of certain anterior pituitary extracts.[5]

F. D. W. LUKENS
F. C. DOHAN

THE GEORGE S. COX MEDICAL RESEARCH INSTITUTE, UNIVERSITY OF PENNSYLVANIA

THE NEURO-MOTOR MECHANISM OF THE SMALL BLOOD VESSELS OF THE FROG

THE mechanism which regulates capillary blood flow has not been definitely established. In Krogh's laboratory, Vimtrup[1] reported the contraction of Rouget cells in Amphibia, which caused folding of the endothelium. Field,[2] using the frog and rat, and also Beecher,[3] using the rabbit's ear, confirmed Vimtrup and in addition observed the swelling of endothelial nuclei which blocked the lumen of the capillary. The Clarks[4] reported endothelium to be contractile in the tadpole's tail but not in the rabbit's ear. They deny the contractility of extra-endothelial cells (Rouget cells) in mammals and amphibians, with the possible exception of the nictitating and hyaloid membranes of the frog. Zweifach[5, 6] reported endothelial contractility in the frog and mouse. In response to mechanical stimulation, contraction of the endothelium in the frog "completely closed the lumen of the vessel only at its ends." At the "capillary exit in those regions where the capillary offshoot leaves the arteriole," he observed valve-like folds of endothelium which opened and closed passively with dilatation and constriction of the arteriole. In the mammal Zweifach[7] comes to the conclusion that the contractility of capillary endothelium has little physiological significance.

We have examined, by means of stimulation with a micro-electrode, the distribution of the contractile elements of the small blood vessels in the retrolingual membrane of the frog. In contrast to the uniform layer of the typical smooth muscle of the arteriole, and the somewhat scattered arrangement on the precapillary, the modified smooth muscle cells of the capillary are confined to the region of its origin. If the capillary branches before emptying into a venule, the branches are devoid of smooth muscle cells and do not contract. The region of the capillary origin may act as a unit with its adjacent blood vessels, but frequently it acts independently of them as a sphincter-like mechanism. This concept of the control of capillary blood flow is supported by the evidence presented below.

In the frog with brain and medulla pithed, the retrolingual membrane was prepared for illumination by transmitted light, after the method of Pratt and Reid.[8] A micro-electrode, 1–5 micra, was placed in the field by an Emerson micromanipulator. Cinephotomicrographs were obtained, using a light-splitting prism.

Brief faradic stimulation of the small vasomotor nerves produced dilatation of the small blood vessels, followed by constriction. Weak stimulation usually

[1] Bj. Vimtrup, *Zeitsch. f. d. ges. Anat.*, 65: 150–182, 1922.
[2] M. E. Field, *Skand. Arch. f. Physiol.*, 72: 175–191, 1935.
[3] H. K. Beecher, *Skand. Arch. f. Physiol.*, 73: 1–6, 1936.
[4] E. R. Clark and E. L. Clark, *Am. Jour. Anat.*, 66: 1–49, 1940.
[5] B. W. Zweifach, *Anat. Rec.*, 59: 83–108, 1934.
[6] B. W. Zweifach, *Anat. Rec.*, 73: 475–495, 1939.
[7] B. W. Zweifach, *Am. Jour. Physiol.*, 120: 23–35, 1937.
[8] F. H. Pratt and M. A. Reid, SCIENCE, 72: 431–433, 1930.

[3] F. M. Allen, *Jour. Metab. Res.*, 1: 5, 1922.
[4] E. F. F. Copp and A. J. Barclay, *Jour. Metab. Res.*, 4: 445, 1923.
[5] J. Campbell, R. E. Haist, A. W. Ham and C. H. Best, *Am. Jour. Physiol.*, 129: P328, 1940 .

produced only dilatation. Strong stimulation of the same nerve frequently produced only constriction. These results suggest that the nerves stimulated contained vasodilator and vasoconstrictor fibers, and that the vasodilators possessed a lower threshold. Furthermore, the area constricted was frequently only a portion of that originally dilated. As additional evidence of dual innervation, vasomotor nerves were found which produced only one type of response to all strengths of stimulation. Although our histological preparations show an anatomically continuous loosely-meshed non-myelinated nerve plexus continuous with the perivascular plexus, it is conceivable that dilator and constrictor fibers might occasionally become segregated.

Faradic stimulation of small nerves produced responses confined to limited vascular areas. Therefore, although the nerve plexus appears to be anatomically continuous, functional innervation is discontinuous. Stimulation of any one of several small nerves in the field produced a response in the same limited area. This fact suggests the concept of a smooth muscle motor-unit. Limited vascular areas were seen to beat rhythmically at times. No central reflex could be involved, and we have found no ganglion cells in the membrane.

Faradic stimulation of small nerves produced dilatation and contraction of the capillary only in the region of its origin. This region may respond independently of the supplying arteriole or precapillary, and function as a sphincter. Such sphincter-like regions sometimes show spontaneous rhythmic contractions, quite independent of the supplying vessel. Nuclei of contractile pericapillary cells were always seen in this region. In preparations vitally stained with methylene blue the capillary origins possessed a few modified smooth muscle cells with branched cytoplasmic processes. They are probably the type of cell originally described by Rouget,[9] redescribed by Vimtrup[10] in Amphibia, and reported by Field[11] in the rat. Furthermore, the perivascular nerve plexus was rich on the arterioles and precapillaries but sparse on the capillaries. Various pericapillary cells were found farther along the capillary. Except for an occasional cell, these did not respond to electrical stimulation. Further experiments are in progress, with drugs and with denervated preparations, to determine the nature of the independent activity and the rhythmic responses.

Both direct observation with a water immersion lens and careful study of the cinephotomicrographs of the active capillary origins failed to disclose the swelling of endothelial nuclei into the lumen, or the presence of endothelial valves. Endothelial contraction in response to stimulation of the nerves or to direct electrical and mechanical stimulation did not occur. It appears, therefore, that in the retrolingual membrane of the frog, the capillary origins are provided with modified smooth muscle cells and thus regulate capillary blood flow in a sphincter-like manner without the aid of the supplying vessel.

GEORGE P. FULTON
BRENTON R. LUTZ

BOSTON UNIVERSITY

[9] C. Rouget, *Arch. de Physiol. Norm. et Path.*, 5: 603–663, 1873.
[10] *Loc. cit.*
[11] *Loc. cit.*

EGG-WHITE INJURY IN CHICKS AND ITS RELATIONSHIP TO A DEFICIENCY OF VITAMIN H (BIOTIN)

THE action of Vitamin H in protecting against the injury caused by a diet containing egg white is somewhat unique in that the diet can not be considered to be deficient in an essential food constituent. Omission of the egg white from the injury-producing diet gives a ration which apparently does not lack any of the needed vitamins. This appears to be in contrast to the action of the various members of the vitamin B group in curing or preventing nutritional injuries, for the diets in these cases have always been found to be definitely deficient in the vitamin in question.

The recent observations of György, Melville, Burk and du Vigneaud have shown that vitamin H is probably identical with biotin (and co-enzyme R).[1, 2] In view of their results, it appeared that a study of the biotin intake and excretion and the biotin content in the tissues of chicks receiving egg-white injury diets might be helpful in throwing some light on the manner in which vitamin H functions.

Day-old chicks were placed on the following diet: yellow corn, 55 per cent.; wheat middlings, 20 per cent.; purified casein, 20 per cent.; bone meal, 1.5 per cent.; limestone, 2 per cent.; cod liver oil, 1 per cent.; and iodized salt, 0.5 per cent. When ten days old, the chicks were divided into two groups. One, the controls, was continued on this same diet, and the other group was given a ration in which the purified casein was replaced by dried egg white. Samples of the two diets, digested in 20 per cent. sulfuric acid for 18 hours at 100° C., gave the following assay values for biotin by the method of Snell, Eakin and Williams[3]: control diet, 0.39γ per gram; injury diet, 0.67γ per gram. Twenty-four-hour samples of the feces from the two groups were collected at intervals throughout a month, dried, weighed and carefully sampled. Aliquots were tested, both for free (extractable) biotin,

[1] Paul György, Donald B. Melville, Dean Burk and Vincent du Vigneaud, SCIENCE, 91: 243, 1940.
[2] Since this investigation was started, private information from Dr. du Vigneaud to one of us confirms the identity of vitamin H and biotin.
[3] E. E. Snell, Robert E. Eakin and Roger J. Williams, *Jour. Am. Chem. Soc.*, 62: 175, 1940.