1941

The regulation of capillary blood flow.

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Boston University

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THE REGULATION OF CAPILLARY BLOOD FLOW

by

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(S.B., Boston University, 1936; A.M., Boston University, 1938)

submitted in partial fulfilment of the requirements for the degree of

Doctor of Philosophy

1941
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INTRODUCTION

The regulation of capillary blood flow is of fundamental importance since oxygen and nutrients ultimately reach the individual cells of the body through the wall of the capillary. Until 1920, it was believed generally that contraction and dilatation of the arterioles alone controlled the flow of blood in capillaries. According to this view, the capillaries did not respond actively. They were expanded passively by the increased capillary pressure during the dilatation of the arterioles. Because of their elasticity, they collapsed passively as the capillary pressure decreased during the contraction of the arterioles.

The need for a local regulation of capillary blood flow became obvious to Krogh (1919a, 1919b), following an investigation of the supply of oxygen to skeletal muscle. He reasoned that a much more effective distribution of blood would be obtained if the capillaries themselves were contractile and a limited number were open in a resting organ at any one time. On the basis of this hypothesis, Krogh (1919c) commenced an investigation of capillary contractility. In 1922 he published the book, "The Anatomy and Physiology of Capillaries". This volume, revised and enlarged in 1929, contained an extensive review of the literature which supported the concept of the independent contractility of capillaries. As the mechanism of capillary contraction, Krogh proposed muscular pericapillary cells, the Rouget cells, which caused folding of the endothelium.
The classical volume by Krogh stimulated numerous investigators to study the control of capillaries. Various workers have confirmed the contractility of pericapillary cells, while others have refuted it. The contraction of endothelial cells and also the swelling of endothelial nuclei have been reported as alternative mechanisms of capillary contraction. Other investigators denied capillary contraction and reported the contraction and dilatation of arterioles as the mechanism which regulates capillary blood flow. The present investigation had its origin in Krogh's laboratory at Copenhagen, where Dr. Brenton R. Lutz first worked on capillary circulation. At Boston University, he applied micromanipulative methods to the investigation of capillary contractility in the retrolingual membrane of the frog. Antimony-glass and also platinum-quartz micro-electrodes were used to stimulate small nerve fibers in the field under the microscope. A technique was perfected for recording the responses on motion picture film. Early experiments indicated that the capillaries possessed active contractility and that they were under nervous control. (Unpublished material).

Under the direction of Dr. Lutz, the author has continued this investigation. Silver-glass micro-electrodes have been perfected for use in stimulation of small nerve fibers. The cinephotomicrographic technique has been used to record significant experiments. By this method the innervation and distribution of the contractile elements of small blood vessels has
been investigated. A sphincter-like mechanism has been observed at the capillary origin, which may dilate or contract independently of the supplying arteriole to regulate capillary blood flow.

A motion picture, "The Control of Small Blood Vessels" has been made from cuttings taken from the composite film records in this laboratory.
EVIDENCE FOR INDEPENDENT CAPILLARY CONTRACTION

Certain obscure papers on blood capillaries, published during the early part of the nineteenth century, were reviewed by Stegemann (1927). Philip (1800) observed dilatation and constriction of capillaries of the frog. Bichet (1818) noted that only a part of the capillary bed was open to circulation at a given time. Hastings (1820), Koch (1823), Burdach (1825), and Wedemeyer (1828) observed dilatation and constriction of capillaries, without establishing the nature of the reaction. Schultz (1836) described the constriction of capillaries as swelling of the wall of the vessel without change in the outside diameter. As pointed out by Krogh (1929), these early workers were searching for structures in the periphery which might aid the heart in propelling the blood. From their observations of the contraction and dilatation of small blood vessels, Philip and others concluded that these vessels were propulsive agents. Wedemeyer and others maintained that the contractions of blood vessels controlled the blood flow to the periphery. However, no attempt was made in these studies to distinguish between capillaries and arterioles. In fact the structure of capillaries was not understood clearly at that time.

J. F. Fulton (1929), in a letter to the editor of the Lancet, stated that James Black in 1825 observed beyond doubt the independent contractility of capillaries. As evidence for his contention, Fulton quoted certain protocols and conclusions
from Black. On the basis of the quoted excerpts, it is rather optimistic to concede to Black the priority in the observation of independent contraction of capillaries.

Hooker (1920) stated that the first evidence for capillary contractility independent of the supplying arteriole was published by Lister in 1858. In camera lucida drawings of the same capillary at two different times, a change in caliber was detected. However, Lister stated that the dilatation of capillaries was a passive phenomenon caused by the increased pressure from the dilatation of arterioles. Although reporting the constriction of capillaries in the web of the frog when the spinal cord was stimulated, he interpreted the phenomenon as a passive collapse following contraction of the arterioles. Although Lister may have published the first evidence for independent capillary contractility, he did not interpret it as such.

It is generally agreed that Stricker (1865) was the first to report the independent contractility of capillaries. He observed irregular spontaneous contractions and relaxations of single capillaries in the excised nictitating membrane of the frog. Since blood pressure could not be involved, Stricker reasoned that the capillaries themselves were contractile. The outside diameter of the capillary remained unchanged, while the nuclei on the wall appeared to project into the lumen. Consequently, Stricker proposed that the swelling of the cells on/in the capillary wall was the mechanism of capillary contraction.
Since the experiments by Stricker, much of the evidence for active capillary contraction has been obtained from the use of excised transparent membranes. Golubew (1869) confirmed Stricker using the excised nictitating membrane of the frog. Following stimulation of the entire membrane with tinfoil electrodes, he reported that spindle elements on the capillaries became thicker and appeared to narrow the lumen. Tarchanoff (1874) also reported the active contraction of capillaries in a similar preparation. Following electrical stimulation of the membrane, the spindle elements shortened, thickened and extended into the lumen. Steinach and Kahn (1903) likewise observed capillary contraction in the excised nictitating membrane of the frog. They reported the swelling of endothelial nuclei into the lumen and also a longitudinal folding of the endothelium in the region of pericapillary cells. Both responses were induced by electrical stimulation of the membrane and also by stimulation of the sympathetic in a nictitating membrane with intact innervation but no circulation. Kahn and Pollak (1931) confirmed the observations of Steinach and Kahn. They stated that the circulation must be eliminated in order to demonstrate that capillary constriction is an active process.

However, evidence for capillary contractility gained from experiments on excised tissue is open to the criticism that the conditions are not physiological. A number of investigators have eliminated the blood pressure factor in the intact animal without resorting to excision.
Roy and Brown (1880) determined the blood pressure in capillaries of the web, tongue, and mesentery of the frog by measuring the amount of extracapillary pressure required to stop the circulation. They noticed that hardly any change in capillary caliber took place until a pressure sufficient to collapse the wall was attained. They reasoned that changes in blood pressure within the capillary could not be expected to produce the spontaneous variations in diameter which actually occur. They pointed out that reduction of the intracapillary pressure obtained by severing the web does not cause the capillaries to collapse. As a result, Roy and Brown concluded that capillaries were capable of active contraction.

Cotton, Slade and Lewis (1917) presented indirect evidence for the independent contraction of capillaries in man. By means of a sphygmomanometer on the upper arm they stopped the arterial inflow and venous outflow of the forearm. Under this condition a light stroke on the skin produced a white line. The authors reasoned that if the arterioles were responsible for the constriction, the capillaries would not empty but would fill with blood. "Closure of the capillaries themselves alone suffices to explain the phenomena observed and we believe that this closure is affected by some essential element in the capillary wall."

Hooker (1920) reported the constriction of capillaries and venules in the cat's ear following stimulation of the cervical sympathetic nerve. Since the ear was maintained below the heart level, he concluded that only an active contraction of the
If our society is to continue to exist, the world to exist, of course, requires some order and structure. In a world of countless possibilities and continuing growth, it is essential to create a framework that guides our actions and decisions. This framework can be based on a simple set of values, which are the foundation of our society. Values provide a sense of direction and purpose, helping us to navigate the complexities of life.

When we talk about values, we are referring to certain beliefs and principles that guide our behavior. These values can shape our decisions, influence our relationships, and determine how we interact with others. In order to live a fulfilling life, it is important to have a clear understanding of our values and how they align with our actions.

Creating a society based on shared values requires cooperation and collaboration. When people work together towards a common goal, they can achieve great things. This is why it is important to have a system in place that encourages and supports collaborative efforts.

In conclusion, a values-based society is essential for the well-being of individuals and communities. By focusing on shared values, we can create a world that is more just, equitable, and fulfilling for all.
capillary itself could force out the blood against the hydro-
static column in the veins.

Krogh (1920) reported that stimulation of the underside of
the frog's tongue with a hair produced a dilatation of the cap-
illaries, even if the arterial pressure was reduced by clamping
the lingual artery. Furthermore, he observed that small drops
of acetylcholine dilated the arterioles but produced no effect
on capillaries. On the other hand, drops of urethane dilated
the capillaries but produced no effect on arterioles. Conse-
quently he concluded that capillaries possessed the property of
independent contractility.

Krogh, Harrop and Rehberg (1922) measured the diameter of
capillaries before and after stimulation of the sympathetic.
They found a marked decrease in diameter of certain capillaries
following stimulation. The authors maintained that the capil-
laries responded independently of the arterioles because a fall
of arteriolar blood pressure, even to the zero level, would not
produce a measurable passive change in capillary caliber.

Harris and Marvin (1927-1929) reported the independent
contractility of capillaries in the ear of the albino rabbit.
They eliminated the influence of blood pressure by tying off
the circulation to the ear. Electrical stimulation of the cer-
vical sympathetic caused capillaries in the ear to disappear
from view. In a long capillary the red corpuscles were
squeezed in both directions from the middle.
adapted expressions inside and then added these comments:

"The problem is not "increased" risk; it is the risk-perception. Risk perception is subjective and can be influenced by personal biases, cultural factors, and societal norms. It is important to recognize that risk perception is not an objective measure but rather a reflection of individual experiences, beliefs, and values.

It is also important to consider the role of communication in shaping risk perception. As information about risks is often disseminated through media and other channels, it is crucial to ensure that messages are accurate, balanced, and presented in a way that is understandable to the public. The use of clear, concise language and avoiding jargon can help to improve comprehension and reduce confusion.

In summary, it is essential to address the issue of risk perception by focusing on understanding individual perspectives and communicating information in a clear and accessible manner. This approach will help to ensure that people make informed decisions and can take appropriate actions to manage risks effectively."
Evidence for capillary contractility obtained under conditions of reduced blood pressure does not prove that capillaries can contract independently under normal circumstances. Direct microscopic observations on transparent membranes with unimpeded circulation are of greater significance.

Among the first of such preparations to be used was the transparent tailfin of amphibian larvae. Using this particular preparation Charles Rouget first proposed the concept of contractile pericapillary cells. In an histological and embryological study of capillaries in various amphibian larvae, as well as in the hyaloid membrane of the frog's eye, he described branched pericapillary cells. In 1874 he reported the contraction of these cells in the swimming membrane of larval amphibia. Vimtrup (1922) observed spontaneous variations in the diameter of capillaries in the tailfin of larvae of the salamander and the frog. He explained the activity on the basis of contractile pericapillary cells. In extensive investigations, Clark and Clark (1925a, 1925b) noticed the spontaneous contraction of capillaries in the tails of various amphibian larvae and explained the activity on the basis of contractile endothelial cells. Using micromanipulative methods, Nagel (1937) confirmed the observations of Clark and Clark.

In the adult frog independent contraction of capillaries has been reported in intact transparent membranes such as the web and the mesentery. In the web Vimtrup (1922), and Bensley and Vimtrup (1923) noticed that contraction started at the
location of a pericapillary cell and proceeded in both directions from that point. Ni (1922) reported local contractions of capillaries in the web. In the mesentery Zweifach (1934) reported the contraction of capillary endothelium. Field (1935) observed the contraction of capillaries in the mesentery and explained the activity on the basis of the swelling of endothelial nuclei and the contraction of pericapillary cells. Michels (1936) observed variations in the diameter of capillaries in the web and concluded that the endothelium was responsible. Ferguson (1937) reported the contraction of the endothelium in the mesentery of the frog.

In the mammal the problem of capillary contraction has been investigated in intact transparent membranes such as the omentum and mesentery. Rouget (1879) reported the contraction of pericapillary cells in the omentum of embryonic and newborn mammals. Tannenberg (1926) observed the contraction of capillaries in the mesentery of the rabbit. Field (1935) reported the contraction of capillaries in the mesentery and subcutaneous tissue of the rat. Rogers (1935) observed slight responses of the endothelium of capillaries in the cat's mesentery without interference with the peripheral circulation. Ferguson (1937) reported slight contractions of the endothelium in the mesentery of the kitten, but concluded that blood pressure changes regulated capillary blood flow. Zweifach and Kossmann (1937) reported that, although the endothelium of capillaries was slightly contractile in the mesentery of the mouse, endo-
Hi - Infor. Thx
thelial contractility was of little importance in the physiology of the mammalian capillary.

The technique for inserting transparent chambers in the rabbit's ear presented new opportunities for observations on capillary contractility in the mammal. This technique was perfected in Clark's laboratory by Sandison (1928) and has been used there in extensive investigations. Clark and Clark (1940) stated that they never observed active contraction of capillaries in such preparations. On the other hand, Beecher (1936a, 1936b) reported the contraction of pericapillary cells and also the swelling of the endothelium within a similar transparent chamber inserted in the rabbit's ear. Sanders, Ebert and Florey (1940), using an improved chamber, reported the swelling of endothelial cells on capillaries in the rabbit's ear following stimulation of the cervical sympathetic nerve.

There is some evidence for capillary contractility in man, apart from the indirect observations of Cotton, Slade and Lewis (1917). This evidence has been obtained through the use of the method for skin illumination developed by Lombard (1912). According to this method a drop of oil is applied to the skin. By means of a strong light the blood flow can be seen through the microscope, although the vessel walls remain invisible. Using this method Hooker (1920) reported the independent contractility of capillaries in the cat's ear. In the nailfold of man Lennartz (1921) observed a variation in the rate of blood flow in different capillaries and in the same capillary over a period of time. Using Lombard's method Carrier (1922) concluded that
the blanching of skin, following a light stroke, was due to capillary constriction. Heimberger (1926) stimulated single capillaries in the nailfold and observed local constrictions of the blood column. He concluded that capillaries in man were capable of independent contraction.

The problem of capillary contractility has been investigated in opaque tissues of amphibians and mammals by means of transillumination with glass or quartz rods. Using a glass rod for conducting light, Hartman, Evans and Walker (1929) observed an increased capillary blood flow in the cat's sartorius muscle following injection of adrenalin and stimulation of the sympathetic. Wearn and co-workers (1934) reported spontaneous intermittency of capillary blood flow in the cat's lung using a quartz rod for transillumination. By means of a new quartz tissue illuminator, Knisely (1938, 1939) obtained evidence for the contractility of the sinusoids in the liver lobule.

Evidence for the contraction of capillaries obtained through the use of Lombard's method is open to the criticism that the walls of the capillaries cannot be seen. Since it is unsafe to assume contraction merely because of the cessation of blood flow, the results obtained with Lombard's method must be interpreted carefully. The same objection applies, to a less extent, to the use of transillumination by quartz rods.

With the development of micromanipulative methods, investigators were able to stimulate capillaries independently of the arterioles. In all previous work the form of stimulation
and that we should still fundamentally desire to promote our

goals, regardless of any immediate short-term consequences. And we must remain vigilant in our commitment to

never lose sight of the ultimate goal. To achieve this, we must

strive for excellence in all aspects of our work.

In essence, we must be willing to make sacrifices and

persevere through challenges. It is only through this dedication that we can truly

realize our potential. Each step we take should be

approached with careful consideration and a focus on

improvement. By doing so, we can continue to grow and

advance our goals.
was not localized adequately. Electrical stimulation was applied to the tissue as a whole or to peripheral nerve trunks. Chemical stimulation was applied by submerging the tissue in a bath or by means of drops from a small rod or pipette. Mechanical stimulation was applied by stroking with blunt needles or fine hairs. The new technique of micromanipulation made it possible to stimulate not only individual capillaries but also individual cells on the capillary wall, independently of each other. It made it possible to determine by direct methods the mechanism which regulates capillary blood flow.

Zweifach (1934) first applied micromanipulative methods to capillaries. In the mesentery of the frog he reported the contraction of the endothelium following direct mechanical stimulation with a micro-needle. In the mesenteries of the frog and mouse Field (1935) observed the contraction of pericapillary cells and the swelling of the endothelium in response to stimulation with a micro-electrode. In the cat's mesentery Rogers (1935) and also Ferguson (1937) obtained only slight responses of the endothelium to mechanical stimulation with a micro-needle. In the tadpole's tail Nagel (1937) reported the contraction of the endothelium following direct mechanical stimulation with a micro-needle. Zweifach and Kossman (1937) concluded that the contraction of capillary endothelium was of little physiological significance in the mesentery of the mouse. Zweifach (1940) concluded that the perivascular muscle elements on arterioles and "arterio-venous capillaries" were the effective factors which regulated the flow of blood.
In order to understand the implications of these findings, we must consider the context in which they were obtained. The data from the study were collected through a series of surveys administered to a representative sample of individuals. These surveys included questions about their income, education, and employment status.

The results indicate that there is a significant correlation between income and education levels. Individuals with higher education tend to earn higher incomes, with the difference being statistically significant. This finding supports the idea that education plays a crucial role in determining economic outcomes.

Furthermore, the data show that employment status also affects income. Full-time employment is associated with higher wages compared to part-time or unemployed status. These findings highlight the importance of stable employment in achieving financial security.

In conclusion, the results of this study suggest that efforts to improve education and provide stable employment opportunities could have a significant impact on the economic well-being of individuals. Further research is needed to explore these findings in greater depth and to consider potential policy implications.
through capillaries.
Swelling of the endothelium

The first mechanism to be proposed for capillary closing was the swelling of endothelial cells in the region of the nucleus. During capillary constriction in the excised nictitating membrane of the frog, Stricker (1858) observed that the nuclei on the wall appeared to project into the lumen, whereas the outside diameter of the capillary remained unchanged.

Subsequent investigations on the same preparation have confirmed the observations reported by Stricker. Golubew (1869) and also Tarchanoff (1874) reported the swelling of the spindle elements on the capillary wall. Steinach and Kahn (1903) and also Kahn and Pollak (1931) reported the swelling of endothelial nuclei into the lumen, as well as the longitudinal folding of the endothelium in the region of pericapillary cells.

The importance of endothelial swelling as a mechanism for capillary contraction under physiological conditions can not be evaluated from investigations on excised membranes. However, endothelial swelling has been reported in preparations with an intact circulation. In the mesentery of the frog and also the rat, Field (1935) observed the swelling of endothelial nuclei, as well as the contraction of Rouget cells. Beecher (1936a, 1936b) reported the same phenomena in newly-formed capillaries within transparent chambers inserted in the ears of rabbits.
...
He observed the swelling of endothelial nuclei when the rabbit was exposed to fright, pain, or anoxemia. Sanders, Ebert and Florey (1940) reported the swelling of endothelial cells in capillaries within an improved transparent chamber inserted in the rabbit's ear. They stated that the endothelium swelled spontaneously and in response to stimulation of the peripheral end of the cut cervical sympathetic nerve.

**Contraction of the endothelium**

Clark and Clark (1925b) reported the contraction of capillaries in the tail of the tadpole. Although they observed bulging of endothelial nuclei into the lumen of capillaries, they noticed that narrowing often occurred independently of nuclei of endothelial cells, as well as those of pericapillary cells. Consequently, they concluded that the endothelial cells were contractile.

Zweifach (1934) reported that the endothelium was definitely contractile in the frog. When prodded with a micro-needle the endothelial cell contracted and its nucleus bulged into the lumen. Zweifach (1937) described longitudinal fibrils (tonofibrils) in endothelial cells stained with Heidenhain's iron hematoxylin or Mallory's phosphotungstic acid hematoxylin. He stated that the tonofibrils resembled those of smooth muscle in their staining reaction.
Mycelium knot 1/4" hole under inflorescence 1/2" presence and frequency in "low chanter" medicine on upper surface or between the 1/2" holes of inflorescence to catalyze 1/2" infusion from a 1/2" transverse section. Mycelium knot 1/4" hole under inflorescence 1/2" presence and frequency in "low chanter" medicine on upper surface or between the 1/2" holes of inflorescence to catalyze 1/2" infusion from a 1/2" transverse section. Mycelium knot 1/4" hole under inflorescence 1/2" presence and frequency in "low chanter" medicine on upper surface or between the 1/2" holes of inflorescence to catalyze 1/2" infusion from a 1/2" transverse section.
Michels (1936) observed the contraction of capillaries in the web of the frog. He obtained no evidence for the contraction of pericapillary cells and concluded that the endothelium, "in virtue of its inherent ameboid activity" was the mechanism of capillary contraction. Nagel (1937) prodded the capillary wall, in the tails of amphibian larvae, with a micro-needle and reported the contractility of the endothelium. He considered that the endothelial contractility was merely an example of the fundamental property of movement possessed by epithelium in general.

Endothelial contractility has been reported in invertebrates. Federighi (1928) observed a peristalsis-like contraction of capillaries in the sandworm, *Nereis*. He attributed this phenomenon to contraction of the endothelium.

In the mammal various investigators have concluded that endothelial contractility is of little significance in the control of circulation. Rogers (1935) stimulated individual endothelial cells in the omentum of the cat with a micro-needle. He reported contraction of the endothelium which did not interfere, however, with the peripheral circulation. In the mesentery of the mouse Zweifach and Kossmann (1937) obtained only slight contractions of the endothelium upon gentle prodding. Clark and Clark (1932, 1935, 1940) observed no contraction of the endothelium of capillaries within transparent chambers inserted in the rabbit's ear. They concluded, "It would appear that in mammalian vessels there is considerable doubt as to whether
true active contractions of capillary endothelium occur spontaneously or in response to most types of stimulation and that in any case contractions if present are so sporadic and slight as to be negligible as a factor in the control of peripheral circulation."

Clark and Clark (1933, 1935) proposed an interesting hypothesis to account for the discrepancies with regard to endothelial contractility. They suggested that there may have been an evolutionary loss of the property of contraction by endothelium, from invertebrates to mammals, accompanying the acquisition of an highly developed muscular layer on arterioles.

As pointed out by Vimtrup (1922), Krogh (1929), and Nagel (1937), the swelling of endothelium as the mechanism of capillary contraction is difficult to accept for physical reasons. It implies rapid imbibition or absorption of fluid sufficient to block the lumen of the capillary. How this can take place on nerve stimulation is not clear. Furthermore, Barksdale (1925-1926) observed no thickening of the endothelium during the contraction of capillaries in the tongue and also the mesentery of the frog. He stated, "This disproves the cell-turgor theory which has been advanced to explain capillary constriction and dilatation."

As already indicated, Nagel (1937) thought the apparent swelling of the endothelium represented a contraction. However, endothelial contractility is difficult to accept for physiological reasons. Zweifach (1937) presented histological
evidence for longitudinal, supposedly contractile fibrils (tonofibrils). However, the shortening of longitudinal fibrils implies a decrease in length of the capillary during contraction. There is little evidence for this in capillaries.
Michels (1936) believed the endothelium was contractile because of inherent ameboid activity. However, it is doubtful if this explanation could account adequately for the rapid, decisive contraction of capillaries reported in the literature.

Contraction of pericapillary cells

Charles Rouget in 1873 was the first to distinguish clearly between endothelial cells and pericapillary cells. He described the structure of small blood vessels in the tails of various amphibian larvae and also the hyaloid membrane of the eye of the frog. The arterioles possessed typical, spindle-shaped smooth muscle cells, with nuclei arranged at right angles to the axis of the vessel. Smaller arterioles possessed branched cells, with nuclei arranged obliquely. Capillaries possessed finely branched cells, with nuclei arranged parallel to the longitudinal axis. The fine processes of the cells on capillaries encircled the endothelium like a hoop. Rouget described a transition from the smooth muscle cells of arterioles to the branched cells of capillaries.

Rouget (1874) reported the contractility of the branched pericapillary cells in the swimming membrane of larval amphibia. Mechanical, chemical, and electrical stimulation produced
always advisable whenever available, to cooperate in the manner in which the following

material and ideas will be discussed and developed. The main scope of the

merits and the conclusions drawn should be kept

with all the ramifications and consequences of the concept and its

should be avoided. These are not fully present in the initial treatment

material but in full evidence in the literature. If

material and ideas to supplement the initial material

and to indicate the possible extent and the implications

and the consequences of the treatment of such conditions a

nificant, but in addition to this, the evidence in the literature

material should be supplemented by a detailed and detailed

and the consequences of the treatment of such conditions a
contraction of capillaries, accompanied by indentations in the wall at points of refractive annular bands containing nuclei. The nuclei and refractive bands were the branched pericapillary cells. In 1879 he reported the contractility of similar branched pericapillary cells in the "membrane capsulo-pupillaire" and omentum of embryonic and newborn mammals. He concluded that a contractile tunic enveloped all the blood vessels, including capillaries, throughout the vertebrates.

The publications of Rouget were overlooked by his contemporaries. In connection with an histological study of blood vessels, Mayer (1902) brought to light the publications of Rouget. He criticized severely the authors of current textbooks for omitting the discovery of contractile pericapillary cells. In his own investigations Mayer described a transition from typical smooth muscle cells on arterioles to branched cells on capillaries in the urinary bladder of the salamander and also the hyaloid membrane of the eye of the frog. On the basis of preparations stained with methylene blue, he considered that the branched pericapillary cells were muscular and similar to those described by Rouget. Since Mayer did not publish a detailed, illustrated account of his work, contemporary investigators remained unconvinced.

The longitudinal folding of the capillary endothelium reported by Steinach and Kahn (1903), in the excised nictitating membrane of the frog, was important physiological evidence for the contraction of pericapillary cells. However, this significant work received little recognition.
Krogh (1920) suggested that contractile pericapillary cells might account for the active contractions of capillaries. In Krogh's laboratory Vimtrup (1922a, 1922b) investigated this possibility by histological methods. In the tongue and also the urinary bladder of the frog he studied the blood vessels in supravital methylene blue preparations and in the usual preparations stained with Heidenhain's hematoxylin or saponin-indigo-carmine-picric acid. He described a transition from the smooth muscle cells on arterioles to the pericapillary cells. The nuclei of pericapillary cells were, for the most part, parallel to the longitudinal axis of the capillary. A few nuclei were arranged obliquely. Although the cytoplasm stained with difficulty, delicate transverse processes extended around the capillary forming a complete ring in several instances. At narrow places on the capillary the cells were stained more densely. In 1933 he described similar pericapillary cells in the human skin.

Vimtrup (1922a, 1922b) observed the contraction of capillaries in the tongue of the adult frog, the tailfin of the tadpole, and the larval salamander. The contraction started at a pericapillary cell and spread in both directions. The nucleus changed in shape. The transverse processes shortened and the cytoplasm collected about the nucleus. Because these cells resembled those described by Rouget, Vimtrup named them "Rouget cells".

Zimmerman (1923) reported pericapillary cells (Pericyten)
in numerous kinds of fish, amphibians, reptiles, birds, and mammals, including man. From preparations impregnated with silver nitrate he illustrated innumerable varieties of profusely-branched, extensive elements on the walls of capillaries. Zimmerman believed that these elements were muscular in nature.

As reported by Krogh (1929), Schaly (1926) described pericapillary cells similar to those of Rouget in the retina, choroid, ciliary body, iris, and other parts of the human eye. He reported similar cells on capillaries in the tongue and also the hyaloid membrane of the adult frog and in the tail of the tadpole.

Bensley and Vimtrup (1928) confirmed the previous observations of Vimtrup concerning the contraction of pericapillary cells. In the excised nictitating membrane, the tongue, and the web of the frog, they reported Rouget cells at places where the capillary first constricted. They described thin fibrils (myofibrils) in Rouget cells on capillaries perfused with Janus green.

Kahn and Pollak (1931) while confirming the previous experiments of Steinach and Kahn (1903) on the capillaries in the excised nictitating membrane of the frog, observed the longitudinal folding of the capillary wall in the region of the pericapillary cells. Their photographic records present convincing evidence for the contraction of pericapillary cells.
In Krogh's laboratory Field (1935) observed longitudinal folding of capillaries, as well as swelling of endothelial nuclei. Nuclei of pericapillary cells (Rouget cells) were seen at places where the endothelial folds appeared. She reported the contractility of Rouget cells in the excised nictitating and hyaloid membranes, the mesentery, and the tongue of the frog and in the mesentery and the subcutaneous tissue of the rat. By means of a transparent chamber inserted in the rabbit's ear, Beecher (1936a, 1936b) confirmed Field's report of contractile pericapillary cells in the mammal.

Jones (1936) concluded that there were two kinds of pericapillary cells in his methylene blue preparations of blood vessels in the iris of the albino rabbit. The first type were neurilemma cells of the non-myelinated nerve fibers composing the perivascular nerve plexus. The second were smooth muscle cells, "separated from one another, sometimes by a greater distance than the width of the cells themselves, which present a twined, or elongated spiral formation."

Parker (1923) reported that branched cells similar to Rouget cells were described on the blood vessels of invertebrates by Retzius. In Parker's laboratory Federighi (1928) observed two types of contraction in the capillaries of the sandworm, Nereis. One type was peristaltic. The other was local and occurred only in response to direct stimulation. Federighi attributed the peristaltic contraction to the endothelium and the local contraction to Rouget cells.
The contractility of pericapillary cells has been denied by various investigators on histological grounds. Marchand (1923), Aschoff (1924), and Volterra (1925) considered that Rouget cells were merely adventitial cells. They noticed that pericapillary cells stored vital dyes, similarly to histiocytes. Benninghoff (1926) reported that Rouget cells possessed the properties of adventitial cells. Nagel (1934) and also Michels (1936) concluded that the Rouget cells were fibrocytes.

Bensley and Vimtrup (1928) claimed that there were several kinds of pericapillary cells. They maintained that Rouget cells were distinct from the adventitial type. On capillaries perfused with Janus green they reported cells with delicate fibrils (myofibrils) similar to those of smooth muscle. These were the Rouget cells. Concerning the adventitial cells on capillaries, Krogh (1929) stated, "they have nothing to do with the Rouget cells, which are very difficult to stain and which take up intra vitam only certain diffusible dyes which are temporarily deposited in their fibrils, the appearance of which when thus stained cannot be distinguished from the myofibrils of undoubted smooth muscle cells."

However, several investigators have denied the presence of myofibrils in pericapillary cells. Benninghoff (1926) obtained no evidence for them in preparations of the diaphragm and uterine mucosa of man. Rogers (1932), using Janus green, failed to demonstrate myofibrils in pericapillary cells in the omentum of the cat. Zweifach (1937) found none in preparations of the
frog's mesentery stained with Janus green.

Clark and Clark (1925a) followed the development of capillaries in the tadpole's tail by means of daily observations of the same region. They reported that the pericapillary cells were adventitial cells which developed from stellate connective tissue cells. They were not able to determine whether the adventitial cells on capillaries developed into smooth muscle cells or connective tissue cells on arterioles. Clark and Clark (1940) repeated their observations on the growth of blood vessels in the rabbit's ear. In daily observations of capillaries they saw fibroblasts approach the exterior of a new capillary and fasten to the wall, remaining attached as an adventitial cell. In vessels which received a continuous blood supply for several days, the number of pericapillary cells (extra-endothelial cells) increased. The axis of the cell changed from longitudinal to transverse, with respect to the direction of the blood flow. The nuclei changed in shape, becoming round and compact. Thus the pericapillary cells became transformed into smooth muscle cells.

Certain observations on the activity of living capillaries refute the concept of the contraction of pericapillary cells. Clark and Clark (1925b) reported that capillaries in the tadpole's tail contract before pericapillary cells are developed on their walls. Furthermore, when pericapillary cells appeared, contraction occurred at places where no such cells were located. Zweifach (1934) and Rogers (1935) reported that the endothelium
pulled away from pericapillary cells during the contraction of capillaries. Zweifach (1934) distinguished seven kinds of pericapillary cells in methylene blue preparations of the mesentery of the frog. Several types responded to prodding with a micro-needle by changing shape and withdrawing their processes. However, none were contractile. Zweifach and Kossmann (1937) obtained no contraction of pericapillary cells in response to micromanipulation in the mesentery of the mouse. In extensive studies Clark and Clark (1932, 1935, 1940) have not observed the contraction of pericapillary cells in the rabbit's ear.

It may be that the number and extent of contractile pericapillary cells varies from species to species and even from tissue to tissue in the same animal. Clark and Clark (1940) have concluded with fairness, "From the descriptions given by the workers who have studied the extra-endothelial cells on the vessels of the nictitating and hyaloid membranes, of the arrangement of these cells with prongs extending around the vessel walls and of their apparent response to electrical stimulation, it appears possible that these cells, as Rouget (1879) originally suggested, may represent a form of primitive smooth muscle cell which is transitional between the longitudinally arranged, sparsely distributed and apparently non-contractile cells present on the vessels of the tadpole's tail, frog's mesentery, and on the capillaries and venules of mammals, and the more highly specialized contractile smooth muscle cells on the mammalian arteries and arterioles."
Sphincter-like contraction of the capillary origin

The point of branching of the capillary from the arteriole, the capillary origin, is strongly contractile and a number of investigators have observed this property. Golubew (1869) emphasized that the oblique and transverse spindles were frequent at the angles of branching of capillaries. He noted that the angles of dividing capillaries were the most strongly narrowed by swelling of the spindle elements. Tarchanoff (1874) observed that the spindle elements at the origin of capillaries were the first to thicken and extend into the lumen. Rouget (1874) noted that the annular bands of constriction associated with pericapillary cells were especially prominent at points of emergence of vessels. According to Krogh, Schaly (1926) emphasized the occurrence of Rouget cells at the points of branching of capillaries. Endo (1935) reported the constriction of arterioles and also the branching points of capillaries from arterioles in response to electrical stimulation and to application of adrenalin, pituitrin, or histamine in the nictitating and perioesophageal membranes of the frog and also the omentum of the rabbit.

A sphincter mechanism at the capillary origin has been postulated to explain the intermittency of blood flow in capillaries. Richards and Schmidt (1925) observed such an intermittency in the capillaries in the glomerulus of the frog's kidney. Although the capillary walls were not visible, there was no evidence from the column of blood corpuscles for constriction of any considerable portion of the capillary wall. They suggested that a
ring at the origin of the capillary might produce the intermit-tency. They report the observations of Schmidt that intra-venous injection of adrenalin produced constriction which was more conspicuous at the branching of small vessels than along their course.

Heimberger (1926) stimulated single capillaries in the nailfold of man. Blood ceased to flow temporarily. The capillary either remained packed with corpuscles or became clear, except for a few corpuscles which continued to move to and fro. Since the circulation continued in adjacent capillaries, Heimberger reasoned that the response occurred in the capillary which was stimulated, rather than the arteriole. He concluded that the capillary was narrowed by something at its place of origin from the arteriole. He actually observed a ring-like constriction of the blood column close to the origin of a capillary. Although the mechanism of the constriction was not determined, he believed it was muscular in nature (Schleusenmuskeln).

Wearn and co-workers (1934) observed spontaneous intermit-tency of capillary blood flow in the lung of the cat. They could not see the capillary wall and therefore obtained no proof for the contraction of capillaries. However, certain observa-tions were explained best on the assumption of contraction at the capillary origin. Thus, the blood flow stopped in several capillaries but continued in the arteriole. The capillaries gradually emptied. The authors suggested that plasma may have skimmed through the constricted capillary origin to
force the corpuscles into the venules.

Bordley, Grow and Sherman (1938) observed intermittency of blood flow in the capillaries of the skin over the tibia in man. When the circulation stopped corpuscles were usually present in clumps, and clear spaces were seen at the limbs of the capillary loop. The authors suggested that the clear columns indicated occlusion not far from the arteriolar-capillary junction. They proposed that individual capillaries might possess an occlusive mechanism to prevent passage of blood through the lumen. They suggested that such an hypothetical mechanism could operate independently of neighboring capillaries and the supplying arteriole.

According to Marchand (1923), Klemensiewicz observed no contraction of capillaries in the nictitating membrane of the frog in response to electrical stimulation. However, in reviewing the work of Klemensiewicz, Marchand states "Nur die sog. Ventilästchen haben an der Abgangsstellung von der Arteriole einen Ringmuskel, der bei der Kontraktion Wandverdickung und Verengung macht."

Jacobj (1920) reported that adrenalin produced local narrowing of the terminal arterioles beyond their point of bifurcation (hinter die Gablungen), in the swimming membrane of the frog. Since the capillary network remained dilated, he suggested that the ring of contraction (Kontraktionsringe) at the bifurcation of the arteriole might apportion the blood stream in the capillary network. He speculated that the ring of
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contraction might be controlled by a local reflex arc. "Es liegt der Gedanke nahe, dass diese Schleusenmuskeln auf Grund lokaler Reize eventuell auch unter Vermittlung kurzer lokaler reflexbogenartiger nervöser Bahnen erregt werden können, so dass unabhängig von der zentralen Gefässregulation einer den Bedürfnissen des einzelnen kleinen Gewebsdistriktes dienenden Blutverteilung damit Rechnung getragen wäre."

The first clean-cut direct evidence for a sphincter mechanism at the capillary origin was presented by Tannenberg (1925). He observed that blood corpuscles merely trickled through certain capillaries in the mesentery of the rabbit. At the origin of the capillary (Abgangsstelle einer Kapillare), he noted a spur-like structure (spornartiges Gebilde) which extended into the capillary and, for the most part, excluded the blood stream in the arteriole. Using vital trypan blue, Tannenberg stained cells with protoplasmic processes at the capillary origin. He observed their activity during the application of heat and cold to the mesentery. He concluded that these cells were sphincters (Pfortnerzellen). "Es gelang uns auch einige Male, die feineren Vorgänge in der Kapillarpfortnerzelle selbst mit aller Deutlichkeit und Sicherheit zu beobachten, welche bei der Ausbildung und Wiedereinziehung des verschließenden sporns ablaufen."

Ffuhl (1934) reported an accumulation of nuclei at the point of origin of capillaries from small arterioles in the omentum of the cat. The nuclei were partly circular and
partly longitudinal. Pfuhl proposed that they belonged to smooth muscle cells. He stated, "Ich vermute, dass wir hier den 'Pfortner' vor uns haben, der die Füllung der Kapillaren reguliert."

Knisely (1938) reported that "a sphincter guards each sinus's exit" in the liver lobule of the frog. The sphincters acted individually, in groups, or all together. Bloch (1940), in Knisely's laboratory, reported that each sinusoid possessed an afferent sphincter guarding its junction with the portal vein, and an efferent sphincter guarding its junction with the central vein. Adrenalin (10^{-4} to 10^{-6}) deposited on the surface of the liver contracted the majority of afferent sphincters but not the efferent. Acetyl-beta-methylcholine chloride (10^{-3} to 10^{-6}) dilated the afferent sphincters and some of the efferent to a lesser extent. In a personal communication, Knisely stated that the nature of these sphincters has not yet been determined, although Bensley and Warner have stained myofibrils in similarly-placed sphincters in the liver of the guinea pig.

The presence of sphincters at the capillary origins was denied by Ferguson (1937). He observed that the junction of the capillary and its parent vessel was narrowed. However, this portion of the capillary did not alter during the spontaneous changes in capillary blood flow. It could not be modified to any extent by prodding with a micro-needle. "That this was in no sense sphincter-like in action was evident from the observation of periodical eddyings of cells from the parent vessels into the mouth of the capillary."
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Endothelial valves have been reported at the capillary origin. Zweifach (1934) stated that mechanical stimulation with a micro-needle produced complete closure of the lumen of a capillary at its end. In 1939 he observed valve-like folds of endothelium at the "capillary exit in those regions where the capillary offshoot leaves the arteriole." The valve-like folds of endothelium opened and closed passively with dilatation and constriction of the arteriole. The valve behaved like an "endothelial sphincter." According to Zweifach smooth muscle cells were found occasionally at these places and might aid in the response.

In a preliminary report Fulton and Lutz (1940) described the activity of capillary origins in the frog's retrolingual membrane as sphincter-like. In response to stimulation of small vasomotor nerves with a micro-electrode such regions constricted in a sphincter-like manner, independently of the supplying arteriole, to regulate capillary blood flow locally. They described modified smooth muscle cells at the capillary origins in methylene blue preparations and concluded that these cells constituted the sphincter mechanism.
THE INNERVATION OF SMALL BLOOD VESSELS

The newer concepts concerning the innervation of smooth muscle, including that of blood vessels, imply the presence of a continuous plasmodial network of non-myelinated Remak fibers. Numerous investigators have reported dense, closed nerve networks in preparations stained with methylene blue. Prominent histologists such as Stöhr and Boeke formerly believed that the nerve supply to smooth muscle was scanty, as few as one muscle cell in one hundred being innervated. In recent years they reversed their earlier conclusions and presented evidence for copious, anastomosing terminal networks in silver-impregnated preparations.

The nature and mode of termination of the plasmodial nerve nets is a matter of considerable controversy. The staining methods are difficult and much personal interpretation is involved.

Woollard (1926) described a continuous perivascular nerve plexus in methylene blue preparations of the iliac arteries of various mammals. The plexus was continuous from the aorta to the periphery. Branches from the peripheral nerve trunks contributed to the perivascular plexus at intervals. Concerning the mode of termination, Woollard concluded, "From the individual strand in the net tiny side branches are given off and these end in small swellings after an extremely short course. I believe these terminals are always pericellular and not intracellular."

Hill (1927) investigated the innervation of the gut in preparations stained with methylene blue. She described a
complicated network of fibrils on the surface of the smooth muscle cells. The fibrils possessed small varicosities from which delicate fibrillae took origin and actually penetrated into the cell substance.

Busch (1929) investigated the innervation of blood vessels in methylene blue preparations from the frog, guinea pig, rabbit, and man. He concluded that the mode of innervation was similar in all species and consisted of closed networks of neurofibrils placed extracellularly between the individual muscle cells.

In methylene blue preparations of the frog's palate Leontowitsch (1930) reported a dense nerve plexus on the blood vessels. He distinguished two nerve networks on arteries. The first consisted of fine non-myelinated fibers and was concerned, presumably, with vasoconstriction. The second consisted of finer fibers and was concerned, presumably, with vasodilatation.

As a result of extensive studies of Bielschowsky preparations, Boeke (1932a, 1932b, 1940) described the termination of the sympathetic nervous system as the "ground-plexus". The sympathetic ground plexus was composed of protoplasmic or plasmodial strands interspersed with Schwannian nuclei. Within the plasmodial strands non-myelinated nerve fibers or neurofibrillae coursed as small anastomosing bundles. The network of neurofibrillae seemed to extend into the cytoplasm of smooth muscle cells to form a delicate, granular, sarcoplasmic structure, the "periterminal network."
In Bielschowsky preparations Stöhr (1934, 1938) described a fine protoplasmic network, the "terminal reticulum," in the adventitia, media, and intima of arteries. Since the terminal reticulum originated from the Schwannian-nucleated plasmodial strands, Stöhr concluded that it constituted the mode of termination of the autonomic nervous system. The reticulum was so dense it came in contact with every cellular component of the vessel wall. It was continuous from the aorta to the capillaries. Furthermore, it was not limited to the blood vessel wall, but extended everywhere throughout the entire organism. In the case of smooth muscle the terminal reticulum formed a protoplasmic continuity between neuroplasm and sarcoplasm.

Stöhr claimed that his terminal reticulum was comparable with the periterminal network of Boeke. However, Boeke did not agree and pointed out that the periterminal network was intracellular. Nonidez (1936, 1937a, 1937b) concluded that the terminal reticulum of Stöhr and the ground plexus of Boeke were identical. He attributed the slight differences in structure to slightly different techniques in staining and suggested that Boeke's ground plexus might be the result of incomplete impregnation of the terminal reticulum. Michels (1935) concluded, "At most the term 'terminal reticulum' is applicable to what Boeke had previously called the 'periterminal network,' i.e., an extremely fine plexiform net connected with the vascular smooth musculature whereby every muscle cell is innervated, the innervation being accomplished by the gradual transition from
neuroplasm to sarcoplasm (one-half protoplasm, one-half neurofibrillar structure)."

As indicated by Boeke (1940), the concept of the periterminal network, and the terminal reticulum imply that discrete autonomic neurones do not exist.

Hinsey (1934) was not convinced of the nervous nature of Boeke's sympathetic ground plexus, particularly in its relation to the innervation of skeletal muscle. Wilkinson (1934) maintained that the periterminal network was an artifact, since methylene blue and also gold chloride did not reveal its presence.

In the omentum of the rabbit, Michels (1935) described a widely-meshed nerve net composed of homogeneous plasmodial strands or Remak fibers interspersed with Schwannian nuclei. These plasmodial strands were comparable with those described by Stöhr and Boeke. However, even in silver-impregnated preparations Michels found no delicate neurofibrillae within the plasmodial strands. In preparations stained with Rio Hortega's modification of the Bielschowsky method, he observed a dense argyrophil network of connective tissue fibers. He suggested that Stöhr and Boeke may have impregnated similar elements. Michels concluded that there was no such structure as a terminal reticulum subserving a nervous function.

Nonidez (1936, 1937a, 1937b, 1939) questioned the nervous nature of the terminal reticulum. Using the reduced silver nitrate method of Cajal which is specific for nerves, he failed
to stain the terminal reticulum on blood vessels. Using the Rio Hortega silver carbonate method which is specific for connective tissue, he impregnated successfully the terminal reticulum and traced its continuity with collagenous fibers in the media and adventitia. Consequently he concluded that the terminal reticulum was non-nervous in nature. Since the Bielschowsky method combines the reduced silver nitrate method of Cajal and the silver carbonate method of Rio Hortega, Nonidez suggested that Stöhr and Boeke may have impregnated argyrophil connective tissue and nerves at the same time.

Nonidez reported that the bundles of nerve fibers in the arteries of the cat's tongue did not anastomose. He found no extensive networks in the tunica media. Nonidez still believed in the "neuro-neuronal" synapsis and the concept of Langley.

S. L. Clark (1937) investigated the innervation of the smooth muscle in the iris and also the ciliary body in the cat's eye. Using Ranson's silver pyridine method he obtained no evidence for a terminal reticulum. However, Clark reported sufficient terminal nerve fibers for separate innervation of each muscle cell. He described knobbed endings, or varicosities closely related to the surface of the muscle cells. Clark concluded, "We have not been able to observe, as Boeke maintains, that the nerve fiber ends within the protoplasm of the muscle cell."

In methylene blue preparations Weddell, Harpman and Lambley (1939-1940) reported networks which resembled the peri-
terminal network and the terminal reticulum. Such networks could not be traced to nerve trunks and persisted in denervated preparations.

Ganglion cells are present in the smooth muscle of certain organs, but not in others. Gruber (1933) summarized the evidence with reference to the ureter and the uterus. He concluded that the presence of ganglion cells in the plexus of the ureter was still doubtful, although there appeared to be good evidence for it. Concerning the uterus, reports were equally contradictory. In his investigations on the uterus Bozler (1938a, 1938b) assumed that no ganglion cells were present. Hill (1927), Stöhr (1932), and others have found ganglion cells in the gut and urinary bladder.

Along the course of peripheral blood vessels Leontowitsch (1930) reported small, primitive ganglion cells associated with the diffuse nerve plexus in the frog's palate. Using ordinary methylene blue and also Bielschowsky staining methods, he failed to find such cells. Demonstration of ganglion cells depended on the addition of a small amount of thiopyronin to the methylene blue.

Using Nissl's stain Michels (1935) observed no ganglion cells associated with blood vessels in the "plexus omentalis" of the rabbit. He suggested that Leontowitsch may have confused sheath cells of Schwann with ganglion cells. Among others, Woollard (1926), Hinsey (1928), Busch (1929), Stöhr (1933) and Boeke (1940) have reported no ganglion cells in the walls of
peripheral blood vessels in various tissues.

Thus it may be concluded that ganglion cells are absent from the smooth muscle of peripheral blood vessels. They are limited, for the most part, to the adventitia of the carotid artery and the aorta.

Competent investigators of innervation problems, such as Stöhr, Woollard, Hinsey, and Busch, have commented on the difficulties involved in demonstrating nerves to capillaries. This may be due in part to imperfect staining methods. As a result the concepts regarding capillary innervation are varied and conflicting.

Barksdale (1925-1926) reported that capillaries were innervated by contiguity and not by continuity. Woollard (1926) found no definite nerve endings on or near capillaries in methylene blue preparations. He reported that the perivascular nerve plexus invested capillaries only in part and many capillaries possessed no innervation. S. L. Clark (1928, 1929-1930) found no nerve fibers on capillaries in silver pyridine preparations of the choroid plexus, brain stem, and spinal cord of cats and dogs.

In silver pyridine preparations Hinsey (1928) reported that a small portion of the capillary bed in skeletal muscle possessed a sympathetic innervation. He described a few nerve endings on the capillaries and concluded, "It would seem that some of the fibers become smaller and smaller and end in free fibrils."
The impact of human factor considerations in design on the overall success rate of a project cannot be underestimated. It is crucial to involve stakeholders who possess the necessary expertise and experience in the project planning stage. This ensures that the project is aligned with the organization's strategic goals and objectives.

communication is key in project management, especially when dealing with teams from different backgrounds and cultures. Effective communication helps in aligning team members and ensuring a smooth execution of the project.
Busch (1929) investigated the innervation of capillaries in the amnion, and in the mucous membrane of the guinea pig's bladder. During progressive staining with methylene blue the nerves appeared and later faded before the Rouget cells came into view. Busch drew the nerve plexus as soon as it had stained and later superimposed the Rouget cells on the drawing. He reported that nerve fibers approached the Rouget cells and divided into 3 to 6 fine fibrils which united again beyond the cell. Although he assumed that Rouget cells were innervated, he saw no nerve endings. "I have never succeeded in demonstrating free nerve-terminations here, and furthermore I have never seen one single picture which made it even probable that the nerve penetrated into the cell . . . . ."

Michels (1935) studied the innervation of capillaries in the omentum of the rabbit stained with hematoxylin-azur-eosin. He projected the capillary bed with an Edinger apparatus, and drew the nerve plexus as it appeared under oil immersion in "approximately 325 contiguous fields." The nerve plexus consisted of plasmodial meshes which were much wider than the meshes of the capillary network. Michels concluded that actual nerve endings did not exist on capillaries and suggested that diffusion of a neurohumor might account for contraction of the capillary endothelium.

In Cajal silver nitrate preparations Nonidez (1936) reported no nerve endings, and also no nerve networks on capillaries.
In his early work on innervation Stöhr (1925-1926) stated that capillaries were generally supplied with one to several non-myelinated nerve fibers which occasionally spiralled around the wall. The fibers extended from one capillary to another, forming a loose, closed network. At places on the endothelium, fibers possessed fibrillar loosenings (Auflockerung). In an examination of thousands of slides Stöhr found no nerve endings on capillaries. Only in a few exceptional instances in the pia mater did he observe knob-like endings on the endothelial wall. Stöhr concluded that the capillaries were innervated by contact.

In his later work Stöhr (1934, 1938) reported that the terminal reticulum extended upon capillaries, "wobei ein direkter plasmatischer Zusammenhang jeder Endothelzelle, sowie jedes Pericyten mit allerfeinsten, fibrillären Ausläufern des Terminalretikulums ausser Zweifel gestellt wurde."

Boeke (1940) reported that the sympathetic ground plexus extended upon capillaries.
THE PRESENT INVESTIGATION

Methods

The present investigation of the regulation of blood flow in small vessels was conducted on the retrolingual membrane of the frog, *Rana pipiens*. Pratt and Reid (1930) first recognized the advantages of the retrolingual membrane for the study of single skeletal muscle fibers. This membrane is thin and may be illuminated readily by transmitted light. The skeletal muscle fibers, nerve fibers, and blood vessels are arranged in a single plane. A comparatively large field comprising several local vascular areas may be studied. Pratt and Reid described an operative technique for the exposure of the membrane and a method for transillumination. Their methods have been used in this investigation.

The brain and medulla of the frog were pithed. The retrolingual membrane was exposed by dissecting away the papillary epithelium and the muscle from the dorsal surface of the tongue. In most instances a large median vein was divided between two ligatures. Care was taken to avoid interference with the lateral blood supply and severed vessels were cauterized promptly. The frog was placed in a Petri dish possessing a glass shelf cemented to the bottom and surrounded by paraffin. The everted tongue was stretched gently over the glass shelf and pinned to the paraffin. By this procedure the retrolingual membrane was brought to rest on the glass shelf. Sufficient Ringer's solu-
tion was added to cover the membrane. The entire preparation was placed on the stage of the microscope and illuminated by transmitted light.

Unipolar micro-electrodes were used for the stimulation of small vasomotor nerves in the field of the microscope. Electrodes of this type were devised by Taylor (1925). He inserted platinum wire in a quartz capillary and drew it in a minute oxy-acetylene flame. He obtained insulated electrodes less than one micron in diameter. Pratt and Reid (1930) have used similar electrodes for the study of single muscle fibers. In the present investigation quartz-platinum micro-electrodes were used at first. However, such electrodes require the use of oxygen to make and are expensive because of the high cost of platinum. They break easily because of the brittle characteristic of the quartz. Consequently, a search was made for a more convenient and economical type of electrode.

Sen (1930) deposited metallic platinum, gold, or silver on the surface of quartz and also glass micro-needles. He silvered needles by Brashear's method, but obtained best results by sputtering with a high voltage discharge in a vacuum. Sen insulated the micro-electrodes by applying shellac with a small brush. This type of electrode was tried in the present investigation, but was discarded because of the difficulties involved in maintaining an insulation. During faradic stimulation of moderate strength the heat of resistance was great enough to disrupt the coating of shellac.
Nonpolarizable micro-electrodes (micro-saltbridges) consisting of capillary tubes filled with an electrolyte and connected with a large metal electrode were devised by Ettisch and Peterfi (1925) and also Taylor (1925). Field (1935) used this type for direct electrical stimulation of individual capillaries and also nerves in the frog and rat. In the present investigation nonpolarizable micro-electrodes have not been used. A polarizable electrode was preferable for the motion picture recording. When the stimulus was made a minute bubble of hydrogen appeared at the electrode tip (the cathode). This bubble was photographed on the moving film preceding the response, and presented visual proof that stimulation had occurred.

A silver-glass micro-electrode has been devised. Silver suture wire (#28 or #30) is inserted in a closely-fitting glass capillary and drawn in a minute gas flame. The type of micro-burner described by Chambers and Kopac (1937) is used for this purpose. When a satisfactory tip has been obtained the end of the silver wire is fused to a piece of copper wire. The copper wire and the initial portion of the shank of the electrode are sealed in a five-inch length of glass tubing (6 mm. in diameter), by means of a beeswax-resin cement. This tube constitutes the holder and is ready to be inserted in an Emerson micromanipulator in place of the holder supplied with the instrument. The micro-electrodes are stored conveniently by suspending them in a jar through perforations in the cover.
Micro-electrodes of one to five micra in diameter at the tip are obtained by this method. If the silver core is sealed by glass at the tip the insulation may be removed by passing a strong induced current through the electrode. Tissue debris has a tendency to accumulate at the tip of used electrodes. However, a single electrode may be used almost indefinitely if it is cleaned carefully after using by stroking with a small camel's hair brush beneath the surface of the electrolyte in which it is being used. Silver-glass micro-electrodes are easy to make, inexpensive, and resistant to breakage.

For electrical stimulation induced currents from an induction coil (Harvard apparatus) were passed through the micro-electrode. For chemical stimulation micro-pipettes were used, according to the method described by Chambers (1918), and Chambers and Kopac (1937). An Emerson micromanipulator was used to place the electrodes and pipettes in the field of the microscope.

Significant experiments were recorded on motion picture film (Agfa Superpan Supreme Negative), by means of an Eastman Ciné-Kodak special and a Spencer light-splitting prism. By means of a water immersion objective cinemicrographs were taken at magnifications as great as 900 times. At high magnifications a carbon arc was used for illumination.

In order to study the structure and innervation of the perivascular cells numerous preparations of the retrolingual membrane were stained differentially with methylene blue, fixed in saturated ammonium picrate and mounted in glycerine.
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Additional information:
- Task 10: Note for additional details.
- Task 8: Detailed notes for Task 8.
- Task 7: Additional comments.
- Task 6: Significant note.
- Task 5: Notes for Task 5.
- Task 4: Important details.
- Task 3: Notes for Task 3.
- Task 2: Specific notes.
- Task 1: General notes.
THE APPARATUS

(Illustration 1)

(A) Emerson micromanipulator
(B) Spencer side tube
(C) light-splitting prism
(D) Eastman Cine-Kodak special camera
(E) Harvard Apparatus induction coil
(F) Petri dish
(G) glass shelf cemented to the Petri dish with Canada balsam
(H) paraffin
(I) level of Ringer's solution
(J) silver-glass micro-electrode
(K) indifferent electrode
(L) pithed frog
(M) frog's tongue
(N) frog's retrolingual membrane
(O) stage of the microscope
THE EMERSON MICROMANIPULATOR
(one-half size)

Courtesy of Dr. F. H. Pratt

The manipulator operates in the horizontal plane by movement of a single lever. The electrode holder (A), provided with coarse adjustment, is fitted to the sliding carriage plate (1). This is supported by a second sliding plate (2) having a pair of transverse parallel ridges which fit into corresponding grooves in (1). A third plate (3) is fixed, but has longitudinal ridges engaging with similar grooves in (2). The holder thus is subject to universal horizontal transit without rotation. Motion is imparted by the lever (B), the fulcrum of which lies in the hinged plate (4) which by variable spring tension keeps the short arm of the lever firmly applied at a semi-spherical bearing to the carriage plate (1). Range and speed are together varied by screwing the lever (carrying the set-nut, b) up or down in a semi-spherical nut sunk in the bearing at the fulcrum, and so changing the leverage ratio. Direction of transmitted motion is such that the apparent movement under the compound microscope of an actuated electrode or other instrument is in exact directional accordance with the movement of the lever. Vertical fine adjustment is provided by a second lever (C) which raises and lowers the entire system by virtue of similar ridge and groove contact between the support (D) and the base (E). Three or four of the manipulator units may be brought to bear upon a single preparation, each unit being bolted to the base-plate that supports the microscope.
Structure and innervation of the perivascular cells

The perivascular cells on the small blood vessels in the retrolingual membrane were examined in preparations stained differentially with methylene blue. Typical smooth muscle cells were numerous on the arterioles but somewhat scattered on the precapillaries. The pericapillary cells at the origin of certain capillaries possessed nuclei arranged obliquely with reference to the capillary wall, while those scattered farther along the wall possessed nuclei with a longitudinal arrangement. The perivascular cells on venules possessed nuclei with an irregular arrangement.

The protoplasm of perivascular cells stained poorly with methylene blue. However, the cells at certain capillary origins possessed several distinct, coarse branches. An occasional pericapillary cell farther along the wall possessed numerous fine processes. When the protoplasm of several contiguous cells was stained, the processes appeared to anastomose, although direct protoplasmic continuity could not be established definitely.

The perivascular cells could be followed from the arterial to the venous side throughout the capillary network. A transition was observed from the longitudinally-arranged pericapillary cells (adventitial cells) to the branched, obliquely-arranged cells (modified smooth muscle cells) at the capillary origins to the spindle-shaped circularly-arranged smooth muscle cells on the arterioles.
THE PERIVASCULAR ELEMENTS ON SMALL BLOOD VESSELS

(Illustration 2)

The photograph is taken from a preparation stained differentially with methylene blue. The drawing is a key to the photograph. (x200).

(A) typical circularly-arranged smooth muscle on an arteriole. (B) typical smooth muscle on a precapillary. (C) branched obliquely-arranged smooth muscle on a capillary origin. (D) longitudinally-arranged pericapillary cells.
The innervation of the small blood vessels was studied in other membranes stained with methylene blue. In favorable preparations only the nerves were stained. Because of the differential action of methylene blue the nerves could be stained and the tissue fixed before the perivascular cells, endothelium, and connective tissue, elements appeared. The pattern of the blood vessels was traced by the perivascular nerve plexus. Non-myelinated nerve fibers, presumably branches of the glossopharyngeal and hypoglossal nerve trunks, formed a loosely-meshed plexus throughout the retrolingual membrane, the primary or gross plexus. Nerve fibers from the gross plexus approached the perivascular nerve plexus and were continuous with it. The perivascular plexus consisted of wide-meshed loops, the secondary plexus, and finely-meshed networks, the tertiary plexus.

The secondary perivascular plexus was continuous from arterioles to venules. The tertiary plexus was copious on the walls of arterioles and precapillaries, but sparse on the capillaries. Although actual nerve endings were not found, sufficient nervous tissue was present to innervate all the contractile elements. Ganglion cells were never found associated with the blood vessels in the tongue.

**Nature and distribution of the contractile elements**

The nature and also the distribution of the contractile elements on the blood vessels were examined by means of stimulation with a micro-electrode. The smooth muscle cells on the arterioles
and precapillaries, and the modified smooth muscle cells at certain capillary origins, contracted in response to direct stimulation. These were the cells involved in the dilatation and constriction of the small blood vessels to nerve stimulation. Except for an occasional cell, the pericapillary cells peripheral to the origin did not contract (Seq. 2, fig. 10; Seq. 3, fig. 7; Seq. 7, fig. 5; Seq. 9, fig. 3; Seq. 11, fig. 5 and 8).

Under magnifications of 400 to 900 times, nuclei of pericapillary cells sometimes appeared to thicken following stimulation with a micro-electrode. Although the nuclei appeared to project into the lumen, red corpuscles progressed without deformation. Consequently, the response was probably a transverse movement of the cell over the wall of the capillary presenting a face view of the nucleus which had been seen previously in profile.

Strong faradic stimulation sufficient to produce local injury, accompanied by sticking of leucocytes to the capillary wall, did not produce contraction of the endothelium. Endothelial nuclei were not observed to swell and block the lumen of the capillary. The endothelium did not respond to mechanical stimulation, direct electrical stimulation (Seq. 5, fig. 2 and 5; Seq. 6, fig. 3), or indirect electrical stimulation (Seq. 2, fig. 10; Seq. 3, fig. 7; Seq. 7, fig. 5).

It is concluded that the contractile elements of the small blood vessels in the frog's retrolingual membrane are typical smooth muscle cells on the arterioles and precapillaries and modified smooth muscle cells on certain capillary origins.
The local vascular pattern

Each incoming arteriole and its immediate branches may be said to constitute a local vascular pattern. In the retrolingual membrane there are several local vascular patterns, since two to four small arterioles enter from each side. The contractile perivascular cells extend a variable distance toward the periphery in each pattern. The precapillaries are provided with scattered smooth muscle cells throughout their length. The capillaries may possess a few modified smooth muscle cells at their origins. In some membranes the capillaries divide several times forming an extensive network devoid of contractile elements. In other membranes or in other local patterns of the same membrane long capillary loops provided with contractile origins converge directly to form venules without an intervening network. Direct pathways from arterioles to venules, serving as shunts for the capillary circulation, have not been found.

The vascular patterns in certain membranes appeared to be undergoing a change. Numerous capillary buds were noticed. Many aimless and duplicating loops were observed. Extensive capillary networks were present. Pericapillary cells were few in numbers and non-contractile. The capillaries had the appearance of newly formed blood vessels.

In active frogs the typical vascular pattern appeared to consist of an incoming arteriole, precapillaries, and long capillary loops provided with contractile modified smooth muscle cells at the origins.
Responses to nerve stimulation

Brief faradic stimulation of the non-myelinated nerves composing the gross nerve plexus produced dilatation of the small blood vessels in a local vascular pattern, followed by constriction (Seq. 1, fig. 1-5; Seq. 3, fig. 4-7; Seq. 7, fig. 1-5). The area constricted was frequently only a portion of that originally dilated (Seq. 3, fig. 4-7). Weak stimulation of a nerve frequently produced only dilatation, while strong stimulation of the same nerve sometimes produced only constriction (Seq. 2, fig. 4-10).

These observations suggest the concept of discrete vaso-dilator and vasoconstrictor nerves with different thresholds to electrical stimulation. Although the most frequent response to nerve stimulation was diphasic, a few vasomotor nerves produced either dilatation or constriction to all strengths of stimulation. It is conceivable that dilator and constrictor fibers might be segregated occasionally near their destination.

The vascular responses cannot be due to spread of current. In control experiments the micro-electrode was placed on the epithelium near a small nerve. No response occurred to brief faradic stimulation. The electrode was shifted to the nerve and stimulation was repeated. This time the typical diphasic response occurred (Seq. 2, fig. 1-6; Seq. 3, fig. 1-6).

Apart from the dilatation and contraction of certain capillary origins, capillaries did not participate actively in vasomotor responses. During dilatation within a local vascular
pattern the capillaries appeared to be increased slightly in diameter. During constriction they remained open beyond their origins. The presumptive decrease in intracapillary pressure did not collapse the wall. (Seq. 1, fig. 8; Seq. 2, fig. 10; etc.)

Spontaneous reversals in the direction of capillary blood flow frequently occurred. In addition, these were seen in portions of the capillary network following constriction in a local vascular pattern. It is probable that the direction of blood flow in portions of the patent capillary network is determined by pressure differences between adjacent local vascular patterns.

Faradic stimulation of small vasomotor nerves produced responses confined within a local vascular pattern. Nerves were found at times which produced constriction limited to the terminal arteriole, the precapillary, and the capillary origin (Seq. 3, fig. 7; Seq. 8, fig. 1-4). In other instances, nerve stimulation produced constriction confined to single precapillaries, or capillary origins (Seq. 9, fig. 1-3; Seq. 12, fig. 4-7). Stimulation of the wall of a capillary frequently produced a constriction confined to the capillary origin. (Seq. 5, fig. 1-8).

The dilatation produced by nerve stimulation is generally more extensive than constriction. It usually extends centrally along the arteriole to a point outside the field of the microscope. However, dilatation is confined within a local vascular pattern, since the vessels within adjacent patterns are not involved.

Although the nerve plexus appears to be anatomically continuous, it is physiologically discontinuous. Each local vascular pattern appears to be innervated separately.
Stimulation of the wall of an arteriole generally produced constriction confined to a portion of the local vascular pattern. The response was usually discontinuous at the place of origin of either the stimulated arteriole or its supplying vessel. A weak stimulus applied to certain places on the wall of an arteriole frequently produced an extensive dilatation within the local vascular pattern. Presumably, these conducted, limited responses were due to the physiologically discontinuous perivascular nerve plexus.

In general, two types of contraction of the smooth muscle were detected to both direct and indirect stimulation through the nerve. One type consisted of an abrupt contraction, occurring simultaneously throughout the responding portion of the vascular pattern (Seq. 8, fig. 3; Seq. 9, fig. 3). The other consisted of a sluggish, "out of phase" contraction, frequent in cases of rhythmicity (Seq. 7, fig. 4 and 5). In one experiment, the arteriole and precapillary responded to nerve stimulation in an abrupt manner, while the capillary origin contracted several seconds later in a sluggish manner (Seq. 2, fig. 9 and 10).

Stimulation of vasomotor nerves produced responses confined to restricted vascular patterns. These limited responses suggest the concept of a smooth muscle motor-unit. Stimulation of any one of several small nerves produced a response confined within the same pattern (Seq. 10, fig. 1-8). Such observations are in accord with the concept of the smooth muscle motor-unit and imply that axon reflexes are operating in efferent neurones.
Spontaneous rhythmicity

Spontaneous contractions within local vascular patterns were frequently observed (Seq. 12, fig. 1-3; Seq. 13, fig. 1-6). Such contractions were sometimes rhythmic over long periods. In other instances they were irregular. Stimulation of vasomotor nerves sometimes initiated a rhythmic response (Seq. 11, fig. 1-8).

Within certain local vascular patterns possessing rhythmicity, different portions of the wall of the same vessel responded at different rates. Occasionally one portion of an arteriole would be dilating while an adjacent portion would be constricting. In one preparation a précapillary was observed to beat in this manner for some time.

The explanation for spontaneous activity of the blood vessels was not determined. It occurred in preparations with the extrinsic nerves severed. Consequently no central reflexes could be involved. Discharges from ganglion cells are not a likely explanation since no such cells have yet been found in methylene blue preparations of the retrolingual membrane. Furthermore, spontaneous rhythmicity occurred in lightly cocainized preparations after nerve fibers had ceased to give a vasomotor response to stimulation. This suggests that the spontaneous activity may be a property of the smooth muscle itself.
**Sphincter mechanism at the capillary origin**

Sphincter-like activity of the capillary origin has been observed in certain preparations under high magnification. Following nerve stimulation pericapillary cells at the origin contracted to completely block capillary blood flow (Seq. 11, fig. 1-8). Spontaneous sphincter-like activity of such regions has been observed (Seq. 13, fig. 1-6). The capillary origin may respond independently of the supplying arteriole or precapillary and function as a sphincter to control capillary blood flow locally (Seq. 5, fig. 1-8; Seq. 9, fig. 1-3).

In methylene blue preparations modified smooth muscle cells with branched cytoplasmic processes are found at the capillary origin. They are probably the type of contractile pericapillary cell reported by Rouget (1874), Vimtrup (1922), Tannenberg (1925), and others. As proposed by Clark and Clark (1940), it is possible that the distribution of such cells may vary in different species or in different tissues of the same animal. In the retrolingual membrane of the frog it is concluded that modified smooth muscle cells at the capillary origin may respond independently of the supplying vessel and function as a sphincter.
Responses to acetylcholine and adrenalin

Solutions of acetylcholine hydrochloride (Lamate and Boinot), and adrenalin chloride (Parke, Davis) in Ringer's solution were applied directly to the walls of arterioles by means of a micro-pipette. Sufficient methyl green was added to make the small drops visible under the microscope. In control experiments adequate concentrations of methyl green produced no effect on the blood vessels.

In a few preliminary experiments acetylcholine in concentrations of 1:2,000 and 1:200,000 produced vasodilatation. A concentration of 1:2,000,000 had a doubtful effect. The dilatation persisted for two to three minutes and was followed at times by a brief period of rhythmicity. Although confined to a local vascular pattern, the response was extensive. The approximate extent of diffusion of the acetylcholine was detectable, because of the methyl green. Diffusion was insufficient to account for the widespread dilatation.

Adrenalin applied directly to the walls of arterioles usually produced constriction. Concentrations of 1:10,000, 1:100,000, 1:500,000, and 1:1,000,000 were effective. In contrast to the results with acetycholine and nerve stimulation, the response to adrenalin was localized to the smooth muscle cells near the tip of the micro-pipette. In a few experiments, constriction was followed by an extensive dilatation. In several experiments an initial extensive dilatation occurred.
The ongoing surge of empirical and computational work indicates a renaissance in formal methods for handling
complex data, aiming to balance between the flexibility of
algorithms and the completeness of their specification. Although
many modern computing systems have reached high levels of
complexity and are challenging to model adequately, there is
a growing reliance on computational techniques to assist in
understanding and analyzing these systems. As such,
methods are needed to capture the essential features
and dynamics of complex systems in a comprehensive and
accurate manner.
Intraperitoneal injections of adrenalin produced an initial increase in the rate of blood flow in the vessels of the retro-lingual membrane. This was probably due to action of adrenalin on the heart. Arterioles and capillary origins usually constricted or became rhythmic.

By means of a micro-pipette small drops of acetylcholine were placed on capillary origins possessing three or four modified smooth muscle cells. Such regions dilated. Adrenalin applied to the same place produced constriction. The same concentration of adrenalin produced constriction at one time and later produced dilatation of the identical place. The capillary origins appeared to be quite sensitive to acetylcholine and adrenalin.

Adrenalin and also acetylcholine produced no effect on capillaries apart from muscular capillary origins. Venules were not affected.

Responses in cocainized preparations

Three or four drops of a solution of 1% cocaine hydrochloride in Ringer's solution were placed on the retrolingual membrane. The arterioles and muscular capillary origins dilated. After several minutes the vessels narrowed considerably but did not close completely.

In these preparations stimulation of small vasomotor nerves, and also motor nerves to skeletal muscle, produced no responses. However, stimulation of the walls of arterioles produced
constriction of the same extent and limitation as before treatment with cocaine. The constriction was simultaneous in all parts of the responding portions of the vessels.

After treatment of approximately 20 minutes with cocaine, stimulation of the walls of arterioles produced a constriction confined to the smooth muscle cells at the tip of the micro-electrode. Stimulation of the wall of an arteriole at scattered points produced sharply localized constrictions. After prolonged treatment with cocaine an increase in the strength of stimulation was needed to constrict the smooth muscle. Greater doses of cocaine rendered the smooth muscle inert to strong stimulation.

When the cocaine was replaced or diluted with Ringer's solution stimulation of the walls of arterioles once more produced an extensive response. Later stimulation of small nerves again produced the typical diphasic response in preparations examined for reversibility.

Several instances of rhythmic vessels were observed in lightly cocainized preparations. After short treatment the rhythmicity ceased. It returned when the cocaine was diluted with Ringer's solution. Stimulation of vasomotor nerves during the period of rhythmicity failed to produce a response.

The limited, conducted response in lightly cocainized preparations implies a non-nervous conducting mechanism, such as a muscle syncytium, discontinuous at the junctions of certain vessels within a local vascular pattern. Stimulation of
The provided document contains a section about mid-life

problems. It discusses the challenges faced by adults who have

reached middle age. It highlights the importance of addressing these

issues to maintain overall well-being and adapt to the changing

demands of life. The text emphasizes the need for continuous

learning and personal growth to stay connected and engaged in

society. It suggests that embracing new experiences and hobbies

can help individuals find fulfillment and maintain a sense of

purpose as they navigate the mid-life phase.
the capillary wall sometimes produced constriction at the capillary origin but no response at the point of stimulation. Assuming the perivascular cells to be syncytial, this implies that conduction may occur without contraction.
DISCUSSION

In the mesentery of the mouse Zweifach and Kossmann (1937) distinguished two kinds of capillaries: the true or non-muscular capillary, and the "arteriovenous bridge". The arteriovenous bridge is a central pathway from the arterial to the venous side, from which the true capillaries take origin as side branches. When the tissues are in a resting state the "A-V bridge" remains open and serves as a shunt.

Zweifach (1939) reported that the ratio of A-V bridges to non-muscular capillaries varied in different tissues according to the metabolic level. Capillaries in the frog's skin and mouse's ear were almost entirely of the A-V type, whereas those in striated muscle were mostly of the non-muscular variety. In the nictitating membrane the two types were present in equal numbers. The true capillaries slightly outnumbered the A-V capillaries in the mesentery. In a recent paper Zweifach (1940) reported that non-particulate perfusion fluids passed through the A-V bridges only, whereas particulate fluids entered the true capillaries.

In the retrolingual membrane of the frog arteriovenous bridges have not been detected. The circulatory pattern consists of bifurcating vessels and is not built around a central pathway. According to Zweifach the A-V bridge remains open at all times, although it is a muscular vessel. In the retrolingual membrane the terminal arteriole and all its muscular branches may contract to stop blood flow completely in a local vascular pattern.
The origin of the nerve fibers forming the perivascular plexus in the frog's retrolingual membrane is not known. Krogh (1920) assumed that the blood vessels in the frog's tongue were innervated by sensory nerves because the threshold for mechanical stimulation was low, and the response was abolished by treatment with cocaine. In the web Doi (1920-1921) obtained vasodilatation following stimulation of posterior roots. Krogh, Harrop and Rehberg (1922), and Bozler (1936) have confirmed Doi. However, there is no definite proof that the vasodilators in the frog's tongue and retrolingual membrane are of posterior root origin.

Krogh (1921) reported that arterioles and capillaries in the frog's web responded to weak mechanical stimulation by dilatation, and to strong mechanical stimulation by constriction. He concluded that the reactions were due to stimulation of posterior root fibers and sympathetic fibers respectively. Krogh, Harrop and Rehberg (1922) observed contraction of arteries and capillaries in the web following electrical stimulation of sympathetic ganglia eight to ten, and also the sciatic nerve. They concluded that the capillaries received a sympathetic innervation.

Krogh (1920, 1929) obtained no evidence for sympathetic innervation of capillaries in the tongue of the green frog; Rana esculenta. The capillaries did not contract upon stimulation of the glossopharyngeal nerve, although occasionally small arteries and arterioles contracted. The usual response to stimulation of this nerve was dilatation. In curarized frogs stimulation of
information on several methods used to analyze the
results. These methods are based on statistical
analysis of the data. However, due to the
complexity of the data, the results obtained may
not fully reflect the true situation. Therefore,
much of the data should be interpreted with
caution. It should be noted that these methods
are not universally applicable, and each
method should be selected based on the
specific characteristics of the data and the
research objectives.
the hypoglossal nerve elicited no vasomotor responses except in a few cases where the skeletal muscle fibers contracted.

At Boston University Smith obtained dilatation, but no constriction of the blood vessels in the frog's tongue, except for an isolated case, following stimulation of the glossopharyngeal and hypoglossal nerve trunks (unpublished material). In the mixed lingual nerves it is possible that the vasodilator fibers greatly outnumber the vasoconstrictors. Consequently vasodilatation might be expected to predominate following stimulation of the nerve trunks. Near their destination in the retrolingual membrane, vasoconstrictors may possibly become sufficiently segregated to be detected in micromanipulative investigations.

The diphasic response is explained best on the basis of dual innervation, since the dilatation and constriction are frequently of unequal extent.

On the other hand, the concept of fiber specificity is by no means axiomatic. Bozler (1940) reported a diphasic response, contraction followed by inhibition, in uterine muscle of the cat, after stimulation of the hypogastric nerve. Since purely excitatory and purely inhibitory effects were infrequent, he stated that the hypothesis of specific motor and inhibitor fibers was inadequate to explain the mixed responses. Bozler proposed that sympathetic impulses possess a dual action on the smooth muscle of the uterus. First, they tend to set up impulses in the muscle and initiate contraction. Second, they have a tendency to lower the excitability of the muscle. A decrease in excitability
of human knowledge contained in textbooks, articles, and other written materials. It is

understood that there are limitations to what can be learned and understood from such resources. However, the information contained in textbooks and articles is often considered to be authoritative and reliable. The process of learning involves not only reading and understanding the material, but also thinking critically and applying the knowledge gained to new situations. It is important to remember that learning is an ongoing process and that knowledge evolves and expands over time. It is essential to stay informed and continue to learn throughout life, both for personal growth and professional development.
during stimulation of the hypogastric nerve was demonstrated experimentally by the dimished response of the uterus to direct electrical stimulation. This dual action could account for the diphasic response in the following way. Nerve impulses would first cause a contraction of the smooth muscle. Then the excitability would be lowered and the muscle would relax. If the excitability were depressed rapidly, pure relaxation might occur, but if it were not sufficiently depressed pure contraction might occur.

Innervation studies have contributed little to an understanding of the diphasic responses of the small blood vessels in the retrolingual membrane. In methylene blue preparations the non-myelinated nerve strands appear to separate and recombine at times, but no evidence has been obtained for possible conducting neurofibrillae within the nerve strands. However, in transverse sections of Remak fibers stained with osmic acid, Nageotte (1932) described trabeculae each of which possessed a neurite appearing as a white spot.

Krogh (1920) reported that the extent of dilatation in the frog's tongue following local mechanical stimulation depended approximately upon the strength of the stimulus. He stated, "it is necessary to assume that the nervous process set up by a stimulus is weakened at the points of branching by being diverted into two channels instead of one."

In the frog's retrolingual membrane conduction with a decrement, as proposed by Krogh, has not been confirmed.
Rosenblueth and Rioch (1933) reported that the concept of
the motor unit did not apply to the smooth muscle of the cat's
nictitating membrane. They recorded the responses of the nicti-
tating membrane to different frequencies of maximal stimulation
of the cervical sympathetic, before and after cutting a varying
number of the efferent branches of the superior cervical gang-
lion. As the frequency of stimulation was increased, the
height and also the tension of the responses of nictitating mem-
branes with reduced nerve supply became identical with that of
nictitating membranes with intact nerve supply. In other words,
the ratio of the response with intact nerve supply to the re-
sponse with partially cut nerve supply was a function of the
frequency of stimulation and not a function of the number of
fibers cut. Rosenblueth and Rioch pointed out that such a phe-
nomenon can be due only to a mechanism by which any nerve fiber
can affect all the muscle cells. The neurohumoral hypothesis
would provide such a mechanism. Thus, each impulse in a nerve
fiber produces a constant quantum of mediator. Consequently the
concentration of mediator is dependent upon the frequency of
stimulation, and the same amount of mediator would be liberated
with one-half the fibers discharging at twice the frequency as
with all the fibers discharging at one-half the frequency. Pre-
sumably diffusion of the mediator would affect the smooth muscle
cells with severed nerve supply. In skeletal muscle where the
motor unit and all-or-none principle apply, cutting a portion of
the nerve supply reduced the tension of contraction in proportion
to the number of fibers cut. The response was then independent
of the frequency of stimulation. The assumption was made that the mediator did not diffuse from the point of liberation in the case of skeletal muscle.

As Rosenblueth and Rioch have indicated, an alternative mechanism would be provided if the smooth muscle were a syncytium. Then the nictitating membrane would constitute a single motor unit with multiple innervation and the all-or-none law would apply. However, if such were true the responses in the nictitating membranes with partially severed nerve supply and the responses in those with intact nerve supply should be the same to all frequencies of stimulation. Since this was not found to hold, the authors concluded that the all-or-none principle did not apply to smooth muscle. For this reason Rosenblueth and Rioch discarded the alternative explanation of a muscle syncytium and explained the responses on the basis of diffusion of the chemical mediator.

Bozler (1938a) obtained a propagated contraction in uterine strips from the guinea pig, rabbit and cat, following direct electrical stimulation of the smooth muscle. He concluded that nervous tissue was not involved, since the response occurred after application of cocaine in concentration sufficient to block all nervous conduction (1:200). Furthermore, stimulation of the nerve supply to the uterus in the cat and guinea pig produced inhibition, and not contraction. Bozler explained the conducted contraction by the assumption of a muscle syncytium. As evidence for this explanation he reported that the responses were all-or-none and thus resembled the responses of single
I
skeletal muscle fibers.

Bozler (1938a, 1939) suggested that there are two kinds of smooth muscle: visceral muscle, such as that of the uterus and ureter; and muscle with a motor innervation, such as that of the nictitating membrane and the blood vessels. "Smooth muscles supplied by true motor nerves, in contrast with visceral muscles, consist of a great number of muscular units. This difference explains why the responses of the two types of smooth muscles are quite different from one another."

It should be noted that the concept of a muscle syncytium does not preclude the neurohumoral basis of the conducted contraction. Chemical substances could be liberated locally and initiate contraction at certain points from which the response might spread through the syncytium. In the retrolingual membrane treated with cocaine, some evidence has been presented for syncytial muscle segments, discontinuous at the branching points of certain vessels. However, sufficient perivascular nerve plexus is present so that it is unnecessary to assume either diffusion of the chemical mediator or the presence of a muscle syncytium to explain the conducted response in non-cocainized preparations. Furthermore, in preliminary, qualitative experiments variation of the frequency of stimulation did not appear to vary the extent of the response, indicating that temporal summation and spread of neurohumeror were not appreciable factors.
The concept of two types of smooth muscle requires further confirmation. The present investigation suggests that, contrary to the opinion expressed by Bozler, the perivascular smooth muscle may not be so different from that of the uterus and ureter.

Cannon and Rosenblueth (1937) suggested that parasympathetic fibers innervate certain smooth muscle cells and sympathetic fibers innervate others. To account for the excitation produced by adrenin under certain circumstances and the inhibition under others, they assumed that any given smooth muscle cell could respond in only one way, by either contraction or relaxation, dependent upon the presence of intracellular, hypothetical substances, E. or I, respectively. It is difficult to reconcile these assumptions with the direct observations of the contractions and relaxations of what appear to be the identical few modified smooth muscle cells at the capillary origin, following local application of acetylcholine and adrenalin with a micro-pipette.
SUMMARY

1. A review of the literature concerning the regulation of capillary blood flow has been presented.
2. A technique for making silver-glass micro-electrodes has been developed.
3. By means of stimulation with a micro-electrode, the nature and distribution of the contractile elements of small blood vessels have been examined in the retrolingual membrane of the frog, *Rana pipiens*.
   a. Pericapillary cells in the region of the capillary origin were contractile; those farther along the capillary were inert. These are probably the type of contractile pericapillary cell first reported by Rouget.
   b. The endothelium did not contract or swell to block the lumen of the capillary.
4. Brief faradic stimulation of small vasomotor nerves in the field of the microscope produced a diphasic response, dilatation followed by constriction. The diphasic response is interpreted as evidence for dual innervation. Additional evidence is presented and discussed.
5. Vasomotor responses were confined to local vascular patterns. Although the perivascular nerve plexus appears to be continuous in methylene blue preparations, it is physiologically discontinuous.
6. Stimulation of any one of several nerves produced a response in the same local pattern suggesting a smooth muscle motor-unit.
7. Spontaneous rhythmicity of undetermined peripheral origin has been described.

8. Responses to acetylcholine and adrenalin applied locally with a micro-pipette have been investigated. Experiments relevant to the neurohumoral hypothesis are discussed.

9. Responses of perivascular smooth muscle in cocainized preparations have been investigated. It is suggested that perivascular smooth muscle may constitute syncytial segments discontinuous at certain vessel junctions.

10. Sphincter-like activity of certain capillary origins has been observed. In methylene blue preparations modified smooth muscle cells have been described at the origin of the capillary. It is concluded that such cells may contract and relax, independently of supplying vessels, to regulate capillary blood flow.
within developmental psychology to psychological anthropologists. The development of the theory of psychological anthropology has been influenced by the work of several key figures in the field. Among these are the anthropologists who have developed the concept of cultural relativism. This concept is based on the idea that all cultures have their own unique values, beliefs, and practices, and that these cannot be judged by the standards of other cultures. This has led to a recognition of the importance of understanding the cultural context in which behavior and thought occur. The development of psychological anthropology has been characterized by a growing awareness of the need for a more holistic approach to the study of human behavior. This approach takes into account the interplay of biological, psychological, and social factors in shaping human experience. The field has also seen a growing interest in the role of culture in the development of psychological disorders, and the development of interventions that are culturally sensitive. This has led to a greater emphasis on the importance of cultural competence in the delivery of psychological services. The future of psychological anthropology is likely to be characterized by a continued focus on the importance of cultural context in understanding human behavior, as well as a growing recognition of the need for cultural sensitivity in the delivery of psychological services.
The cinephotomicrographs are enlargements from the motion picture records obtained in this laboratory. Sequences 1 and 5 are taken from the film records obtained by Dr. Brenton R. Lutz and Mr. Jack Seltzer, with their kind consent.

Many of the sequences reproduced here are taken from cuttings which have been incorporated into a film, "The Control of Small Blood Vessels", produced by Dr. Brenton R. Lutz and the author.
Sequence 1 (8 figures)

Micro-electrode on a nerve. Faradic stimulation when bubble appears causes dilatation of the arteriole and precapillary followed by constriction. The capillary does not constrict (x60, x250).

Figure 1. Normal condition. Electrode is placed on a nerve. Figure 2. Appearance of the bubble at tip of the electrode indicates stimulation of the nerve. Figure 3. Dilatation occurs in the arteriole and precapillary. Figure 4. Constriction takes place in the arteriole and precapillary. Figure 5. Return to normal. Figure 6. Normal condition. Electrode is placed on a nerve. Figure 7. Dilatation occurs in the arteriole and precapillary. Figure 8. Constriction takes place in the arteriole and precapillary. The capillary remains open.
Sequence 1, cont.
Sequence 2 (10 figures)

Control experiment. Electrode is placed on the epithelium near a small nerve. No response occurs to faradic stimulation. Electrode is shifted to the nerve. Weak stimulation produces dilatation of the arteriole, precapillary and the capillary origin. Strong stimulation of the same nerve produces constriction of the same vessels. The capillary remains open beyond the origin (x150).

**Figure 1.** Normal condition. Electrode is placed near a small nerve.

**Figure 2.** Appearance of the bubble at tip of the electrode indicates stimulation.

**Figure 3.** No response takes place.

**Figure 4.** Electrode is shifted to the nerve.

**Figure 5.** Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.

**Figure 6.** Dilatation occurs in the arteriole, precapillary and capillary origin.

**Figure 7.** Return to normal.

**Figure 8.** Appearance of the bubble at tip of the electrode indicates strong stimulation of the same nerve.

**Figure 9.** Constriction occurs in the arteriole and precapillary.

**Figure 10.** Constriction of the capillary origin occurs at a different rate. The capillary remains open beyond the origin.
SEQUENCE 2

Fig. 1

Fig. 2

Fig. 3
Sequence 3 (7 figures)

Control experiment. Electrode is placed on the epithelium near a small nerve. No response occurs to faradic stimulation. Electrode is shifted to the nerve. Weak stimulation produces dilatation followed by constriction (x100).

Figure 1. Normal condition. Electrode is placed near a small nerve.

Figure 2. Appearance of the bubble at tip of the electrode indicates stimulation.

Figure 3. No response takes place.

Figure 4. Electrode is shifted to the nerve.

Figure 5. Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.

Figure 6. Dilatation occurs in the arterioles and precapillaries.

Figure 7. Constriction takes place, confined to a precapillary and capillary origins.
SEQUENCE 3

Fig. 1

Fig. 2

Fig. 3

(cont.)
Sequence 4 (4 figures)

Electrode is placed on a nerve. A weak stimulus dilates the vessels which were completely closed (x100).

**Figure 1.** Initial state of constriction. Electrode is placed on a nerve.

**Figure 2.** Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.

**Figure 3.** Dilatation occurs in the arterioles and precapillaries.

**Figure 4.** The vessels return to their previous state.
Sequence 5 (8 figures)

Electrode is placed on the capillary wall. Stimulation with a single shock produces constriction confined to the capillary origin (x150, x250).

**Figure 1.** Initial condition. Electrode is placed on the capillary wall.

**Figure 2.** Following stimulation, constriction begins at the capillary origin.

**Figure 3.** The capillary origin constricts completely, in a sphincter-like manner.

**Figure 4.** Initial condition. Electrode is placed on the capillary wall at the same place.

**Figure 5.** Following stimulation, constriction begins at the capillary origin.

**Figure 6.** The capillary origin constricts in a sphincter-like manner.

**Figure 7.** A red corpuscle enters the reopening capillary.

**Figure 8.** Return to the initial condition.
Electrode is placed on a pericyte. No response of this cell or the endothelium takes place to strong faradic stimulation (x900).

**Figure 1.** Electrode is placed on a pericyte.

**Figure 2.** Appearance of the bubble at tip of the electrode indicates stimulation of the pericyte and the adjacent endothelium.

**Figure 3.** Electrode is moved away. No response has taken place.
Sequence 7 (5 figures)

Electrode is placed on a nerve. Constriction occurs at three capillary origins and along the arteriole. No capillary constriction occurs a short distance from the origin (x200).

**Figure 1.** Normal condition. Electrode is placed on a nerve.

**Figure 2.** Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.

**Figure 3.** Dilatation occurs in the arteriole and capillary origins.

**Figure 4.** Constriction starts at the capillary origin in the lower right-hand portion of the field.

**Figure 5.** Constriction of the arteriole and all three capillary origins takes place.


Conclusions:

In conclusion, it is important to address the multifaceted nature of the issue. By examining the various factors at play, we can gain a deeper understanding of the problem. It is crucial to consider not only the immediate causes but also the underlying systemic issues that contribute to the situation. Furthermore, it is essential to explore potential solutions that can be implemented to address the problem effectively.

- Address the immediate causes.
- Consider systemic issues.
- Explore potential solutions.

The interplay between these factors is crucial in developing effective strategies. By closely examining the situation, we can identify the most impactful areas to focus on and develop comprehensive solutions that address the root causes.

- Analyze the interplay.
- Identify impactful areas.
- Develop comprehensive solutions.

In summary, a thorough examination of the multifaceted nature of the issue is necessary to develop effective strategies. By considering all relevant factors, we can work towards finding sustainable solutions that address the problem comprehensively.
Sequence 8 (4 figures)

Electrode is placed on a nerve. Constriction takes place, confined to the terminal arteriole and its branches (x100).

Figure 1. Normal condition. Electrode is placed on a nerve.

Figure 2. Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.

Figure 3. Constriction takes place, confined to the terminal arteriole and its branches.

Figure 4. Return to normal.
Section 17: Language

Please note that the text in this section is not clearly legible. It appears to be a mix of words and phrases, possibly indicating a need for further clarification or context. The content seems to be discussing language-related topics, possibly including terms related to phonetics, grammar, or lexicon. Due to the unclear nature of the text, a detailed transcription or interpretation is not possible.
Sequence 9 (3 figures)

Electrode is placed on a nerve. A strong stimulus causes constriction confined to the capillary origin (x600).

Figure 1. Normal condition. Electrode is placed on the nerve.
Figure 2. Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.
Figure 3. Constriction takes place, confined to the capillary origin.
Sequence 10 (3 figures)

Electrode is placed on a nerve. Stimulation produces a diphasic response, dilatation followed by constriction. Electrode is shifted to another nerve. Stimulation produces the same response in the identical vessels (x90).

Figure 1. Electrode is placed on a nerve.

Figure 2. Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.

Figure 3. Dilatation occurs in the small blood vessels.

Figure 4. Return to normal. Electrode is shifted.

Figure 5. Electrode is placed on another nerve.

Figure 6. Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.

Figure 7. Dilatation takes place in the small blood vessels.

Figure 8. Return to normal.
Sequence 10, cont.

Fig. 5

Fig. 6
Sequence 11 (8 figures)

Electrode is placed on a nerve. Stimulation produces a rhythmic response of the arteriole and the capillary origin. Pericapillary cells at the origin contract and relax to control capillary blood flow (x600).

Figure 1. Electrode is placed on a nerve at the edge of the field.

Figure 2. Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.

Figure 3. Dilatation occurs in the arteriole and capillary origin.

Figure 4. Constriction occurs in the arteriole and capillary origin.

Figure 5. The capillary origin constricts in a sphincter-like manner.

Figure 6. Dilatation occurs in the arteriole and capillary origin.

Figure 7. Dilatation progresses.

Figure 8. Constriction occurs again, indicating rhythmicity.
Sequence 12 (7 figures)

Spontaneous rhythmicity of a precapillary. The arteriole is not involved. Electrode is placed on a nerve. Stimulation produces constriction confined to the same precapillary (x200).

Figure 1. Normal condition.
Figure 2. Spontaneous contraction confined to the precapillary.
Figure 3. Return to normal.
Figure 4. Electrode is placed on a nerve.
Figure 5. Appearance of the bubble at tip of the electrode indicates stimulation of the nerve.
Figure 6. Contraction occurs confined to the same precapillary.
Figure 7. Return to normal.
Chapter VI: Discussion

In conclusion, the following are the conclusions and recommendations:

1. The findings suggest that:
   a. Factor A contributes significantly to outcome B.
   b. Further analysis is required to confirm these findings.

2. Recommendations:
   a. Implementing strategy C could mitigate the effects of factor A.
   b. Additional research is needed to validate the conclusions drawn.

Data collected from:

- Sample 1
- Sample 2
- Sample 3

Analysis conducted using:

- Statistical Package
- Qualitative Methods
- Mixed Methods

Conclusion:

The study has provided valuable insights into the relationship between factor A and outcome B. Further work is needed to refine the findings and develop practical applications.
Sequence 13 (6 figures)

Spontaneous rhythmic contraction takes place. The capillary origin contracts in a sphincter-like manner (x600).

**Figure 1.** Normal condition.

**Figure 2.** Contraction takes place at the capillary origin. Pericapillary cells are involved.

**Figure 3.** Sphincter-like activity of the capillary origin continues.

**Figure 4.** The capillary origin dilates.

**Figure 5.** Contraction occurs again at the capillary origin, indicating rhythmicity.

**Figure 6.** Dilatation occurs again.
Contact and Accommodation

- Phone:...
- Email:...
- Address:...

Availability and Facilities

- Rooms: 20
- Meals:...
- Activities:...
- Parking:...

Rates and Bookings

- Single: $50
- Double: $75
- Triple: $90

Check-in/Check-out

- Check-in: 14:00
- Check-out: 11:00

Cancellations

- Full refund within 7 days
- No refund after 7 days
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It would be best not to be genealogically tied to one group, for example, to be related to a clan or tribe, as this could lead to misunderstandings or conflicts. It is important to have a wide and diverse network of relationships.
THE REGULATION OF CAPILLARY BLOOD FLOW

Abstract of a Dissertation

Submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy

BOSTON UNIVERSITY GRADUATE SCHOOL

By

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1941
There are several views concerning the mechanism which regulates capillary blood flow. Using the frog and rat, Field (1935) reported the swelling of endothelial nuclei which blocked the lumen of the capillary, and the contraction of pericapillary cells (Rouget cells). Beecher (1936) confirmed Field in studies on the blood vessels within transparent chambers inserted in the rabbit's ear. Using a similar preparation Sanders, Ebert and Florey (1940) reported the swelling of endothelial nuclei following electrical stimulation of the peripheral end of the cut cervical sympathetic nerve. Clark and Clark (1940) observed the contraction of endothelial cells in the tadpole's tail but not in the rabbit's ear. They have not seen the contraction of pericapillary cells but concede that it may take place in certain tissues such as the nictitating and hyaloid membranes of the frog. Zweifach (1939, 1940) maintained that capillary blood flow was regulated chiefly by the contraction of small arterioles and that changes in capillary caliber were merely passive.

In preliminary work at Boston University, Dr. Brenton R. Lutz applied the micromanipulative methods used by Pratt and Reid (1930), for the study of single skeletal muscle fibers, to the investigation of the control of capillary blood flow in the retrolingual membrane of the frog. Using antimony-glass and platinum-quartz micro-electrodes, he stimulated small nerve fibers, individual endothelial cells, and pericapillary cells in the field under the microscope. He perfected a technique for recording the responses on motion picture film. His early experiments indicated that the capillaries possessed active contractility and that they were under nervous control.

The author has confirmed the results obtained by Dr. Lutz and has extended the original investigation.

Silver-glass micro-electrodes, 1 to 5 micra in diameter at the tip, have been perfected for use in stimulation. These are made by inserting silver suture wire (#28 or #30) in a closely-fitting glass capillary and drawing it in a minute gas flame, produced by a microburner of the type described by Chambers and Kopac (1937). Electrodes of this type are advantageous because they are easy to make, inexpensive, and resistant to breakage. Since they are polarizable, a bubble appears at the electrode tip during stimulation and affords visual proof that stimulation has occurred. This is an important feature for the photographic records.

Significant experiments have been recorded on motion picture film, using an Eastman Cine-Kodak Special camera and a Spencer light-splitting prism. By means of a water immersion objective, cinephotomicrographs were taken at magnifications as great as 900 times. At high magnifications a carbon arc was used for illumination.

Numerous preparations of the retrolingual membrane were stained differentially with methylene blue, fixed in saturated ammonium picrate and mounted in glycerine.

By the use of methylene blue staining, micromanipulation, and cinephotomicrographic recording, the author has investigated the nature, distribution, and innervation of the contractile elements of the small blood vessels in the frog's retrolingual membrane.

Stimulation of small non-myelinated nerves produced a diphasic response, dilatation followed by constriction, involving the arterioles, precapillaries and muscular capillary origins in a local vascular pattern. The region constricted was frequently only a portion of that originally dilated. Occasionally nerves were found which produced only one kind of response, either constriction or
dilatation, to all strengths of stimulation. These observations are evidence for dual innervation.

In preparations stained differentially with methylene blue, the perivascular nerve plexus consisted of a dense network sufficient to innervate all the contractile elements, although actual nerve terminations were not found. At frequent intervals the perivascular plexus was supplied by nerve fibers from a loosely-meshed gross plexus. In stained preparations the plexus appeared to be anatomically continuous but was physiologically discontinuous, since stimulation of small nerves, in living preparations, produced responses which were confined to local vascular patterns. The restricted response suggests the concept of a smooth muscle motor-unit.

Stimulation of any one of several small nerves produced a response confined to the same local vascular pattern. This supports the concept of a smooth muscle motor-unit and implies that axon reflexes may operate in efferent vaso-motor neurones.

In lightly cocainized preparations (1% cocaine hydrochloride in Ringer's solution), stimulation of the vessel wall produced constriction of the same extent and limitation as before treatment. The nerve plexus was non-functional since stimulation of small vasomotor nerves produced no response. Consequently, the limited, conducted response implies a non-nervous conducting mechanism, such as a muscle syncytium, discontinuous at the junctions of certain vessels.

Spontaneous rhythmic contractions were observed frequently confined to local vascular patterns. Rhythmic contractions were initiated at times by nerve stimulation. The reason for the spontaneous and induced rhythmicity has not been determined. Discharges from ganglion cells are not a likely explanation since no such cells have been identified in the methylene blue preparations.

By means of a micro-pipette, minute drops of acetylcholine and adrenalin were placed on the smooth muscle cells of arterioles and capillary origins. Acetylcholine produced dilatation and adrenalin produced contraction of the same region. It appeared that the identical cells were involved in both responses. The relevancy of such observations to the neurohumoral hypothesis is considered in the discussion.

The capillary origin was the only portion of the capillary to be involved in the vascular responses. Active pericapillary cells were located at this place. Those farther along the wall were inactive, and did not respond to direct stimulation or indirect stimulation through the nerve. The endothelium did not appear to contract or swell so as to block the lumen.

Stimulation of small vasomotor nerves sometimes produced dilatation and constriction of the capillary origin, independently of the supplying arteriole or precapillary. Such capillaries possess a sphincter-like mechanism which regulates their blood flow.

In preparations stained differentially with methylene blue, capillary origins possessed modified smooth muscle cells with branched, obliquely-arranged processes. Presumably, these are the contractile elements involved in the sphincter mechanism. They are probably the type of cell discovered originally by Rouget (1873) and redescribed by Vimtrup (1922) in Krogh's laboratory.

In order to present the results of this investigation, cuttings were taken from the film records of the experiments and a motion picture, "The Control of Small Blood Vessels", was produced by Dr. Brenton R. Lutz and the
author. An attempt was made to make the film self-explanatory by the use of adequate titles and subtitles, so that it might be used for teaching purposes. For that reason, a few elementary sequences were included, showing typical circulation in the frog's retrolingual membrane, the structure of the perivascular elements, and the perivascular nerve network.

The film is copyrighted by the Trustees of Boston University and printed copies are offered for rental or for sale to educational institutions.

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