

VARIATION OF CAPILLARY DIAMETER AND
ANTIDROMIC ACTION IN THE FROG.
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SINCE the date of Stricker's description of independent contractility in the capillaries of the excised nictitating membrane of the frog, capillary contractility has been affirmed by several investigators. A summary of the previous work has recently been given both by Krogh⁽¹⁾ and by Langley⁽²⁾ so that I need not give it here. The conclusiveness of the evidence that a decrease of capillary diameter is due to active contraction is greatly dependent, in the ordinary conditions of the circulation, upon a knowledge of the degree to which the diameter varies with arterial pressure. It was to determine this question that my observations were begun; they have been extended to some other controversial questions.

Method. In all experiments the cerebral hemispheres were destroyed and a small dose of curari given. The capillaries were observed under a microscope with 200 or 400 magnification and ocular-micrometer. Observations on spontaneous variations in diameter were made, and on the same or following day the posterior roots of the lower nerves were prepared for stimulation, the cord cut above the 7th spinal root, and the part below excised. If the frog is kept cold and moist after such operation it may survive four to five days with good circulation. Observations were made both on spontaneous variations and on the effect of stimulating the posterior roots on more than ten frogs each of them allowing many series of observations.

Concurrent variations in the diameter of arteries and capillaries. The earlier observers took for granted that contraction of arteries in one region of the body would cause dilatation of both arteries and capillaries in the regions with uncontracted vessels. Doubt was thrown on the degree to which this occurred by the observation of Roy and Graham Brown⁽³⁾ that extra-capillary pressure caused very little variation in the diameter of capillaries. From this and other results they concluded that the diameter of the capillaries depended mainly on their intrinsic tone. Instances of vascular dilatation caused by increased arterial pressure

were given by Langley (4), but he stated that increased rate of circulation was generally more obvious than dilatation of vessels. Krogh (5), as Roy and Graham Brown, came to the conclusion that capillary diameter was very little affected by arterial blood-pressure.

In the many observations I have made on spontaneous variations, I have found definitely independent contraction in two cases only and then only in two capillaries. In the first case, a part of a capillary contracted from 25μ to 6μ and a spindle-shaped bulge formed just centrally of it. Circulation ceased just after this contraction. In the second case a capillary of 19.2μ diameter contracted to 13μ . Circulation was good. This capillary was the last branch of the trunk of an arteriole, which had sent off many side branches. None of these side branches showed any contraction.

In the other cases, and in all the circulation was good, there was a variable increase or decrease of the diameter of capillaries but this always corresponded with increase or decrease of arteriole diameter. The following is a marked example of variation of capillary diameter.

Exp. 1.

Time of obs.	Arteriole diam. in μ	Percentage variation	Capillary diam. in μ	Percentage variation
3.51	33	—	13.2	—
3.53	33	—	13.2	—
3.55	46	+39	26.5	+100
3.58	40	-13	20.0	-24.5

If there was no variation in the diameter of the arterioles, then the capillaries showed no variation of their size.

In order to determine further the effect of variation of blood-pressure on capillary diameter, experiments were made in two ways:

(a) A loose thread was passed round the femoral artery, or the abdominal aorta, and the circulation through the artery was stopped by pulling up the thread. After compression of the femoral artery a very slow circulation usually remained in the web. If the circulation before compression was very good, there was, on compression, a slight diminution of the diameter of capillaries which returned to the former size when blood was allowed to flow again through the artery. The diminution was, however, usually less than that observed in the spontaneous variations.

Exp. 2.

	Size of capillary in μ	
	(a)	(b)
Before compression	23.0	19.8
Artery compressed	19.8 (-14 %)	13.2 (-33 %)
Compression off	23.0	26.4

(b) The middle of the thigh was gradually compressed with the finger. By this means the vein was closed without closing the artery. The calibre both of arteries and capillaries increased.

Exp. 3.

	Size of arteriole	Size of capillaries	
		(a)	(b)
Before compression	—	25.0	16.0
Vein compressed	—	37.5	22.5
		(c)	
Before compression	38.5	15.0	
Vein compressed	48.5	19.2	

With regard to the compression experiment it must be remembered that arterioles and capillaries dilate as the result of cutting off the supply of blood. In one of my experiments with compression of the abdominal aorta in which the circulation in the web completely stopped, the dilatation of arterioles and capillaries began 1 min. after compression and attained a maximum after 2 mins.

The results given above show, I think, that, as a rule, in the given conditions, arteriole variation is accompanied by capillary variation of the same sign, *i.e.* that, as a rule, the diameter of the capillaries varies with the blood-pressure. A given arteriole variation in diameter, is however, accompanied in different conditions by different degrees of capillary change. In fact, as I have to mention presently, I have not found any distinct dilatation of capillaries to accompany the arteriole dilatation produced by posterior root stimulation, and sometimes there was no decrease of capillary size during reflex arterial contraction, and further it is known that complete occlusion of the arteries does not cause collapse of the capillaries.

Effect of brushing the web. Krogh⁽⁶⁾ found contraction of part of a capillary on local mechanical stimulation. This local effect I have not investigated, but I made some observations on the effect of brushing the web with a brush moistened with Ringer's fluid. This readily caused strong contraction of the arterioles. The capillaries decreased somewhat in size, but the decrease was slight and was equal in the whole area of the capillaries observed. No evidence of independent capillary contractility was obtained. The arteriole contraction was not reflex, for it was obtained after section of the sciatic. It was apparently caused by direct stimulation of the muscle coat, for it was obtained after applying cocaine to the web. I conclude that mechanical stimulation of moderate strength does not directly affect capillary diameter.

Innervation of capillaries. Steinach and Kahn⁽⁷⁾ found that some

capillaries in the frog's nictitating membrane can be brought to complete obliteration by stimulation of sympathetic fibres. Krogh and his co-workers⁽⁸⁾ found also that stimulation of the lower ganglion of the sympathetic chain brings about a constriction first of arteries and a few seconds later also of the capillaries of the web. They believe that every Rouget cell which surrounds a capillary is supplied by a sympathetic nerve fibre capable of causing contraction of the cell and so constriction of the capillary. I investigated the question in the following ways.

After cutting both roots of the 7th, 8th and 9th spinal nerves close to the cord, the spinal cord was cut just above the level of the 7th spinal nerve and the part caudal of the section was excised. Then, observing the web under the microscope, I pinched the flank of the same side. Reflex arterial contraction was always produced but the capillaries were usually only slightly affected and sometimes not at all.

		Size of arteriole	Size of capillary
<i>Exp. 4.</i>	Before pinching	46.0 μ	12.8 μ
	Pinching of flank	Contract	9.6
<i>Exp. 5.</i>	Before pinching	53.0	13.2
	Pinching of flank	39.6	13.2

In these cases the nervous impulses causing vaso-constriction leave the cord by the upper rami communicantes, pass down the sympathetic chain and reach the sciatic nerve by the lower rami communicantes.

I tried also direct electrical stimulation of the upper part of the cord after removal of the lower part; it caused greater contraction of arterioles than that produced reflexly. In one experiment out of ten local constriction occurred in a few capillaries (see *Exp. 6*).

	Size of capillaries	
	(a)	(b)
Before stimulation	9.6 μ	16.0 μ
Spinal cord stimulated	3.2 (-67 %)	9.6 (-40 %)
After stimulation	—	22.4

In other cases there were only variations concomitant with that of the arterioles. These variations did not take place at a particular point of a capillary, as they did in *Exp. 6*, but occurred along its whole length. The following two examples show the usual range of variation.

	Size of capillaries	
	(a)	(b)
Before stimulation	19.8 μ	12.8 μ
Stimulation of spinal cord	13.2 (-33 %)	9.6 (-25 %)

Stimulation of posterior roots. Doi⁽⁹⁾ found dilatation of arterioles as well as of capillaries in the web on stimulating the posterior roots. After dilating the arterioles by injecting acetyl-cholin the posterior roots caused dilatation of the capillaries only, and Doi concluded that the dilatation of the capillaries was due to a direct effect upon them. Krogh and his co-workers⁽⁸⁾ confirmed this result. Twelve years ago I tried the antidromic action of posterior roots on the frog's web without success. Possibly the failure was due to the outspread of the stimulating current to the spinal cord. In my present experiments, stimulation of the posterior roots on frogs from which the hinder half of the spinal cord had been excised, always caused distinct dilatation of arterioles. I did not find any dilatation of capillaries, but it happened that in the experiments in which the arteriole dilatation was most marked, my attention was given to this and not to the effect on the capillaries. Antidromic action on capillaries was also absent so far as I could see in the experiments to be mentioned presently on the skin of the back and on the tongue.

Effect of some drugs upon capillaries. Krogh⁽⁶⁾ describes the application of 0.1 p.c. adrenaline to the tongue of the green frog as causing capillary dilatation accompanied usually by dilatation of most of the smaller arteries. In the web, he found^(1, p. 136) that adrenalin had no effect on the capillaries. In my experiments the application of 0.1 p.c. adrenaline to the frog's web caused such distinct contraction of arterioles that they sometimes closed completely and if the adrenaline was not washed off, its action continued for a very long time. The capillaries, on the contrary, dilate. There is, however, a preliminary contraction which may be due to the fall of blood-pressure by the contraction of arterioles. Capillary dilatation occurs usually during contraction of arterioles, and as a result of the contraction a dilated capillary is sometimes quite free from blood corpuscles, and sometimes congested further by blood streaming back from the vein. The result shows that if there are sympathetic constrictor nerve endings in the capillaries, adrenaline does not stimulate them.

Exp. 8.

	Diameter of capillaries in μ		
	(a)	(b)	(c)
Before application	19.8	26.5	19.8
Adrenaline applied	26.5	39.5	26.5
Blood streaming back from vein	33.0	—	—

Application of 0.1 p.c. histamin to the web had no effect either on arterioles or capillaries. Krogh⁽⁶⁾ describes also inactivity of histamin on the blood-vessels of the frog's web.

It is well known that local application of mustard oil causes distinct dilatation of arterioles and capillaries. I confirmed this on the frog's web and found an exact correspondence between the variation in the capillaries and that in the arterioles.

Exp. 9.

Time of observation	Size in μ of	
	Arteriole	Capillary
3.50	39.5	19.8
3.51*	33.0	13.2
3.53	33.0	13.2
3.55	46.0	26.5
3.58	40.0	20.0

* One drop of mustard oil on the web.

Mechanism of antidromic action on arterioles. As I have said above, I always found in this series of experiments that dilatation of arterioles was caused by stimulation of the peripheral end of the posterior roots. The extent of the dilatation is illustrated in Exps. 10 and 11.

<i>Exp. 10.</i>	Diameter of arterioles in μ		
	(a)	(b)	(c)
Before stimulation	46.0	19.8	19.8
Stimulation of 8th posterior roots ...	53.0 (+15 %)	26.5 (+22 %)	33.0 (+40 %)
After stimulation	46.0	19.8	26.4

<i>Exp. 11.</i>	(a)	(b)	(c)
Before stimulation	19.8	13.2	22.5
Stimulation of 8th and 9th posterior roots ...	33.0 (+40 %)	19.8 (+33 %)	32.0 (+29.5 %)
After stimulation	19.8	13.2	22.5

As these figures show, the maximal increase of diameter was 40 p.c., the minimum 15 p.c., the average of eight cases was 28 p.c. The response begins, in good condition of the frog, in 10 seconds from the beginning of a faradisation lasting 15 to 30 seconds, and reaches its maximum during stimulation. If the animal is not very excitable, the response appears one to two minutes after cessation of stimulation. The currents were of a strength which caused a distinct pricking sensation on the tip of the tongue. Cooling of the web with ice prolongs the latent period of response. In one experiment with cooled web, the dilatation began in 10 seconds and reached its maximum 20 seconds after cessation of the stimulus.

The use of curari prevented recognition of escape of current to the anterior roots. The anterior roots of the 9th and sometimes those of the 8th nerve cause contraction of the bladder and cloaca. Although it is not very probable, it is conceivable that the contraction by compressing the blood-vessels might raise the blood-pressure, and the raised blood-

pressure distend the arteries of the web. In consequence, experiments were made to test this possibility.

The sciatic nerve on one side was exposed in the middle of the thigh and a small sheet of india-rubber placed under it. After testing the vasodilatation by stimulating the posterior roots, the part of the sciatic nerve on the rubber sheet was wrapped round with a small piece of cotton wool soaked in novocaine solution. The completeness of the paralysis of the nerve was tested by the disappearance of vaso-constriction on pinching the flank or on stimulation of the spinal cord. Complete paralysis was usually obtained 15 minutes after the novocaine application. Then the effect of stimulating the posterior roots was tested on two or three different arterioles. After this, the cotton wool with novocaine was removed, the sciatic nerve washed with Ringer solution and wrapped in cotton wool with Ringer. When the conductivity of the nerve had returned the effect of the posterior roots was tested again.

The experiments were decisive. Abolition of the conductivity of the sciatic abolished the vaso-dilator effect of the posterior roots. In one case only, a slight dilatation—from $56\ \mu$ to $59\ \mu$ —was obtained. Thus the effect is not a passive effect brought about by constriction elsewhere, but is a direct effect of posterior root fibres on the arterioles. Examples of the results obtained in three frogs are given in Exps. 12 to 15.

		Diameter of capillaries in μ		
		Before application of novocaine	During paralysis by novocaine	After recovery
<i>Exp. 12.</i>	Before stimulation	52.8	59.3	52.8
	Stimulation of posterior roots	66.0	59.3	59.3
<i>Exp. 13.</i>	Before stimulation	19.8	39.6	26.4
	Stimulation of posterior roots	39.6	39.6	36.3
<i>Exp. 14.</i>	Before stimulation	39.6	33.0	16.5
	Stimulation of posterior roots	43.0	33.0	26.4
<i>Exp. 15.</i>	Before stimulation	66.0	79.0	59.2
	Stimulation of posterior roots	79.0	79.0	72.5

Another form of experiment was tried. The femoral artery was clamped and the posterior roots then stimulated. The stimulation in some cases, but not constantly, caused dilatation of the arterioles. The results in such experiments are complicated by the effect of anæmia.

In the course of these experiments, I found that pinching the skin of the flank during the abolition of sciatic conductivity by novocaine usually caused distinct dilatation of the arterioles, thus giving evidence in addition to that already given of passive dilatation. On recovery of

sciatic conductivity, pinching caused the normal vaso-constriction. Pinching the skin also caused dilatation instead of constriction of arterioles when the sympathetic trunk was cut just above the 8th ganglion. Examples of these effects are given in Exps. 16 and 17.

Exp. 16.

	Diameter of arterioles in μ		
	Before narcosis	During paralysis	After recovery
Before pinching	39.5	36.4	33.0
Pinching of flank	26.2	46.2	26.4

Exp. 17.

	Before cutting of sympathetic trunk	After cutting of sympathetic trunk
	Before pinching	19.8
Pinching of flank	13.2	26.4

Effect of stimulating the nerves of the dorsal skin. Langley(4) found that stimulation of a cutaneous nerve to any part of the skin caused vaso-constriction in the part adjoining the anatomical ending of the nerve in it and that successive branches of the dorsal cutaneous nerves supplied successive areas which overlapped slightly. I have made 15 observations on nine frogs, stimulating the peripheral ends of the dorsal cutaneous nerves after curarisation. In three cases I found no effect, in two cases contraction of arterioles, and in ten cases dilatation of arterioles. It may be assumed that the dilatation is due to antidromic action; it appears then that the balance of effect of the sympathetic vaso-constriction and of the posterior root vaso-dilatation turns in one direction or the other according to yet undetermined body conditions. I reproduce some examples of dilatation and constriction.

Exp. 18.

	Diameter of arterioles in μ				
	(a)	(b)	(c)	(d)	(e)
Before stimulation	75.0	106.0	39.5	26.4	50.0
Stimulation of cutaneous nerve	87.5	119.0	46.2	33.0	37.5
After stimulation	75.0	106.0	—	29.7	50.0

Effect of stimulating the glossopharyngeal nerve. Dilatation on stimulating the peripheral end of the glossopharyngeal nerve in the frog was first described by Lépine(10). He found that the stimulation caused secretion and flushing of the corresponding half of the tongue. Krogh(1) obtained dilatation on mechanical stimulation of the nerve and observed that it occurred both in the capillaries and in the arteries. It hardly, then, needs further confirmation. I have, however, made some observations on the degree of dilatation which is caused by faradic stimulation of the glossopharyngeal. The increase of diameter ranged from 8.2 p.c. to 64 p.c.

SUMMARY.

The results, unless otherwise mentioned, refer to the vessels of the frog's web.

1. Whilst, as is known, complete contraction of arterioles does not cause collapse of capillaries, decrease or increase of arteriole size is, as a rule, accompanied by decrease or increase of capillary size. The frequency of exceptions to this rule vary in different conditions. Exceptions were not infrequent in reflex contraction of the arterioles, and posterior root stimulation, though it caused arteriole dilatation, was not found to cause appreciable dilatation of capillaries. Further, the degree of capillary variation caused by a given arteriole variation is not constant.

2. It is concluded that capillary size depends partly on the blood-pressure and partly on the condition of the capillaries.

3. Evidence of independent capillary contractility, *i.e.* constriction of a *portion* of a capillary, was rarely obtained (*a*) in spontaneous variations, (*b*) when arteriole contraction was produced reflexly or by stimulating the sympathetic origins in the upper part of the spinal cord or by brushing the web.

4. Adrenaline causes contraction of arteries and (as described by Krogh in the tongue), dilatation of capillaries.

5. Novocaine applied to the sciatic nerve prevents dilatation being produced by posterior root stimulation, but does not prevent dilatation (presumably passive) being produced reflexly by skin stimulation.

6. Stimulation of the dorsal cutaneous nerve was found to cause arterial dilatation more frequently than arterial contraction.

In conclusion I have to record my grateful thanks for the suggestions and kind aid which I received from Prof. Langley.

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