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ON THE PRIMARY VASCULAR DILATATION IN ACUTE INFLAMMATION.

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THE work of which I shall give an account was mainly conducted in the Laboratory of the Brown Institution, under the supervision of Dr Klein, to whose kind assistance I am much indebted. As I venture to bring forward a view which is opposed to that of Dr Cohnheim, I think it will be necessary to begin with a short account of his experimental work and the conclusions he draws from it.

He has, as is well known, studied the inflammatory process by observing the effects of injury on various organs which are sufficiently transparent to allow the changes which occur to be viewed by transmitted light. The experiment which now goes by his name consists in spreading out the tongue of a curarised frog on a plate of glass, which at the same time supports the animal lying on its belly; the glass plate is then fastened to the stage of the microscope and the outspread tongue brought into view. The tongue is then pinched, or irritated in some way, and the effect on the vessels is directly observed. Dr Cohnheim has in this way studied the inflammatory process in the web of the frog's foot, and in the frog's mesentery. The cornea and the membrana nictitans of the frog and the ear of the rabbit were also observed by him with reflected light.

The following[2] is his account of an acute circumscribed inflammation induced by cauterizing the tongue of the frog (*R. esculenta*) with a small crystal of nitrate of silver. The first thing that happens is the rapid dilatation of the arteries in the neighbourhood, and this is quickly followed by the dilatation of the veins, so that the cauterized place is soon surrounded by a zone of hyperæmia. At the same

[1] The chief part of the present paper was presented as a Thesis for the degree of M.B.

[2] *Neue Untersuchungen über die Entzündung.* Dr Julius Cohnheim, Berlin, 1873, p. 12.

time the current in the vessels of this zone increases greatly in velocity. It may be seen that the quickening of the circulation is a purely local effect by comparing the hyperæmic region with other parts of the tongue where the blood-stream will be found to be of normal velocity. This state of things is not of long continuance. The arterial and subsequently the venous current begin to get slow at the cauterized place, and ultimately stop altogether. We have therefore at the spot where the cautery actually took effect a small region of complete stasis, surrounded by a region in which the blood-stream is flowing quickly through dilated vessels. After a time the dilated arteries in the more peripheral parts of this hyperæmic zone begin to contract and the current becomes slower, and ultimately both the velocity of the circulation and the calibre of the vessels return to the normal. The venous current necessarily becomes slower, depending as it does on the supply of blood from the arteries. The dilated veins do not begin to contract till after the arteries, but they also at last regain their normal condition. Between the region of complete stasis, and the peripheral zone where the vessels have recovered and are practically as they were at first, there is a zone of vessels which have not recovered—which have not contracted—but remain permanently dilated. And it is of importance to note, that in these permanently dilated vessels the velocity of the current instead of being above the normal as it was at first, has now fallen below it.

The process of extravasation now commences. This does not affect the arteries, only the capillaries and veins. It is chiefly the coloured corpuscles which leave the capillaries (diapedesis) while only colourless ones "emigrate" through the walls of the veins. In the latter the process is preceded by the phenomenon known as "adhesion." The colourless (amœboid) corpuscles begin one by one to stick to the walls till the whole inner surface of the veins is coated with them. The same process takes place in the arteries, but, as before remarked, it never passes into the stage of emigration. Besides the emigration and "diapedesis" of the formed elements, there is a considerable extravasation of the liquid part of the blood. So that the lymphatic sack at the base of the tongue becomes filled with fluid and with corpuscles. This short account is, I believe, a fair abstract of Dr Cohnheim's account of acute inflammation; and I have observed for my own satisfaction all the chief phenomena of the series.

Dr Cohnheim believes the dilatation which comes on in the arteries directly after the application of an irritant to be due to the paralysis of the muscles in the vascular walls, and that this loss of power is the direct effect of the injury on the tissues of the muscular coat. He does not believe this temporary paralysis to be an essential part of the true process of inflammation, but merely an incidental accompaniment of the injury inflicted. The subsequent changes which the injury produces, viz. the *permanent dilatation*, the slowing of the current and the adhesion and emigration of corpuscles, constitute, according to his views, the true process of inflammation. He insists especially that they are caused by, so to speak, chemical changes which the irritation brings on in the walls of the vessels.

He remarks that in the condition of primary dilatation we have a rapid current flowing through dilated arteries, and since in the state of permanent dilatation the current becomes slow although no alteration has taken place in the calibre of the vessels, the diminution or velocity of the arterial current can only be accounted for by assuming that some alteration has taken place in the walls of the vessel. He also remarks that the passage of formed elements into the surrounding tissues shows a loss of physiological integrity which can only be due to some quasi-chemical change in the vascular coats. Would it not, he asks, be a remarkable thing if an irritant such as nitrate of silver did *not* produce some alteration in such a structure as the wall of an artery?

Dr Cohnheim appears to believe (if I do not misinterpret him) that if his theory be not accepted the only conceivable one is, that the dilatation of the vessels is due to central reflex action. Against any explanation of the phenomena by reflex action, he brings several objections. The most important of these is embodied in the result of the following experiment. The central nervous system of a frog is destroyed, or else the tongue is divided in such a way that it is only attached to the body by the lingual arteries and veins; he then repeats the experiment of irritating the tongue, and finds that the results are identical with those obtained with a normal tongue. His argument is, that the central nervous system being destroyed (or cut off from communication with the tongue), the only reflex action that could take place would be from peripheral vaso-motor ganglia situated in the tongue itself. And this, he concludes, is impossible, because no ganglia have been found in the tongue, and because no peripheral reflex action is known to occur anywhere.

It does not appear to me that all conceivable opposition is destroyed by the above experiment. I shall endeavour to show that the *primary* arterial dilatation which is accompanied by quickened circulation is due to some kind of nervous activity, and not, as Dr Cohnheim believes, to the direct effect of the irritant on the muscular coat of the arteries.

Paralysis may be due either to a lesion of the muscular tissue itself, as in progressive muscular atrophy[1], or it may be due to a loss of nerve-power, as in the paralysis of the lower extremities resulting from injuries to the spinal cord. Since Dr Cohnheim denies the existence of local vaso-motor ganglia, and leaves out of consideration the peripheral terminations of the vaso-motor nerves, he is forced to assume that the dilatation produced by local irritation is due *solely* to the direct effect of the irritant on the *muscular tissue* contained in the walls of the vessels.

When an irritant is applied to a curarised frog's tongue it

[1] Niemeyer's *Text-Book of Practical Medicine* (American Trans.), Vol. II. p. 519.

must act both on the intrinsic muscles of the organ and on the arteries contained in it. As is well known, curare paralyses the peripheral terminations of the ordinary motor nerves, but not those of the vaso-motor nerves; therefore any effect the irritant may produce on the intrinsic muscles of the tongue must be wholly due to its direct effect on the muscular tissue itself. This however is not necessarily the case with the arteries, since the irritant may primarily affect the vaso-motor nerves, and through their peripheral terminations may act on the muscular coat of the vessels. But according to Dr Cohnheim's views an irritant produces its results by its direct effect on the muscular coat of an artery; if this is so we have in a curarised frog's tongue an irritant acting *directly* on the striped muscle of the tongue, and *directly* on the unstriped muscle of the arteries, and we may expect that similar results will follow in the two cases. But this is not the case, for although irritation of the tongue produces dilatation of the arteries, it produces contraction (as I have often observed) in the intrinsic muscles of the tongue. Yet Dr Cohnheim uses this very example of the effects of irritation on the muscular tissue of the tongue to illustrate his theory of paralytic dilatation. He says (*Op. cit.* p. 26) "……as the muscular twitchings (muskelzuckungen) which make their appearance on pinching or irritating a part of the tongue, after a time subside, so also the vessels and their muscles gradually recover from the effect of a sudden pinch."

If an irritant acts directly and solely on the muscles of the arterial walls, it ought to produce the same effect in whatever part of the body the artery acted on may be situated. At any rate in superficial organs like the tongue and the membrana nictitans, arteries considered merely as muscular tubes ought to behave in the same way under similar circumstances. Yet Dr Cohnheim says that in the membrana nictitans the primary dilatation is absent, while in the tongue it is well marked. It appears that in the membrana nictitans the arteries dilate after an interval of some hours, and this corresponds to the permanent dilatation in the vessels of the tongue, and marks the commencement, according to Dr Cohnheim, of the inflammatory process. Dr Cohnheim accordingly concludes, from his own experiments and those of others, that dilatation is the universal

result of irritating an artery[1]. He quotes however Saviotti[2], who states that ammonia and some other irritants produce contraction of the arteries in the frog's foot; but these results are neglected, because on Saviotti's own admission they are somewhat variable, and because Dr Cohnheim believes that researches for which the more tender species of frog, *Rana temporaria*, is employed, are not trustworthy[3].

I worked with *Rana temporaria* before I was aware of Saviotti's results, and I can certainly confirm his assertion, that a solution of ammonia applied to the web of the frog's foot causes contraction of the arteries. I have observed the phenomenon so often that it is impossible to doubt that it is a genuine one. The same result has been produced by scratching the web with the broken end of a capillary pipette and by cauterising with nitrate of silver. The contraction is so intense that the arteries fade out of sight and complete venous stasis supervenes in consequence of the cessation of the arterial current. This condition of intense contraction has been observed to continue for as long as 13 or 14 minutes; as the artery recovers and the current returns, it dilates up to or sometimes beyond the normal calibre. A curious spasmodic condition is sometimes observed when the artery is recovering; the intense contraction coming on and disappearing again rapidly once or twice before the normal tone is fully re-established.

An interval of a few seconds usually intervenes between

[1] The following observers have recorded the fact that *contraction* may result from the irritation of an artery, Mr Lister (*Phil. Trans.* 1858, both papers), Sir James Paget (*Lectures on Surgical Pathology*), Dr Lionel Beale (*Monthly Microscopical Journal*, VIII. p. 58), Mr Wharton Jones (*Guy's Hospital Reports*, 1850, quoted in Carpenter's *Physiology*).

[2] Virchow's *Arch.* L. 592.

[3] Saviotti states (*loc. cit.* p. 610) that if the sciatic nerve be divided no contraction can afterwards be produced by local irritation of the web. This is quite at variance with Lister's, Cohnheim's and my own observations, and implies that reflex action from the central nervous system is essential to the production of the phenomena, and this cannot be maintained.

Again, Saviotti's statement that local irritation produces slowing of the current is considered by Riegel (*Mediz. Jahrbüch.* 1871, p. 99) to be at variance with his own observations. Riegel finds that stimulation of a sensory nerve always produces quickening of the current. With all due deference to the opinions of Stricker (see Riegel, note, p. 102) and Burdon Sanderson (Holmes' *System of Surgery*, v. 738), I believe that the slowing observed by Saviotti was merely the *mechanical* result of the diminution of the blood-supply consequent on the diminished arterial calibre, for he notices that, before the arteries contract, the current is *quickened* (*loc. cit.* p. 595), and he does not distinguish very clearly between the velocities of the arterial and venous currents.

the application of the irritant and the appearance of the contraction. On several occasions I have distinctly observed a transitory dilatation preceding the contraction, and occupying the short interval of time just mentioned. This dilatation is slight and is not a constant phenomenon, for I have several times made quite sure that no such dilatation preceded the contraction of the artery under observation. The variability of Saviotti's and my own results would be difficult to reconcile with Dr Cohnheim's theory of paralytic dilatation. But I hope to show that at any rate this slight variability in my own results can be reconciled with another theory.

In examining into the cause of the contraction produced by local irritation of the frog's foot, we may first exclude both *central reflex action* and the effect on the *heart* of irritating a sensory nerve, because the phenomena may be observed *after the division of the sciatic nerve and destruction of the spinal marrow.*

We must next consider whether the irritant acts directly on the muscular coat of the vessels or on the nerves which supply those muscles. As is well known, curare paralyses the peripheral terminations of the motor nerves, but has no such effect on the vaso-motor nerves; there is therefore no *à priori* reason for supposing that an irritant would act exclusively on the muscular coat and not also on the nervous mechanism of the arteries. The following reasons induce me to believe that the contraction is in great measure the result of nerve-stimulation. If the sciatic nerve is divided and the peripheral extremity irritated with an induced current, the arteries of the web are seen to contract. This contraction, like that resulting from local stimulation, is preceded by a short pause and is of the same intense character, causing disappearance of the arterial current and stasis in the veins. Now it is obviously unimportant at what point we divide the sciatic nerve, and of what length the peripheral piece may be to which the irritation is applied[1]; it therefore seems illogical to deny the possibility that the ammonia placed on the web acts primarily on the peripheral terminations of the vaso-motor nerves, the stimulus being subsequently con-

[1] Unimportant at least as far as the intrinsic nature of the result is concerned, although its *intensity* may be altered (Pflüger) quoted in Wundt's *Physiologie.*

veyed to the constrictor muscles in the arterial walls. Professor Maurice Schiff[1] considers it highly probable that local irritants do in this way take effect on the peripheral terminations of the vaso-motor nerves. This one fact, that local irritation may produce *contraction*, makes it impossible for me to accept Dr Cohnheim's theory, that dilatation when produced by local irritants is the result of the direct paralysis of the arterial walls[2]. He tacitly assumes that the dilatation of a vessel is always due to simple paralysis, and thus neglects the theory of *active dilatation of vessels*[3]. This theory is admirably stated and upheld by Schiff (*Op. cit.*, Leçons 11 and 12). It appears that Claude Bernard and Schiff agree in affirming the existence of a dilatation effected in some way by the activity of a nerve. Schiff supposes that some hitherto unknown mechanism comes into play, whereas Bernard assumes the existence in every case of local vaso-motor ganglia, and believes that the dilatation is the result of "inhibition." As an example of inhibition I cannot do better than quote a passage from Dr Brunton's paper "On inhibition peripheral and central[4]." "Thus the blood-vessels of the penis are kept in a state of moderate contraction by the stimulus which the vaso-motor nerves supply to their muscular coats. This stimulus is derived at least in part from ganglia lying close to the vessels, and to these ganglia proceed certain nerves, the *nervi erigentes* which arise from the sacral plexus. When the nerves are irritated the ganglia cease to stimulate the vascular walls, and these consequently relax and yield to the pressure of the blood which pours into and distends them." Local vaso-motor ganglia have usually been considered essential to active dilatation by inhibition. Thus Dr Brunton considers the ganglia on the nervi erigentes essential to the inhibition of the arteries which he describes (*loc. cit.*) in erection.

On the other hand, Dr Michael Foster and Mr Dew Smith have shown[5] that the snail's heart, which seems to be destitute of both nerves and ganglion-cells, is capable of true inhi-

[1] *Leçons sur physiologie de la Digestion.* Paris, 1868, T. I. p. 248.

[2] Dr Sanderson says (Holmes, *Syst. Surgery*, v. 740) that the effect of irritation is certainly *not* to paralyse the arteries.

[3] John Hunter speaks of "active dilatation," and compares it to the dilatation of the os uteri, Paget's *Lectures on Surg. Path.* 1853.

[4] *West Riding Asylum Reports*, IV. 1874, p. 182.

[5] *Proc. R. Soc.* XXIII., No. 160.

bition. These observers also conclude that the snail's heart, like that of the vertebrate embryo, is capable of rhythmical contraction without the "automatic" ganglia. They suggest that in the fully developed vertebrate heart the ganglia are not essential to the production of the rhythm, but are chiefly of use in co-ordinating its complex movements, &c. Any part of the body stands to the rest of the body in the relation of an organism to its environments. Now those organisms are the most developed which are best able to adapt themselves by internal changes to alteration in their environment. And this higher development is connected with the acquirement of structures which intensify or magnify the effects of changes going on in the external world; that is to say, it is connected with the acquirement of *ganglionated* sense-organs. In the same way the heart will be more able to adapt itself to *its* environment when it possesses ganglia; and since the only way in which the heart can respond to changes in its environment is by altering the strength or rapidity of its beats, it seems logical that ganglia should be intimately connected with the production of the rhythm. It appears indeed that minute portions of the heart which contain ganglia differ from those which do not, in this very particular, for they alone are capable of rhythmic contraction[1]. We have then a simple contractile organ (snail's heart) apparently capable of contracting rhythmically without the help of ganglion cells, and we have a complex contractile organ (frog's heart) in which ganglia are developed, which are apparently essential to the production of rhythm. In the same way, is it not possible that ganglia may be necessary for the inhibition of a complex organ in spite of the possibility of inhibiting a *simple* organ where no such ganglia exist? This supposition is supported by the fact, that in the most perfect and complex cases of inhibition, for instance, in the vertebrate heart, the penis and the submaxillary gland ganglia are found to exist.

We must enquire what evidence there is for the existence of local vaso-motor mechanism in the frog's web, and in some other parts of the body[2] in which we are considering the phenomena of inhibition.

[1] Dr Sanderson in *Handbook for the Phys. Lab.* p. 204.

[2] Since Dr Cohnheim denies the existence of local vaso-motor ganglia, some

Some physiological evidence on this point is contained in a paper by Putzeys and Tarchanoff (*Centralblatt*, Aug. 29, 1874). They begin by referring to an experiment by Goltz which is as follows: A dilatation and a consequent rise of temperature is produced in the feet of various animals (frog among the number) by the section of the sciatic nerve. After a short time the vessels regain their tonus, and the temperature falls to the normal[1]. Goltz argues from this result that vaso-motor ganglia must exist in the feet; because if the maintenance of the arterial tonus were due to stimulus supplied entirely by the central nervous system, the vessels ought to remain permanently dilated when deprived of such stimulus by the section of the sciatic nerve. Dr Cohnheim has himself performed an experiment of this kind, without being aware, as it appears, of the conclusions which must be drawn from his results. He says (*Entzündung*, p. 24) that dividing the tongue so that it remains attached only by the lingual arteries and veins, or that completely destroying the central nervous system, produces only a slight and transitory dilatation of the vessels, which almost at once regain their tonus. In Mr Lister's paper on the vaso-motor nerves of the frog he records experiments of the same nature as those of Putzeys and Tarchanoff, but which are more carefully done, and from which he drew similar conclusions as to the presence of a local vaso-motor apparatus.

Judging from my own observations, I should say that dividing the sciatic nerve has very little effect on the tonus of the vessels[2]. I have seen dilatation ensue; but on other occasions it has been of so slight and doubtful a character that I have not been sure whether or not the artery had dilated. This points to the same conclusion as Goltz's experiment, *and shows moreover how slight in some cases is the share taken by the central nervous system in the maintenance of the tonus.* From the above

evidence in favour of an opposite opinion may be given. In the first place Dr Cohnheim (*Embolischer Processe*, p. 28), in describing the complexity of structure of the walls of an artery, mentions the fact that *ganglion-cells* are found in them. Dr Beale (*Monthly Microscop. Journal*, Aug. 1872, p. 57) says, "in the bladder of the frog I have been able to follow fine nerve fibres from the ganglia both to arteries and capillary vessels." Dr Beale has also described (*Philosophical Transactions*, 1863) a portion of the coat of a branch of the iliac artery of the frog; upon the surface external to the muscular fibres are seen some ganglion-cells in process of developement with their fibres which ramify upon the muscular coat." Lastly, I have described and figured (*Quarterly Journal of Micro. Sc.* XIV. 109) rich plexus of ganglia and nerves accompanying and supplying the vessels in the external coat of the bladders of dogs and rabbits.

[1] A similar experiment has been performed by Schiff, *Op. cit.* I. 258, on the ear of the rabbit. It is hardly necessary to remark that he has not drawn similar conclusions from it.

[2] Dr Sanderson points out (Holmes, *System of Surgery*, V. 736) that there is no single trunk whose division completely paralyses the web. Hence the experiments of Putzeys and Tarchanoff are not complete. Lister's results, however, suffice for my point.

evidence we may conclude that when the vessels of a frog's foot are paralysed, *i. e.* deprived of the stimulus of the central nervous system, they are brought back to a tonic condition by naturally existing internal stimuli, whose effect is probably intensified by a local vaso-motor apparatus. In order to investigate the nature of this apparatus I have made a careful search through a considerable number of webs, by staining them with chloride of gold and cutting horizontal sections. No distinct ganglia have been found, so that if any exist, they must be of such rarity as not to be worth considering. In a few instances I have found places where the nerves possess more or less distinct swellings due to the presence of masses of nuclei. These do not resemble the clear oval nuclei of ganglion-cells as seen, *e.g.* in Auerbach's plexus or the sympathetic plexus in the bladder, &c.; they are, however, very much like the small nuclei which form the swellings figured by Lovén in the nervi erigentes, and regarded by him as ganglionic apparatus[1]. It is possible that nuclei may to some extent perform the functions of ganglia. Beale maintains[2] that ganglion-cells are developed from nuclei, "which cannot at first be distinguished from ordinary nuclei in connection with nerve-fibres." This of course is not conclusive, since the peculiar power of the ganglion-cell might be developed only *pari passu* with the growth of the granular cell-substance around the nucleus. Dr Drysdale[3], however, in speaking of the increased effect produced on the muscle by stimulating the nerve at an increased distance from it says, "the explanation of Pflüger is, that the molecules of the nerve in succession disengage active energy, and each stimulates its successor; but the increase of action (avalanche like) shows that each molecule disengages more force than the one before. Beale's is evidently a much more natural explanation, for in it each little battery of protoplasm is set in action by the passing current, and contributes its quota to the current which is thus really swelled like an avalanche." If by "current" we mean nothing more than the passage of a molecular disturbance along a nerve, I believe that this explanation of Pflüger's observation will be assented to, and

[1] *Leipsig Berichte*, 1866.
[2] Nerve-cells of frog. *Phil. Trans.* 1863, II. 550.
[3] *Protoplasmic Theory of Life*, by John Drysdale, M.D. (Edin.) 1874, p. 121.

that it will not appear improbable that the function of ganglia is performed in the frog's web by nuclei.

Schiff made a careful examination of the rabbit's ear, but found no ganglia. He therefore rejected the inhibitory theory, and concluded that "active dilatation" is effected by some unknown mechanism. But since his active dilatation is identical with that which is usually called inhibitory, I shall mention one of his most striking experiments (*Leçons*, &c., I. 260). He paralyses the ear or the foot of the rabbit by dividing in one case the auricular branch of the fifth, in the other the sciatic nerve. The result is a dilatation of the vessels and a local rise of temperature in the paralysed part. He then produces fever either by injecting pus into the veins or by injuring the pleura. "The first effect of the fever is an increase in the general temperature of the body; this increase shows itself more rapidly in the normal ear, and its temperature is soon higher than that of the paralysed one, which only participates feebly in the febrile rise of temperature." He argues that this experiment proves the possibility of dilatation produced by the *activity* of a nerve, and not by paralysis, because the effect of the loss of nervous supply is not merely to make the vessels dilate, but to prevent them being able to do so. The conclusion becomes inevitable when he shows that by irritating the peripheral end of the auricular branch of the fifth nerve the vessels of the ear can be made to dilate[1].

For the sake of clearness I may be allowed to recapitulate very briefly.

The question under discussion is the cause of the primary dilatation of vessels produced by local irritants.

I. Several reasons were given why the phenomenon cannot be paralytic in nature; the most important being that *contraction* may in certain cases be produced by local irritation. Having shown that local irritants may be supposed to act on the peripheral terminations of the vaso-motor nerves, I passed on to show:—

II. The possibility of dilatation dependent on the activity of a nerve, and produced by the inhibition of the local vaso-motor apparatus. My proposition is, that the primary dilatation is the result of the stimulation of the peripheral terminations of the dilatatory, that is, of the inhibitory nerves. I shall at present confine myself to the result of irritating the frog's web.

In the first place, there can be no doubt that the vessels in this organ are capable of dilating on its being locally irritated.

[1] Lovén, *Leipsig Berichte*, 1866, confirms this result.

I have described the dilatation which I have observed to precede contraction, and Dr Cohnheim believes dilatation to be the universal result of irritation. If these phenomena are to be explained by the stimulation of inhibitory nerve-fibres, it must be shown that the sciatic nerve contains such fibres. Goltz concluded from his experiments that this was the case; but Putzeys and Tarchanoff on continuing the research did not find the assumption of inhibitory nerves necessary, but considered the dilatation to be the result of the exhaustion of the constrictor, or ordinary vaso-motor, nerves.

A similar question has been discussed by Schiff, who found that by dividing the auricular branch of the *cervical plexus* and irritating the central end, he could produce dilatation of the vessels of the ear. In this experiment a central inhibitory ganglion is supposed to be stimulated, and the vessels of the ear are made to dilate by reflex inhibition conveyed to them by the auricular branch of the *fifth nerve*, which remains intact. Donders however (quoted in *Leçons*, T. I. p. 244) imagined the dilatation to be the result of exhausting the ordinary vaso-motor or constrictor nerves. Schiff replies that he finds it impossible to produce dilatation by the most prolonged and violent irritation of the *peripheral* end of the auricular branch of the cervical plexus, *i. e.* of the constrictor nerve.

This is at variance with the results obtained by Putzeys and Tarchanoff, who state that long and protracted irritation of the peripheral end of a divided sciatic produced dilatation in the arteries of the web. On the other hand, it is in agreement with what I have myself observed. I began by irritating the peripheral end of the sciatic with a moderately weak current from a Du Bois inductive coil. The artery under observation contracted, and in a short time dilated in spite of the continuance of the stimulus. I am inclined to think that it was this dilatation which Putzeys and Tarchanoff ascribed to the exhaustion of the constrictor nerves. But it is evident that it is not due to this cause, for while this supposed state of dilatation from exhaustion continued, *the artery contracted on the web being irritated.* The vessels having recovered from the effects of local stimulation, I made the current stronger, and the artery again contracted, but after a time it seemed to become accustomed to the stimulation

as in the first instance, and contracted on local irritation being applied. I strengthened the current several times with the same result, and the very powerful current which I ultimately made use of did not, as I believe, dilate the arteries beyond the normal.

It seems as if the peripheral nervous mechanism has the power of accommodating itself to an excess of stimulation received through the nerves from the central nervous system, and this is in accordance with the independent way in which it can maintain the tonus of the arteries when *deprived* of central nervous stimulation.

It seems then that Putzeys' and Tarchanoff's exhaustion hypothesis is not satisfactory, and that we must return to Goltz's view that dilatatory, *i.e.* inhibitory fibres exist in the sciatic.

In the rabbit's ear, as Schiff has shown, the dilator fibres are collected into one nerve, but in the sciatic, inhibitory and constrictor fibres are mingled together, so that when the central vaso-motor ganglia are irritated both kinds of fibres will be called into action. Dr Sanderson[1] states that contraction in the arteries of the web is produced by irritating the central end of the divided sciatic of the opposite side, that is, when the central vaso-motor ganglia are stimulated. I have performed this experiment with a like result. But on one occasion both Dr Klein and myself several times observed distinct dilatation, and I have confirmed this result by a subsequent experiment.

Having now shown the probability of the existence of inhibitory fibres in the sciatic I shall consider the effects of irritation on this nerve.

It appears to me that when a stimulus is applied to the vaso-motor mechanism of the sciatic nerve, either by irritating the central ganglia, the peripheral end of the divided nerve, or by local irritation of the web (and this is what especially relates to the question under discussion), a struggle commences between the dilatatory (inhibitory) and the constrictor nerves. In the case of local irritation of the web, this struggle usually ends in the victory of the constrictors, in the case of the tongue always in that of the dilators. In the web these are sometimes

[1] Holmes, *System of Surgery*, v. 737.

victorious for a short time, hence the temporary widening of the arteries which I have mentioned as occasionally preceding the contraction. But there are usually no signs of the struggle except the short pause which intervenes between the application of the stimulus and the consequent contraction, and the spasmodic contraction already mentioned. I believe that the primary dilatation in the tongue is in the same manner due to the stimulation of the peripheral terminations of the vaso-motor nerves. This view is rendered probable by Vulpian's results[1]; he finds that the vessels of the tongue (in what animal is not mentioned) are made to dilate where the *peripheral* extremities of the divided lingual and glossopharyngeal nerves are stimulated. The fact that stimulation of the nerves and local irritants both produce dilatation in the tongue, when contrasted with the fact that these agents cause *contraction* in the web, supports my conclusion, that irritants act through the peripheral terminations of the nerves.

The variable results of Saviotti's experiments (so described by Cohnheim, who neglects them for this reason) are exactly what, according to my view of the case, we should expect. As Schiff remarks (*Leçons*, T. I. p. 253), "Les exceptions du reste n'ont rien d'étonnant si l'on considère l'inconstance du trajet des nerfs vaso-moteurs en général, pour tout organe reçevant des nerfs vasculaires de plusieurs sources distinctes." As an example, he mentions the fact, that even the section of the sympathetic in the neck does not produce always the same effect on the vessels of the ear of the rabbit.

Let us once more consider the inhibitory dilatation in the rabbit's ear—Schiff asserts (and he is confirmed by Lovén, *Op. cit.*) that irritating the *peripheral* extremity of one of the auricular nerves (A) causes contraction, while irritating the extremity of another nerve (B) causes dilatation. This cannot be accounted for by different intensities of stimulation, nor by saying that the "nature" of the nerves is different. All we can say is that in passing from nerve (A) to the artery the stimulus remains a stimulus in the ordinary sense of the word[2], but that in passing

[1] *Gazette Hebdom.* No. 52, 1874 (quoted in *Centralblatt*, May 22, 1875).

[2] Brücke (Vienna *Denkschriften*, IV. 1852) in speculating why it is that light which should act as a stimulus produces "paralysis" of the pigment-cells of the chameleon, whereas darkness makes them "contract," remarks that "we are in certain relations to the external world, changes in it produce changes in us;" he goes on to say that anything producing a change may be called a stimulus (reiz),

from nerve (B) to the artery it changes its character and only remains a stimulus in the sense that it produces *some* change in the artery. And the conclusion we seem driven to is, that the means by which the stimulus passes from A to the artery are different from those by which it passes from B to it. That is to say, there must in the latter case be some local mechanism interposed between the nerve and the artery, which has the power of altering the stimuli it receives and passing them on to the artery changed in some way. And we can best conceive such a mechanism taking the form of an arrangement of ganglion-cells or nuclei.

In fact we suppose that an artery contracts under a certain stimulus, but dilates when this stimulus is altered by some local mechanism—or in other words, we assume that its contractile tissue possesses two kinds of excitability. This appears to me to be in accordance with Dr Foster's and Mr Dew Smith's supposition[1], that the nature of the tissue of the snail's heart is such that inductive shocks of different intensities produce exactly opposite results. For this is equivalent to endowing the tissue with two kinds of excitability. By stimulating certain nerves we can produce either flexion or extension of a vertebrate animal's limb, but because by the application of appropriate stimuli we can also produce contraction and extension of a nerveless mass of protoplasm[2], we do not deny that distinct nerves for flexion and extension may exist in more highly developed organisms. This analogy is exaggerated and false, but it may serve to show how the supposition of the existence of distinct nerves for inhibition and contraction is consistent with the simple form of inhibition described by Dr Foster and Mr Dew Smith.

In the course of this paper I have ventured to state the way in which the difficulty of inhibition presents itself to me; and I have tried to show that the only "explanation" or generalization of the facts which I can form, seems to accord with the view that certain forms of inhibition (where the nature of the result

but that "if this word is to be useful in physiological language we must limit it to those agents which when acting in a motor nerve produce contraction (of a muscle), and when acting on a sensory nerve produce sensation....."

[1] *Op. cit.* p. 323.

[2] Stricker, *Handbuch*, &c., Lieferung, 1.

is not determined by the strength of the stimulus applied) require a local vaso-motor apparatus. Also that the supposition of the existence of distinct inhibitory and constrictor nerves is not at variance with the simple form of inhibition of Dr Foster and Mr Dew Smith. I may be permitted to restate the difficulty very briefly. A mere contractile mass of the nature of protoplasm can be inhibited, or the reverse, by varying the *intensity* of the stimulus. We "explain" this by saying that the tissue has two opposite excitabilities. But in the case of the rabbit's ear, (Schiff, *Leçons* 11 and 12,) the same artery can be made to dilate or to contract by applying the same stimulus to different nerves. Here we cannot explain anything by *merely* endowing the tissue of the artery with excitabilities varying with the intensity of the stimulus—because the stimulus we apply to the nerve is the same in the two cases. Nor are we permitted to ascribe different powers of conduction to the nerve-trunks along which the stimuli travel. We seem therefore compelled to say that in passing from the inhibitory nerves to the arteries the stimulus is changed. And to effect such a change we must assume a local mechanism interposed, and this will probably take the form of an arrangement of ganglion cells or nuclei.

The rarity of the collections of nuclei on the nerve-trunks in the frog's web mentioned above may possibly be connected with the preponderance of the contractile over the inhibitory tendency in that part of the body.

Finally I conclude:—

I. That local irritants do *not* cause dilatation by *direct* paralysis of the tissue of the arteries.

II. That Schiff's view is correct: viz. that local irritants produce their effects on vessels by acting on the peripheral terminations of the vaso-motor nerves.

III. That when the vaso-motor nerves include both inhibitory and constrictor fibres, both are stimulated by local irritants, and the resulting alteration in the calibre of the vessel is the result of the victory of one set over the other.