ON A DIFFERENCE IN THE INFLUENCE UPON INFLAMMATION BETWEEN THE SECTION OF THE SYMPATHETIC NERVE AND THE REMOVAL OF THE SYMPATHETIC GANGLION.[1]

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Ever since it was discovered that section of the sympathetic is followed by increased temperature and redness of the corresponding ear in rabbits, the influence of the section of the sympathetic nerve upon the course of an inflammation artificially produced in the rabbit's ear has been the subject of repeated investigations. The influence of the section of the auricular nerves has been also a frequent subject of study. The effect of these nerves, however, was considered to be chiefly a sensory one. In a recent investigation of the vasomotor nerves of the rabbit's ear, we[3] arrived, however, at the conclusion that in a majority of cases the vasomotor action of the third cervical nerve on the rabbit's ear was much greater than that of the sympathetic nerve. On the basis of these results we started to subject to a new revision the old data regarding the influences of the section of the sympathetic and the cervical nerves upon inflammation. Our studies were confined to the observation of the influence of the section of the nerves upon the onset, appearance, and course of a local inflammation in the ear.

Our experiments have demonstrated to us repeatedly that, though the section of either of the nerves has in the great majority of cases a more or less distinct aggravating influence upon the inflammation, this influence is by no means in proportion to the vasodilatation produced by the section of these nerves. We had animals in which section of the third cervical nerve brought on a considerable vasodilatation in the corresponding ear. Nevertheless, the inflammatory process in this ear was far behind that produced in the ear,

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[3] S. J. and Clara Meltzer. The American Journal of Physiology, ix, 1903, p. 147.

the sympathetic nerve of which was cut, and the consecutive vasodilatation was very moderate in comparison. However, it is not this experience which we wish to speak about at this time. We mention it incidentally as we may have to refer to it again later on. The observation which we wish to report here deals with a difference in the influence upon inflammation between the section of the sympathetic nerve and the removal of the superior cervical ganglion.

As an introductory statement we may say that in all our experiments the inflammation in the ear was distinctly aggravated by the preceding operative interference of either kind, whether section of the sympathetic or removal of the ganglion. By aggravation of inflammation we mean that the redness set in first, that hyperemia and edema were more intense and spread over a larger area, that finally the pustules developed earlier and were larger on the operated side than on the other, unoperated side, or in the ears of an unoperated control animal. We have produced inflammations by injecting subcutaneously in the convex side of either ear an equal quantity of an eighteen to thirty hours bouillon culture of staphylococcus pyogenes aureus, or by injections of a drop of spirit of turpentine. In the latter case, care should be taken that the injected quantity is not too large. The same applies to the virulence of the staphylococci which should be not too great, as in either case the inflammation in both ears would become so intense as to make it quite difficult to recognize small differences between the two inflammatory foci. We have lately, however, employed a method which brings out the differences between the two foci very clearly even in extensive inflammations of the ears. The method consists in subcutaneous injections of a sufficient dose of adrenalin. The effect is very interesting and instructive. The difference between the inflammatory focus and the inflammatory area (Entzündungsherd und Entzündungshof) comes out very clearly. All simply hyperemic tissues become very pale, while the redness of the inflammatory focus undergoes almost no change. This demonstrates that blood-vessels within the focus lose the power to react to the effects

of suprarenal extract which otherwise affects normal vessels so readily. It is an instructive demonstration of, and a new proof for the theory that in inflamed tissues the blood-vessels lose many of their normal vital properties.

Now, in the course of these experiments we noticed in animals in which on one side the sympathetic nerve was cut and on the other side the ganglion was removed, that the inflammation on the sympathetic side was invariably greater than on the ganglion side. The cultures employed were the same for both sides, the quantities injected were as nearly equal as possible, and the places of injection were identical points in both ears. As in our previous experience the left ear has shown more pronounced vasomotor changes (after section of the sympathetic or removal of the ganglion) than the right we varied our experiments, operating in one animal the sympathetic nerve on the right and the ganglion on the left, and in another the sympathetic nerve on the left and the ganglion on the right side. Furthermore, in other experiments we have taken for each experiment two rabbits, operating the sympathetic nerve in one and the ganglion in the other animal; here the operation was performed in both rabbits on the same side — either the left or the right. In each animal the inoculations were then made either in both ears, having thus in each animal a comparison between the normal and the operated side; or the inoculations were confined to the operated ear. We can state now briefly that with one single exception the results were in all experiments the same, and that is that the inflammation on the side in which the sympathetic nerve was cut was regularly greater than that on the side where the ganglion was removed. The result was the same whether the inoculation was done soon after the operations or two or three weeks later. The experiments with turpentine have given the same results as those produced by the local infection. Furthermore, in the same animal after the first local lesion was healed or nearly healed, when inoculated again in another part of the ear or when a second lesion was produced by turpentine, the result was again the same, the sympathetic ear has shown the graver symptoms.

We have to say again that the differences were, of course, not so great as to be striking, especially when the inflammations in both ears were intense and covered a large area. By the use of our adrenalin method they could be made apparent even then, but the differences came out best when the lesion was small. The inflammatory process on the ganglion side was then sometimes very insignificant, while that on the sympathetic side was well pronounced, and led to the formation of a pustule.

When Claude Bernard[1] discovered the relation of the sympathetic nerve to the blood vessels of the ear, he set up at the same time the claim that after removal of the superior cervical ganglion the flushing of the ear is more vigorous and the temperature higher than after simple section of the sympathetic. This was soon contradicted by Schiff,[2] Becke van der Callenfels,[3] and others, and the prevailing opinion of our time is not in agreement with that of Bernard. But assuming even that Bernard is right, and assuming further that the aggravating effect upon inflammation of the section of the sympathetic nerve or removal of the ganglion is due solely to the consecutive vasodilatation, to an increase in the blood supply, Bernard's opinion would be available as an explanation only, if the difference we have observed had been in the reverse direction, *i.e.*, if we would have found that after removal of the ganglion the inflammatory process is more flourishing; we could then have assumed that it is due to the greater vasodilatation, which occurs, according to Bernard, after this operation. But what we have found is just the reverse, namely, that after removal of the ganglion the inflammatory process is less vigorous than after section of the sympathetic nerve. If we then should hold that the relation of the nerves to inflammation is due exclusively to the vasomotor influences, we should have to assume, in order to make our observations intelligible, that while the sympathetic nerve is carrying vasoconstrictors which are normally in a tonic

[1] Claude Bernard. Leçons sur la système nerveux. Paris, 1858, ii, p. 492.
[2] Schiff. Archiv für physiologische Heilkunde, xiii, 1854, p. 523.
[3] Callenfels. Zeitschrift für rationelle Medizin, 1855, p. 157.

state, the ganglion adds vasodilating fibers, the tonus of which becomes more apparent as soon as the constrictors are eliminated. The vasodilatation after section of the sympathetic would then be due to two factors: the elimination of the constrictor tonus and the activity of the vasodilating tonus emanating from the ganglion. When, on the other hand, instead of cutting the sympathetic nerve, the ganglion is removed, the vasodilatation coming from the ganglion becomes hereby eliminated and only the dilatation due to the elimination of the constricting tonus is left — hence the reduction in the inflammatory process after the removal of the ganglion, as compared with that occurring after the section of the sympathetic nerve. However, if this assumption were true, a lesser dilatation of the ear vessels ought to be seen after the removal of the ganglion than after simple section of the sympathetic nerve. As far as we know, this has not as yet been claimed by any one. It is true that in two or three experiments quoted by Becke van der Callenfels the flushing of the ear after removal of the ganglion appeared to be less than after section of the sympathetic. Callenfels quotes them, however, only to show the incorrectness of Bernard's claim of the greater effect of the removal of the ganglion, but does not draw the conclusion that the reverse is correct.

Moreover, in some of our experiments there was a distinctly greater vasodilatation on the side on which the ganglion was removed than on the sympathetic side. Nevertheless, the inflammation was more developed on the latter side. We have already quoted above our experience with the section of the third cervical nerve which favored the course of an inflammation very little, although the consecutive dilatation of the ear vessels exceeded that following section of the sympathetic nerve, or removal of the ganglion.

We are then compelled, it seems, to assume that the relations of the sympathetic nerve and the superior cervical ganglion to the course of inflammation, which we have observed in our experiments, are due to some other nervous functions of the sympathetic nerve and the ganglion than vasoconstriction and vasodilatation.

We offer the following provisional hypothesis: Many leading physiologists now hold the view that the metabolic processes of all tissues are under the control of antagonistic nerves: the anabolic nerves which have charge of the building up of the tissues, and catabolic nerves which control the breaking down of the tissues. Gaskel, for instance, considers the vagi as the anabolic and the accelerators as the catabolic nerves of the heart. The building up of tissue makes it, of course, more resistant and the breaking down makes it more susceptible to outside destructive influences. We offer, then, the suggestion that the sympathetic nerve carries the anabolic nerve fibers, and that from the superior cervical ganglion originate catabolic nerve fibers for the tissues of the ear. When the sympathetic nerve is cut, the favorable influence of the anabolic nerves is eliminated and the unfavorable effect of the catabolic nerves remains in activity; hence the greater susceptibility to inflammation. When the ganglion is removed, the detrimental activity of the catabolic nerves is abolished, and only the absence of the anabolic nerves remains as an aggravating factor; hence the lesser susceptibility after removal of the ganglion than after cutting of the sympathetic nerves.

The statements which we make in this paper appear to us to be of such importance that, though they are based on quite a large number of experiments, we feel that much more ought to be done before a final verdict can be given. We consider, therefore, our present report only as a preliminary communication.

However, some of the facts which we have stated in this paper have been sufficiently established in another line of investigation which we have carried out lately, and which we shall mention here in a few words. These facts are that nerve fibers can originate in the superior cervical ganglion and that they can have a function different and, in fact, the reverse from that which is exercised by the fibers of the sympathetic nerve. It has always been stated that the subcutaneous injection of suprarenal extract has no effect upon the blood pressure. We have found that a subcutaneous

injection of a medium dose of the extract causes in a normal rabbit a moderate but distinct dilatation of the blood-vessels of the ears. However, when the sympathetic nerve is cut on one side, the injection caused a constriction on this side every time, while the vessels of the other side became dilated. Furthermore, subcutaneous injection of the extract has no effect upon the pupil of a normal animal. Neither has instillation into the conjunctival sac any effect. Nor has either of these methods of administration any effect upon the pupil when the sympathetic nerve is cut; but when the entire ganglion is removed, twenty-four hours after the operation a subcutaneous injection or an instillation will cause in a few minutes an ad maximum dilatation of the pupil. That means that the nerve fibers originating from the ganglion inhibit the dilatation of the pupil. Now we know that the nerve fibers within the sympathetic nerve favor the dilatation of the pupil. The nerve fibers of the ganglion and the sympathetic nerve possess, then, antagonistic activities.

We have to add that the injection of adrenalin fails to affect the pupil if only a part of the ganglion has been removed, even if this part be more than half. This is a point which has to be kept in mind in cases of failure in the adrenalin experiments as well as in the experiments on inflammation.