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SPINAL CORD.

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DIRECT ACTION OF STRYCHNINE UPON THE SPINAL CORD.

In treating, on a former occasion,* of the physiological action of strychnine, I asserted that, to produce convulsions, the poison mast be first absorbed and conveyed to the spinal cord by the bloodvessels. This being a view directly opposed to the opinion held by almost all the great physiologists of the present day, I feel called upon to support the assertion by something stronger than mere words, lest it should perhaps be regarded simply as a crude theory. I shall therefore quote the results of certain experiments which seem to prove that strychnine exerts no *direct* action upon the spinal cord.

Stilling, Valentin, Budge, Volkmann, Arnold, Ludwig, and, indeed, all recent writers upon the subject, appear to take for granted the doctrine of the direct action of strychnine on the spinal marrow. In corroboration of this view, Stilling† and others have cited numerous experiments upon frogs, where the animals were thrown into violent tetanic convulsions by the direct application of the poison to the spinal cord, even when the circulation had been interrupted by the excision of the heart. These experiments I have repeated, and the results have been in accordance with the statements of previous observers. But the results furnished by other experiments made with the view of still further elucidating the point, have led me to believe that Stilling and his followers, although correct in their observations, have yet erred in concluding that tetanus proceeds from the direct contact of strychnine with the nervous

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* The Lancet, June 7th and 14th, 1856.

† Untersuchungen über das Rückenmark und die Nerven, p. 42. 1842.

substance of the spinal cord, and in not rather imputing the action of the poison to its having been absorbed by the capillaries of the cord and vertebral canal, and conveyed with the blood to the nervous substance.

The following experiments will, I think, prove the justness of the latter supposition:—

When, instead of dropping the solution of strychnine upon the frog's spinal marrow as it lay in the vertebral canal, I first carefully isolated upon a piece of oil-silk about half an inch of the cord, immediately below the brachial enlargement,* and separated throughout a short extent its lateral halves, in order to form a sort of cup for the better reception of the poison, I found that a concentrated solution of the acetate of strychnine might be retained in the hollow of the cord, even when the heart had been left untouched, without any symptoms of tetanus supervening. The animals so treated usually survived the operation for two hours, and remained free from all symptoms of poisoning, unless some of the strychnine accidentally found its way along the side of the cord into the vertebral canal. From this I inferred that strychnine does not act directly upon the spinal cord. There being still, however, a possibility that the poison might have a direct action upon the upper portion of the spinal marrow, even although it failed in producing an effect upon the lower, where, instead of being in contact with the true nervous substance of the spinal cord, it might have only reached the roots of the sacral nerves, whose origins are very high up, (in which case the non-appearance of poisoning might have been due to the previous known fact of strychnine not acting directly upon the nerves,) I turned my attention to another reptile, the toad, (*Bufo vulgaris.*) In this animal, the cord can be isolated in the upper portion of the dorsal region without the operation inducing immediate death. The experiments upon the toad showed, equally with those made on the frog, (*Rana temporaria,*) that the direct application of the acetate of strychnine to the isolated spinal cord is not followed by tetanic convulsions, or by any other symptom of poisoning.

Convinced by a repetition of these experiments that the

* The isolation could not be accomplished higher up without cutting through the origins of the brachial nerves, which would have been speedily followed by the death of the animal.

non-appearance of tetanus was not due to any error in manipulation, I turned from cold to warm-blooded animals, in order to ascertain if the spinal marrow was here equally insensible to the direct application of strychnine. The result of the first attempt was fortunately so decisive, that it did not appear necessary to make further experiments. It was as follows:—

The vertebral canal of a young cat (a third grown) was opened in the dorsal region between the eighth and thirteenth vertebræ, and the cord carefully isolated upon oil-silk to the extent of an inch. The dura mater and arachnoid membrane were then gently removed, and, lastly, the vascular pia mater delicately detached from around the cord throughout half an inch. Having thus rendered the experiment as far as possible independent of the interference of the bloodvessels, the lateral columns of the cord were separated longitudinally, and into the little cavity thus formed was introduced a super-saturated solution of the acetate of strychnine. No symptoms of tetanus presenting themselves at the end of ten minutes, the cavity was slightly enlarged, and more of the solution added. A renewed interval of five minutes having elapsed, and there being still no symptoms of convulsions, the cavity in the cord was sponged out, and refilled with a fresh portion of strychnine. After waiting seven minutes longer (twenty-two minutes in all) without the slightest manifestation of poisoning, I felt perfectly satisfied that strychnine, when directly applied to the nerve-substance of the spinal marrow, does not possess the power imputed to it of producing tetanus. But still further to satisfy myself that the non-appearance of convulsions was not due to any lack of poisonous qualities in the solution employed, I dissected the skin from one of the femoral veins, and brought a third of the quantity of the solution which was applied to the cord into contact with the external surface of the bloodvessel. In one minute and three-quarters the animal became violently tetanic *throughout the whole body*. The cord was divided at the exposed part without the tetanus disappearing from the lower extremities. This shows that the effect of the poison is not limited to any particular part of the spinal marrow.

A more conclusive result than the above can scarcely, I think, be desired, to prove the inability of strychnine to cause tetanus by a direct action upon the spinal cord. Had the membranes of the cord and their vessels not been removed be-

fore the application of the poison, tetanus would most probably have supervened, just as happened in the experiments upon the frogs, when the cord was not carefully isolated. The occasional occurrence of tetanus in frogs after excision of the heart is easily accounted for, on the supposition that the poison, when applied to the cord, finds its way into the neighbouring capillaries, before their circulation has entirely ceased, and is conveyed with the blood to the nerve substance. This supposition is warranted, on the ground that the circulation in the web of the frog's foot is distinctly visible for some time after excision of the heart, and strengthened by the absence of any data disproving the probability of the circulation in other parts of the body being to a similar degree independent of the cardiac impulse. The occasional negative results in the one case cannot therefore be looked upon as lessening the value of the positive effects in the other, although the latter experiments are by far the less numerous. The following is another experiment, which not only confirms the foregoing, but shows the progressive advance of the effects of strychnine on the cord, while at the same time it illustrates in a striking manner the independent action of different parts of the spinal nerve centres.

The vertebral canal of a snake (*Coluber natrix*), three feet long, was opened at the union of the upper and middle third; the cord was next isolated on oil-silk, and an inch of the pia mater, with its vessels, carefully removed. A few drops of the supra-saturated solution of strychnine were kept during thirteen minutes in contact with the exposed nerve substance, without producing the least symptom of tetanus. The oil-silk was then removed, and the cord allowed to slip back into the vertebral canal, and some of the solution of the poison was introduced into an opening made in the thorax. The animal, which had been previously breathing very slowly, began in a short time to respire more rapidly, and in six minutes symptoms of impending tetanus became apparent. The spasms first became visible in the muscles about the neck, and very gradually descended along the vertebral column, till, in about two minutes they had reached the tail. This gradual progress of tetanus is beautifully apparent in a long-bodied animal like a snake, and the distinctness of the advance is also better marked, probably on account of the slow circulation of the blood. The spinal cord was afterwards divided at the exposed part, and

the tetanus in the upper part was seen to be independent of that in the lower, and *vice versâ*. The mutual independence of the different portions of the cord was not so striking until after the animal had become somewhat exhausted. When the intervals between the spasms became considerable, it was interesting to see how irritation applied to the tail caused gradual tetanus up to the point of section, but not beyond it. When, on the other hand, irritation was applied to the head, the tetanus gradually travelled as far down as the point of section, and for about two inches beyond, in the muscles, doubtless, which received their nerves from the lower part of the upper portion of the cord. At first, the tetanic movement in these muscles was sufficiently strong to excite spasm in the lower portion of the body; but afterwards, as the animal became more exhausted, and the spasms less violent, while the stimulus required to call them into play was greater, the tetanus could not be communicated from the muscles in the lower to the upper, nor from the upper to the lower, portion of the vertebral column. This clearly proves that the indirect action of strychnine is not limited to one particular part of the cord.

It appears strange that the poison, when directly applied to the spinal cord, did not affect the nerve substance through entering it, either by imbibition or deosmose. Can it be possible that poisons deosmotically absorbed are not assimilated by the nervous system? or do they first require to undergo a change in the blood before they can act? That strychnine should produce convulsions when carried to the spinal cord by the bloodvessels, and not when directly applied, is certainly very remarkable. The solvent in each case is the same, the liquid part of the blood being nothing more or less than water, and the bloodvessels cannot bring the poison into more intimate connexion with the nerve-tubes than the hand can; for the ultimate capillaries do not enter the nerve-tubes, but only ramify on their exterior. If, therefore, the poison really acts upon the contents of the nerve-tubes, it must, to reach their interior, first pass by deosmose through the external sheath; and deosmose being a purely physical process, it matters not how, or by what means, the substance is brought into contact with the membranous tube of the nerve; for once there, its after-progress is in all cases identical. Now, as we have

brought strychnine into the most favourable circumstances for the development of its action upon nerve substance, and no result has followed, we are forced to conclude that strychnine has *no direct* chemical or physical action on nerve matter. Seeing that the poison acts when conveyed by the blood-vessels, we must try and discover whether or not it is transformed in the blood into a more active poison, or if, though not itself transformed, it yet possesses the power of so modifying the organic constituents of the blood, as to render them not only useless for the purpose of nutrition, but even pernicious. Chemistry has as yet failed to reveal whether or not strychnine is decomposed and transformed in the blood into another substance more baneful than itself; but it has shown,* that the poison possesses the property of so modifying the organic constituents of the blood as to render them incapable of absorbing oxygen, and exhaling carbonic acid, and thus becoming fitted for the purpose of nutrition. It is well known, that "the continual afflux of scarlet blood is a condition very important to the normal molecular constitution of the nervous centres. This proposition especially holds good with mammals and birds; but is less strictly applicable to reptiles and fishes, in whom the interchange of the gases is less active."† When the oxidized materials required as nourishment by the nervous system are either deficient in quantity, or impaired in quality; disordered function of the nerves is the immediate result. We have a most striking example of the former condition in cases of hæmorrhage, where an insufficient supply of the oxidized substances is not unfrequently followed by convulsions; the latter is exemplified in cases where oxygen is prevented from entering the blood, and consequently the organic substances fail to become oxidized and fitted for their peculiar office. Lastly, the same thing occurs when even both the oxygen and the organic substances are present, but where the oxidizing process is either partially or totally arrested by the presence of a foreign substance possessing the property of hindering the constituents of the blood from combining with oxygen. Derangement in the function performed by the molecules of the nervous system

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* The Lancet, June 7th and 14th, 1856.
† Valentin's Physiology, translated by Brinton.

occurs just as surely in the latter example as when either the oxygen alone, as in the second instance, or both the oxygen and the oxidizable materials, as in the first case, are wanting. Strychnine, I believe, from the results of the cited experiments, acts in the third of the three ways—that is to say, it has no *immediate* effect upon the nervous system, but acts indirectly through the power it possesses over the functions of the organic constituents of the blood. Many other poisons, I doubt not, exert their influence in a similar manner; for I have found, that hydrocyanic acid, chloroform, nicotine, alcohol, ether, morphine, and several other narcotics, have the same power of destroying the property possessed by the organic constituents of the blood of absorbing oxygen and exhaling carbonic acid.

A more particular study of the effects of different substances on the blood may yet not only furnish a clue to the actions of poisons in particular, but afford a direct explanation of the physiological action of remedies in general; and the more speedily our knowledge in that direction advances, the more rapidly will medicine be raised to its proper position amongst the inductive sciences.