On the Ultimate Distribution and Function of very Fine Nerve-fibres.

We desire to call the attention of our readers to some important observations and conclusions by Dr. Beale, with reference to the ultimate distribution of nerve-fibres in various tissues recently arrived at from direct observation. Most physiologists have endeavoured to ascertain the functions of nerve-fibres, and the ultimate destination of certain branches, by experiments upon living animals; but Dr. Beale has for many years past devoted himself to the study of this subject in a very different manner. He has sought to establish many general propositions by direct anatomical observation, and has devised new methods for preparing the tissues, and for examining the thinnest possible sections under very high powers varying from 1800 to 3000 diameters.

Perhaps one of the most important and interesting of his conclusions is the demonstration of the existence of nerve-fibres, which probably bear to the vaso-motor nerves distributed to the coats of the small arteries the same relation that afferent or excitor fibres bear to efferent or motor-spinal nerves. The paper in which this inference is arrived at is published in the last number of the 'Archives of Medicine' ("Of very fine Nerve-fibres ramifying in certain Fibrous Tissues," &c. By Lionel S. Beale.)

The author states that researches upon which he has been long engaged have convinced him that the ultimate nerve-fibres in all tissues are much finer and more abundantly distributed than is generally supposed, and that the active terminal branches of many nerves, where they ramify abundantly in tissues, have been included by many authors in the so-called connective tissue. The terminal branches of all nerve-fibres are so very fine as not to be visible by magnifying powers in ordinary use—many in the frog being less than the 1-100,000th of an inch in diameter. In man and mammalia they are wider than this, but appear as faint granular and too often scarcely visible bands. In the frog, although so fine, they are much more distinct, and being firmer, are much more easily studied than in mammalia.

All peripheral nerve-fibres are connected with nuclei (germinal matter), but these nuclei are separated by much greater distances in the nerves distributed to some tissues than others. The nuclei are for the most part oval, but in some cases they are triangular. These bodies, which exist in great
number in many sensitive surfaces, as, for example, just beneath the epithelium of the mucous membrane of the fauces, have been and are still considered by many authorities to be connective tissue-corpuscles. Not a few observers in this country as well as on the continent, following Virchow and his school, consider that they communicate with each other by tubes, and thus form a new canalicul system for conveying nutrient juices.*

The so-called nuclei are never terminal, but a fibre always passes from each nucleus in two or three different directions. Not only nuclei, but nerve-fibres have by many observers been included under the head of connective tissue. Nor, indeed, can these fine terminal nerve-fibres be demonstrated in fibrous tissues in which they exist in great number by the ordinary processes employed in demonstration. They can only be seen in exceedingly thin sections, and with the use of the highest powers. Not only are nerve-fibres present in certain forms of connective tissue, but there are many fibrous tissues destitute of vessels to which nerves are distributed. In the cornea, in the fibrous tissue about the pericardium, the pericardium itself, and the bundles of fibrous tissue in connection with the vessels and various organs in the abdominal cavity of the frog, nerve-fibres are very numerous.

Dr. Beale has succeeded in demonstrating nerve-fibres in connection with the vessels in so many tissues of the frog, and of certain mammalia, that he is strongly inclined to the opinion that in vertebrate animals nerve fibres exist wherever vessels are present. These remarks apply not only to the smallest arteries and veins, but also to the capillaries.† Since the capillaries are devoid of muscular fibre-cells, and do not possess contractile power; it is probable that these fine nerve-fibres associated with the capillary vessels are afferent fibres.

In the papilla of the frog's tongue, for example, besides the bundle of sensitive nerve-fibres passing up the central part of the papillae, there are very fine nerve fibres distributed to the vessels, and some fine fibres in the connective tissue external to the vessels. Similar fibres exist in the small papilla, to which neither vessels nor dark-bordered nerve-fibres are distributed. The nuclei connected with these fibres are about the 1-300th of an inch or more apart. Now these fibres are not ordinary fibres of connective tissue, for the author traced them into undoubted nerve-fibres. More-

* See a paper on the "Distribution of the Nerve-fibres to the Mucous Membrane of the Human Epiglottis." 'Archives,' vol. iii, p. 249.
† See figs. 5 and 9, in plate xxiii, 'Phil. Trans.,' 1860.
over the fibres and nuclei are much more abundant in connection with some capillaries than others. They are very numerous upon the smallest vessels of the ciliary processes of the eye (ox), as well as upon those which are provided with muscular fibre-cells, and many are to be found in the connective tissue upon the free border of the finest vessels. He considers that these branches are in part afferent or excitor and partly efferent or motor nerves of the vessels.

The fact of the presence of undoubted nerve-fibres in tissues destitute of vessels, and deriving their nutriment from the plasma permeating vessels situated perhaps at some distance, is another strong argument in favour of the existence of afferent nerves, bearing to the vaso-motor branches the same relation as the excitor fibres bear to the spinal motor nerves. Such fine nerve-fibres are distributed to the cornea of all animals, and very fine fibres ramify upon different planes in the substance of the proper corneal tissue. From their distribution we are justified in assuming that these fibres are not ordinary sensitive fibres, but are nevertheless concerned in transmitting impressions of some sort from periphery towards nervous centres, while in certain morbid states they are probably instrumental in transmitting impressions which produce the sensation of pain. Ordinarily, these afferent and efferent fibres preside over the nutritive process, and it is easy to conceive how any alteration in the amount of nutrition passing to the tissue must influence, through the nuclei and afferent fibres, the ganglia from which the vaso-motor branches take their rise. Thus the calibre of the minute arteries may be altered by the slightest modification in the supply of pabulum to the tissues outside capillary vessels dependent upon any mechanical or chemical alteration in the tissue whereby the activity of the nutritive changes becomes altered. Normally, the balance between the quantity of pabulum taken up by the tissue and that escaping from the capillaries would be maintained through these afferent and efferent fibres, and it is easy to understand how any derangement of afferent fibres, nerve-centre, or efferent branches would disturb the nutritive process.

Dr. Beale thinks that the rapidity of growth of tissues is determined solely by the supply of pabulum, and this supply is regulated and equalised by a special system of nerves which is, however, connected with the cerebro-spinal system, and may influence it, or be influenced by it. He has been led to the conclusion that nerves invariably form complete circuits, and that there are afferent or excitor nerves and efferent or motor nerves presiding over the nutritive processes, which may act independently of the cerebro-spinal nerves or centres.
It might be asked, if the author holds that there is a complete circuit in the case of the afferent and another in that of the efferent fibres distributed respectively to the tissues and small arteries, or if the afferent and efferent fibres form part of the same circuit, in which case an impression might be transmitted to, and a motor impulse start from, the same ganglion-cell; but he postpones the consideration of this part of the question.

The fine nucleated fibres distributed in the neighbourhood of capillary vessels, and to tissues which do not receive a vascular supply at all, form, in the tissues of the frog generally, fine trunks consisting of several very fine fibres, and these unite to form larger trunks, which, as a general rule, are accompanied by one or more dark-bordered fibres, but in the bladder, in the heart, and also in the mesentery, large trunks exist which are composed entirely of these very fine fibres, and at certain points plexuses are formed. In the cornea the individual fibres are not so distinct, nor are the fibres so decidedly separated from each other as in the drawing accompanying the author's paper. Many seem to be in course of splitting, an appearance more like that seen in the sympathetic branches of birds and mammalia, where the fibres in a trunk appear to be connected together forming bands.*

It is quite certain, therefore, that the fine fibres above described are independent of the dark-bordered fibres. But, it will be asked, are all the fine fibres in the trunks—for example, in those represented in the figure—afferent fibres? In a trunk passing from the cornea, doubtless, all are of this nature, but Dr. Beale has seen many such fibres passing amongst the muscular fibre-cells of the bladder, and also to the contractile coats of the small arteries, so that at least in this case it is probable that some of the fibres entering into the formation of the plexus figured, are afferent and others efferent. There are no characters by which one class of fibres can be distinguished from the other. Amongst the nerves forming the large bundle which supplies a limb, some bundles of fine fibres, which probably belong to the same class, are to be found, but the author has never seen large bundles of very fine fibres like those in the bladder and mesentery, in the voluntary muscles. Such bundles, however, do exist in connection with the heart.

The bundles of fine fibres at their peripheral distribution form plexuses and networks. The author has never seen any termination in any case. The fine nerve-fibres distributed to

* The arrangement of the nerve-fibres in the cornea of various animals is fully described in an elaborate paper by Dr. Ciaccio, of Naples, in No. XI of this Journal.
small arteries and veins also form networks, and very fine fibres can be traced ramifying amongst the muscular fibre-cells on different planes. Kölliker suggests that such fibres ramifying on the outer part of small arteries and veins distributed to voluntary muscle, and on fine vessels on the arterial side of capillaries destitute of a muscular coat, are of the sentient kind. The latter fibres are probably afferent or sentient, but Kölliker’s remarks on this question are very undecided, and he does not profess to have studied the subject carefully. It is very hard to conceive what purpose could be served by the free distribution of sentient fibres upon and in the substance of the muscular coat of an artery. Some of the fibres running with vessels distributed to voluntary muscles are certainly motor branches, for, after running parallel with vessels for some distance, they diverge and are distributed to the muscular fibres. Kölliker considers certain nerves for the most part on the surface of the muscle as sentient fibres, but he adduces no facts which show that this view is correct.*

It is important to state definitely that the bundles of very fine fibres, distributed to the frog’s bladder and in other tissues, are not visible in specimens prepared in the ordinary manner and examined in water or weak glycerine. In the bladder from which the specimen figured in No. xiii of the ‘Archives,’ plate I, was taken, there was no appearance whatever of these very fine fibres when the specimen was first prepared, but after the prolonged action of dilute acetic acid, a great number of bundles, many of which were as much as \( \frac{1}{1000} \) of an inch in diameter, and very many finer compound fibres, made their appearance. The vast majority of these bundles of fine fibres were not only destitute of true dark-bordered fibres, but of any one fibre more than the \( \frac{1}{1000} \) of an inch in diameter.

It is scarcely probable that any observer will doubt that the fibres figured are true nerve-fibres. Their mode of arrangement, the manner in which the trunks branch and ramify amongst the muscular fibre-cells, the character of the nuclei connected with the fibres, and the change produced in them by the action of acetic acid, show them to be nerve-fibres. The author has already proved that very fine fibres invariably form the continuation of dark-bordered fibres, and that fibres, as fine as some of the finest of these, ramify in the same sheath with the dark-bordered fibre, even in the case of the dark-bordered fibres distributed to voluntary muscle (‘Phil. Trans.’ 1862).

But that these very fine fibres in the bladder, which the author

believes have now been demonstrated for the first time in his specimens, are true nerve-fibres, is placed beyond all question by the fact of their being continuous with ganglion-cells. He has seen several ganglion-cells from which such fine fibres alone (every one being less than the \( \frac{1}{1000} \) th of an inch) proceed. From different parts of one ganglion-cell sometimes six or seven or more very fine fibres may be traced, while not a single dark-bordered fibre comes near to the cell or bundle of fibres under consideration.

Dr. Beale fears that the accuracy of these observations will be questioned by many fellow-workers in Germany, and more especially by those of the Dorpat school, and the difficulty of preparing the specimens is so great, that his conclusions are scarcely likely to be confirmed for some time to come. The appearances are, however, so distinct that he has been able to demonstrate the most important points to the students of his physiological class. As the specimens will keep for a considerable length of time, they can be examined by any one desirous of seeing them.

It would seem then that in the frog these fine fibres are distributed to capillary vessels, to fibrous tissues devoid of capillaries, to the tongue and palate, to the unstriped muscle of the bladder, pharynx, gullet, stomach, and intestines, to the unstriped muscle distributed to the coats of arteries, and to the muscular fibres of the heart, and probably they are to be made out in many other tissues than those above named.

The author is unable to enter fully into the question of the distribution of the different classes of nerve-fibres to the various tissues of the frog’s bladder, nor can he discuss satisfactorily their several offices; but on these important questions he offers the following remarks:

With reference to the kind of nerve-fibres, it is certain that—

1. Dark-bordered fibres are distributed to the bladder of the frog, and that the very fine terminal fibres, resulting from the subdivision of these, are freely distributed with the ultimate branches of other nerve-fibres.

2. That there are fine fibres running in the same sheath with the dark-bordered nerve-fibres, as he has described in the case of dark-bordered fibres distributed exclusively to voluntary muscle. See ‘Archives,’ vol. iii, and ‘Phil. Trans.,’ 1862 (just published).

3. That there are very many bundles of very fine fibres which sometimes run with dark-bordered fibres, and sometimes also form special trunks destitute of dark-bordered fibres.
4. That many of these very fine fibres are directly connected with ganglion-cells upon the outer surface of the bladder.

5. It is certain that many ganglion-cells have no dark-bordered fibres whatever in connection with them; but the author has demonstrated that some ganglion-cells are connected with dark-bordered fibres.

In considering the function of this most elaborate and beautiful nervous arrangement, it must be borne in mind—

1. That the muscular fibre-cells and vessels of the bladder are freely supplied with nerves.

2. That nerves ramify upon the surface of the mucous membrane.

3. That the bladder contracts when the nerve-fibres, distributed to the skin of the animal, are irritated, and its contraction seems also to be under the influence of the will of the animal.

The author thinks it probable that the nerves, distributed to the muscular fibre-cells of the bladder, are branches of the same trunks as those distributed to the vessels, and are connected with the ganglion-cells. As already stated, the numerous nerve-fibres in the cornea and other fibrous tissues are purely afferent, and through the centre into which they are implanted, they influence the motor fibres distributed to the nearest vessels. In the bladder there are afferent fibres corresponding to those in the cornea, and efferent or motor fibres distributed to the vessels, and also to the muscular fibre-cells.

Whether the dark-bordered fibres are purely sensitive, or whether some spinal motor fibres thus pass directly to the bladder, the author is unable to say. It is probable that the fine fibres running with the dark-bordered fibres of the bladder correspond to those in the same sheath with purely motor or sensitive dark-bordered fibres. It is, however, not possible to discuss this question advantageously until many points in connection with the general distribution and function of the different classes of nerve-fibres are cleared up.

The most important of the many conclusions arrived at from this investigation is the demonstration of numerous fine nerve-fibres around capillary vessels, and the inference that there are afferent fibres corresponding to and influencing the efferent or vaso-motor branches distributed to the small arteries. The inference that all small arteries and the fibres of unstriped as well as striped muscular fibres are freely supplied with nerve-fibres, is also most important.