X. *On the Development of Striated Muscular Fibre in Mammalia.* By WILLIAM S. SAVORY, *Tutor and Demonstrator of Anatomy of St. Bartholomew's Hospital Medical College.* *Presented by* JAMES PAGET, *F.R.S.*

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THE descriptions which have been hitherto given of the development of muscular fibre may be included in a few words. Little or nothing of importance has been discovered beyond the original researches of VALENTIN and SCHWANN. Concerning these SCHWANN says, "In order briefly to recapitulate our researches into the generation of muscle, the process may be thus stated. Round cells, furnished with a flat nucleus, are first present, the primary cells of muscle. These arrange themselves close together in a linear series; the cells thus arranged in rows coalesce with one another at their points of contact; the septa by which the different cell-cavities are separated then become absorbed, and thus a hollow cylinder closed at its extremities, the secondary cell of muscle, is formed, within which the nuclei of the original cells, from which the secondary cell has been formed, are contained, generally lying near together on its wall. This secondary cell then passes through all the stages of a simple one. It expands throughout its entire length, whereby the nuclei are further removed from one another, and sometimes even become elongated in the same direction. A deposit of a peculiar substance, the proper muscular substance, takes place at the same time upon the inner surface of the cylinder, by which the cavity is at first narrowed and at length completely filled. The cell-nuclei lie external to this substance, between it and the cell-membrane of the secondary cell.

"The transverse striæ in the voluntary muscles become more manifest, and the deposited substance is more distinctly seen to be composed of longitudinal fibres, as the fœtus advances in age. The nuclei are gradually absorbed. The cell-membrane of the secondary muscle-cell remains persistent throughout life, so that each primitive muscular fasciculus is always to be regarded as a cell*."

This account has been generally accepted by those who have since written on the subject. Dr. MARTIN BARRY, however, must be excepted. He entertains a very different view of the origin of muscular fibre, and declares that the cells, by the coalescence of which the tubes are at first formed, are really blood-cells. He says that the blood-corpuscles apply themselves to one another in a linear series. By degrees

* Microscopical Researches into the Accordance in the Structure and Growth of Animals and Plants, translated from the German of Dr. TH. SCHWANN, by H. SMITH, 1847, p. 141.

the appearance of a cylinder is produced, which becomes more perfect as the partitions between the cells disappear*.

These observations have not been confirmed. M. LEBERT has more recently studied the development of striated muscular fibre chiefly in the heart of the chick†. The following is a short abstract of his peculiar description of the process. "The rhythmical contractions of this organ become very manifest and regular towards the thirty-sixth hour of incubation; nevertheless, it is at this time composed of nothing else than organo-plastic globules or elementary cells imbedded in a granular blastema. Between the fourth and fifth days of incubation are seen in the midst of the mass of globular particles certain elongated subcylindrical bodies, sometimes grouped together in a reticular manner; these bodies being the first rudiments of the muscular fibres, not merely in the heart but also in the other striated muscles, are designated by M. LEBERT 'myogenic cells.' Between the seventh and eighth days the 'organo-plastic globules' undergo a considerable diminution, and the muscular substance presents a more complete development. A longitudinal striation shows itself in the contents of the cylinders, which seems partly due to the grouping of the granular particles of which these contents consist; the transverse striations do not show themselves until some time afterwards.....The organo-plastic globules which at first separated the primitive cylinders gradually disappear; the cylinders approach one another, and before the end of embryonic life they are found to be grouped into fasciculi‡."

When many months since I began to study the development of muscular fibre, it was with the hope of being able to add something to what appeared to be a very imperfect explanation of the process. The results of these investigations I have endeavoured to communicate in this paper. It may be as well to state at once that the conclusions I have arrived at are, for the most part and in all important points, completely at variance with the account which is generally believed to be the true one. I can therefore only meet the doubts with which I must expect the following statements to be received, with the assurance that they have not been hastily or carelessly advanced, and by an appeal to the verdict of future inquiry.

These observations have been made for the most part upon fœtal pigs, but they have been confirmed by repeated examinations of fœtal calves, lambs, goats, rabbits, rats, and human embryos.

In very small embryos, specimens of muscular tissue for microscopical examination are most conveniently obtained from the dorsal region. If therefore a portion

* Philosophical Transactions, 1840, 1841. † Annales des Sciences Nat. Juin 1849, Mars 1850.

‡ Principles of Human Physiology, by Dr. CARPENTER, 1853, pp. 305, 306. I have recently read a paper by Dr. HOLST, giving a short account of some observations by REICHERT and himself on the development of muscular fibre. From some of the engravings which accompany the paper, he has probably seen, although I think misinterpreted, the condition of the fibre in what I have described as the second and third stages of development.

of the tissue immediately beneath the surface by the side of the vertebral column of a fœtal pig, from 1 to 2 inches in length, be examined, there will be seen, besides blood-corpuscles in various stages of development, nucleated cells and free nuclei, or cytoblasts scattered through a clear and structureless blastema in great abundance. These cytoblasts vary in shape and size; the smaller ones, which are by far the most numerous, being generally round, and the larger ones more or less oval. Their outline is distinct and well-defined, and one or two nucleoli may be seen in their interior as small, bright, highly-refracting spots; the rest of their substance is either uniformly nebulous or faintly granular, Plate X. fig. 1.

The first stage in the development of striated muscular fibre consists in the aggregation and adhesion of these cytoblasts, and their investment by blastema so as to form elongated masses. In these clusters the nuclei are not at first generally arranged in a single series; but two, three, or even more occasionally lie side by side in apparent disorder. Almost, if not quite as soon as these cytoblasts are thus aggregated into these long masses, they become invested by the blastema, and this substance at the same time appears to be considerably condensed, so that the outlines of the nuclei become almost or completely obscured. The fibre thus appears to be irregularly cylindrical or somewhat flattened. It is so opake that its interior is no longer to be plainly discerned, and its surface is rough and uneven. The appearance of the muscular fibres at this early period of their development is represented in Plate X. fig. 2. It often happens, that here and there, where a nucleus has not become completely invested by condensed blastema, a portion of its well-defined dark margin may be observed standing out in the circumference of the mass. These early fibres measure about $\frac{1}{3000}$th of an inch in diameter. It is almost impossible to estimate their length, as they are so readily broken in being prepared for the microscope; hence the lengths of the masses presented to view vary exceedingly. It has been said that the cytoblasts become invested by a layer of apparently condensed blastema, immediately after or at the same time that they aggregate and adhere together. In some cases, before the nuclei come into contact, this external investment may already be discerned forming around them, giving to them occasionally the appearance, if not very carefully examined, of nucleated cells, and this perhaps may have led to the original description of VALENTIN. But this investment of the nuclei previously to their aggregation is not common: as a very general rule, the nuclei meet each other free as cytoblasts.

In order to obtain a fair view of these early fibres, a portion of tissue should be selected from a perfectly fresh specimen, for if the embryo be kept longer than a few hours, the masses break up and disappear; and this disintegration is much accelerated by placing them in water, for the investing blastema appears to be readily dissolved and the nuclei separate. Indeed the tissue is so moist at this period, that, when prepared for the microscope, the addition of water is scarcely necessary. The action of the weaker acids also rapidly dissolves the investing blastema and sets the cytoblasts free. However, when the fœtal tissue is treated with water, there is a period just before the fibres break up when they become much more transparent, and the nuclei may be seen in their interior clustered together irregularly, and in absolute contact; this fact, that the nuclei are in actual contact, is a most important one, for it proves very conclusively that they do not occupy the interior of cells. I have often earnestly sought for, but never yet detected, the appearance so generally figured in books of a muscular fibre as a string of nucleated cells; on the contrary, the nuclei, when they approach each other, are free cytoblasts, and they may be clearly seen to be in absolute contact.

The nucleated cells which are seen in the blastema are no more concerned in the formation of muscular fibre than are the blood-cells. With regard to their purpose, it is to be observed that they are chiefly found in the layer of tissue investing the embryo, and if this exterior layer be carefully scraped off from the back of the embryo, and a portion of tissue be examined below the surface, nucleated cells, as compared with free cytoblasts, will be extremely rare.

These nuclei, thus aggregated and invested, next assume a much more regular position. They fall into a single row with remarkable regularity, and the surrounding substance at the same time grows clear and more transparent, and is arranged in the form of two bands bordering the fibre and bounding the extremities of the nuclei, so that they become distinctly visible, and the fibre at this stage presents the appearance represented in Plate X. fig. 3. The nuclei have now become decidedly oval and very closely packed together, side by side, so closely indeed that they appear as if compressed. Thus they form a single row in the centre of the fibre with their long axes lying transversely, and their extremities bounded on either side by a thin, clear pellucid border of apparently homogeneous substance. No structure can be discerned between the nuclei; they lie in close contact, except towards their extremities, and even appear as if pressed together. It is here to be remarked that this position of the nuclei is a strong additional argument against the supposition that they are or were contained in cells. If so, what explanation can be offered to account for the present arrangement? It occasionally happens, especially towards the extremities of a fibre, that some irregularity in the position of the nuclei may be discerned. They have not fallen into their places, but still remain as an irregular cluster, dilating the fibre by a separation of the lateral bands to a corresponding extent, Plate X. fig. 4. More frequently, in the course of a fibre an occasional nucleus is seen, which instead of lying transversely is placed obliquely.

The bands of tissue forming the borders of the fibre and bounding the extremities of the nuclei, at first thin and pellucid, soon increase in thickness by the addition of surrounding blastema to their external surface. They increase in breadth, and this increase is due to the addition of fresh material upon their exterior, and not to a deposit upon their inner surface, for the extremities of the nuclei are not encroached upon, and the outline of the fibre, which is at first even and well-defined, soon becomes rough and irregular, obviously from the addition of fresh material, Plate VII. fig. 5. Sometimes these bands appear defective or broken at intervals, or altogether wanting for some little distance. This no doubt is the result of the manipulation required for the microscope. I have occasionally seen fibres, which, either from the same cause or from some defect in their formation, possessed only one lateral band; the extremities of the nuclei being invested on one side only.

If a portion of muscular tissue be examined which has been roughly dissected, or which has been taken from a fœtus previously kept for a few hours in water, fibres will often be seen which are more or less broken up. Some will be found with the lateral bands separated from or partly stripped off the nuclei and variously twisted. The nuclei themselves will be wanting in many places, or considerably disturbed. These and other derangements, the result of violence, assist to explain the construction of the fibres at this period of their development.

It is interesting to compare the arrangement of the nuclei in this stage of development of muscular fibre in Mammalia with the position of the nuclei in the fully-developed fibre of some of the lower classes. Mr. BOWMAN, in his paper in the Philosophical Transactions, has noticed that in the muscular fibre of many insects and of some reptiles, the corpuscles are disposed along the central axis of the fibre with remarkable regularity, and in some instances, as in the *Tipula* (Harry Longlegs), which he figures, the corpuscles are thus arranged with their long axis transversely. (See fig. 6 *a*, and compare it with figs. 3 and 7, Plate X.) The central row of nuclei is well shown in the fibres of the leg of the common Blue Bottle Fly (*Musca vomitoria*) after the addition of a weak acid. In insects, the nuclei are very often visible in the fibre without any previous preparation. I have sometimes distinctly observed them in fibres from the leg of the *Tipula*, and in many other examples.

The fibres next increase in length and the nuclei separate; the nuclei remain no longer in close contact; small intervals appear between them, and as they have more space they increase in width and become more nearly circular. The spaces between the nuclei rapidly widen, until at last they lie at a very considerable distance apart. At the same time the fibre decreases very considerably in diameter, and the cause of this is sufficiently obvious. As the nuclei part from each other and as the spaces between them increase, the bands which they separated fall in,—approach each other and ultimately coalesce*. This fact is placed beyond doubt by the examination of some fibres in which these changes are in progress, Plate X. fig. 8. At one extremity of a fibre may be seen the oval nuclei packed closely together, and bordered at their extremities by the substance of the fibre; further on they may be seen separating and becoming rounder, the bands at the same time are beginning to approxi-

* For example, in a specimen of muscular tissue from a fœtal pig $3\frac{1}{2}$ inches long three fibres were measured. In the first the nuclei were almost in contact, and the width of the fibre was $\frac{1}{1800}$th of an inch; in the second the nuclei were $\frac{1}{1500}$th of an inch apart, and the width of the fibre was $\frac{1}{2000}$; in the third the nuclei were $\frac{1}{1000}$th of an inch apart, and the width of the fibre was $\frac{1}{3000}$.

mate, so that the fibre is at this part much narrower; and still further on the nuclei are more completely separated; they are again oval, with their long axis now in the direction of the fibre; the borders have united, and the diameter of the fibre is consequently very considerably diminished. This falling-in of the lateral bands, as the nuclei separate, and their ultimate coalescence, affords evidence for believing, that when they were separated, there could have existed but very little intermediate substance between them amongst the nuclei.

As a general rule, the changes just described proceed uniformly throughout the entire fibre. But in most specimens some fibres will be found in which development has advanced more rapidly towards one extremity than at the other, and these serve admirably to illustrate the changes which occur.

Soon after the nuclei have separated some of them begin to decay. They increase in size; their outline becomes indistinct; a bright border appears immediately within their margin; their contents become decidedly granular; their outline is broken and interrupted; and presently an irregular cluster of granules is all that remains, and these soon disappear. With regard to these groups of granules, however, it is worthy of remark, that as the fibres continue to increase in length, and the remaining nuclei are still further separated, they are extended longitudinally and the granules become more scattered. It sometimes happens that an irregularity may be observed in the separation of the nuclei. Here and there two or more occasionally remain in contact, as if adherent.

This lengthening of the fibre, and consequent separation of the nuclei, is due to an increase of material, and not to a stretching of the fibre*, for the lateral bands, although they grow firmer, do not decrease in width as they approach each other; they preserve their size. Occasionally, indeed, they appear a little narrower, as if stretched, but this is rare, and is no doubt due to manipulation.

The fact is, as these lateral bands fall in and coalesce, their breadth undergoes no apparent alteration. They remain separated for a time at those parts of the fibre where the nuclei are, but they ultimately join, and the nuclei lie imbedded between them.

The changes described above are generally most obviously marked, and are therefore more readily traced in those fibres which are formed at the earliest period. In those of later growth, the lengthening of the fibres does not commence so early, or proceed so rapidly, and is therefore not so obvious, for the nuclei usually decay before they are separated to any extent. Indeed, in some of the fibres this separation of the majority of the nuclei seems scarcely to occur at all; while but a small interval exists between them, and while their oval form is still preserved, most of them perish in their places, with their long axis still lying transversely; and the position they occupied is marked for a time by clusters of granules extended transversely at frequent intervals along the course of the fibre. (See Plate X. fig. 9*a* & *c*.)

In these fibres, however, the same essential changes occur. They subsequently

* As SCHWANN described it, Untersuchungen, &c.

lengthen and decrease in diameter. The only difference is, that owing to the later period at which this occurs, the majority of the nuclei perish previously, and the distinction between the lateral bands and the central portion of the fibre grows obscure; hence the process is not so obvious, because the separation of the nuclei, when they remain, is a most remarkable feature. But the extension of the clusters of granules longitudinally, the wide separation of the granules from one another, and the remarkable decrease in the diameter of the fibre, are not to be mistaken. (See Plates X. & XI. fig. 9 *d*, *e*, *f* & *g*.)

It is to be observed, that the longer the lengthening of the fibres is delayed, the thicker do the lateral bands become. The addition of fresh material from without, which, when the fibre is elongating, is consumed in maintaining the bands at their original width, now adds very much to their breadth, so that these fibres often attain a very considerable diameter. On the contrary, in those fibres in which the lengthening occurs at an earlier period and is more rapidly accomplished, the lateral bands being as yet very thin, the fibre thus formed is very narrow. Indeed, they are sometimes narrower in the intervals between the nuclei than are the nuclei themselves; so that, where these are situated, the fibre is necessarily bulged to contain them. This appearance may, however, be caused by stretching the fibre while preparing it for the microscope.

The striæ first become visible at this period. A faint indication of their appearance may be sometimes observed in the lateral bands, almost as soon as these are fully formed; and as these bands approximate, the striæ become more plainly marked, and often contrast strongly with the intermediate and apparently homogeneous central portion of the fibre. In any case they can always be readily detected at the time when the distinction between the lateral bands and axis disappears.

The striæ are first discerned immediately within the margin of the fibre, and gradually pass towards the centre. When they first appear, generally the longitudinal but sometimes the transverse lines are most plainly marked. A few streaks are usually seen here and there along different portions of the fibre, and these gradually extend and blend together, giving to the fibre for a time an irregular streaked appearance, until at length they are seen throughout its entire substance, but for a long time they remain most prominently marked towards the margins. When first formed they are certainly much smaller than at a subsequent period. The striæ are much finer, and many more exist in a given space than at a more advanced period of development.

When this stage is completed, the fibre presents a very uniform appearance throughout its entire length, Plate XI. fig. 10. It appears as a narrow flattened band*. The nuclei that remain are seen at tolerably regular intervals in the substance of the

* A form which in insects is often permanently maintained.—Bowman, Phil. Trans.

It is impossible not to remark the close similarity between the appearance of striated muscular fibre at this period of its development and the permanent condition of the highest form of organic muscular fibre.

fibre, generally at an equal distance from either margin. They are large and oval, with their long axis in the direction of the fibre. Between these, widely scattered clusters of granules are seen—the remains of those which have perished, and which soon disappear. The striæ, although faintly and delicately marked, are sufficiently obvious, especially towards the circumference.

The fibre now commences to increase in size, and its development is continued by means of the surrounding cytoblasts, which are very numerous amongst the fibres. These may be seen to become attached to its exterior, and then invested by a layer of the surrounding blastema. Thus, as it were, nodes are formed at intervals on the surface of the fibre. In some specimens the adherent nuclei may be seen attached to the fibre at very regular distances, but in many cases no such uniformity can be detected. Generally, however, the nuclei are so near to each other, that the investing material of one, as it spreads, becomes blended with that of its neighbour, and so a continuous layer of fresh material of greater or less extent is added to the exterior of the fibre. This is at first clear and pellucid, like the original border of the fibre when first formed, and presents a striking contrast to the present substance of the fibre. It is at this period readily detached by a little rough manipulation, but it soon becomes intimately connected and indefinitely blended with the exterior of the fibre. The striæ and other characters of the adjacent portions of the fibre are soon acquired; the nuclei at the same time gradually sink into the substance of the fibre, and an ill-defined elevation, which soon disappears, is all that remains. (See Plate XI. fig. 11, *a*, *b* & *c*.)*

Sometimes these changes occur around a single nucleus which is isolated from any other. More frequently, the blastema surrounding many nuclei, attached at short intervals along the lengths of the fibre, becomes blended into a uniform layer; and this is often of such considerable extent, that it appears as a regular band lying along the whole length of the fibre. With a little dissection these bands may generally be detached, and they then appear as small accessory fibres, lying by the sides of the others. (See Plate XI. fig. 13 *b*).

Between the extreme conditions all intermediate variations may be found; sometimes the investments of different nuclei adhere more firmly to the exterior of the fibre than to each other, but it more frequently happens that as they coalesce they are more readily separated together from the fibre than from each other.

If a portion of muscular tissue be examined at the period when the fibres are increasing by the addition of fresh nuclei, there will be seen in the field, besides a number of free nuclei, many nuclei floating about invested by blastema, and having the appearance of caudate cells. These are nuclei which have adhered to the fibre and become coated, and afterwards detached by violence.

* I think that some sketches published by Virchow in his 'Archiv für Pathologische Anatomie und Physiologie und für Klinische Medicin,' Siebenten Bandes, Erstes Heft, must have been drawn from muscular fibres in this stage of their development.

All the changes which have been described may often be traced in the same specimen: first, the attachment of nuclei to the exterior of the fibre; secondly, their investment by blastema; thirdly, the gradual sinking of the nuclei into the substance of the fibre, the corresponding subsidence of the elevation, the development of striæ, &c.

Authors generally describe and figure, after VALENTIN and SCHWANN, fœtal fibres in which the nuclei in the interior are represented as bulging the fibres or prominent on the surface. I believe such descriptions and representations to have been drawn from fibres which were growing and developing by the addition of fresh nuclei, in the manner I have described.

Fœtal fibres rarely possess the same diameter throughout their entire length; they are seldom uniform in this respect. Now this variation is easily explained by their mode of increase. Those portions to which fresh material has been recently added are for a time increased in diameter, but each inequality gradually disappears. It might be imagined that this condition is due to pressure, and undoubtedly this source of error is very liable to arise; but the variation may be constantly observed, even when the fibre floats freely in the field.

Lastly, the substance of the fibre becomes contracted and condensed. The diameter of a muscular fibre from a fœtus towards, or at the close of intra-uterine life, is considerably less than the diameter of a fibre at a much earlier period.

As the fibre acquires its more perfect characters, so its substance becomes condensed: it diminishes in size. This is continually counteracted to some extent by the addition of fresh material and nuclei; but notwithstanding this, the size of the fibre continues for a time to decrease, so that the diameter of a muscular fibre at birth is considerably less than it was during a much earlier period of its existence *.

That this decrease in the size of the fibre is due to a condensation of its substance, and not to stretching or any like cause, seems proved,—1st, by the relative position of the nuclei, for the decrease in breadth is not accompanied by a corresponding separation of the nuclei; and 2ndly, by the fact, that as the fibre decreases it becomes much less transparent. The nuclei in its interior grow much more obscure, and they are at length concealed by the increasing density of the muscular substance.

At the time of birth muscular fibres present considerable variety in size and other characters. The great majority measure in the pig from $\frac{1}{4000}$th to $\frac{1}{2000}$th of an inch in width, but many will be found beyond either of these extremes. The striæ are very plainly marked, and in many almost as large as in the adult fibre; in some, however, they are much finer. In most of the fibres the nuclei in their interior are obscured or quite hidden by the density of their substance, but in others they are still

* Thus, for example, taking average specimens:—

Diameter of fibre of pig at time of birth, $\frac{1}{3000}$th of an inch.

Diameter of fibre of pig 5 inches long, $\frac{1}{2000}$th of an inch.

visible. Nuclei may be seen in all stages of their progress passing from without into the substance of the fibre, and hence the majority appear placed at or near the border of the fibre. Many granules are visible, scattered irregularly throughout the fibre, Plate XI. fig. 12.

After birth the fibres enlarge with a considerably increased rapidity; they very soon attain a large size, and ere long reach the adult condition; but for some time the variation in the diameter of different fibres is very obvious. In the pig, the striæ (sarcous elements?) attain their full size two or three weeks after birth.

In the development of muscular fibre, then, the following stages may be traced:—

Aggregation of cytoblasts, and their investment by surrounding blastema.

Their regular arrangement into a single series. Formation of lateral bands.

The lengthening of the fibre and separation of the nuclei. Approximation of bands. The appearance of striæ.

The further development of the fibre and its growth, by the addition of fresh substance to its exterior, by means of the surrounding nuclei.

Condensation of the fibre.

Now it may have been understood from the foregoing description, that these several stages do not follow one another as a simple consecutive series. On the contrary, two of the above processes are generally proceeding at the same time. For instance, during the whole period of development, fresh material is being continually added to the fibre, at first independently, and afterwards by means of additional nuclei; while the nuclei are rearranging themselves into a single row, fresh blastema is constantly added to that which already invests them. The bands bordering the nuclei are continually increasing by the addition of fresh material; so that, as previously explained, the longer the separation of the nuclei is delayed, the thicker do they become; and in those fibres especially in which many of the nuclei perish before they have separated, the lateral bands attain a very great breadth, and the fibres a very considerable diameter.

So also, as already stated, the fibres at a subsequent period continue for some time to decrease in diameter, although fresh material is being added by means of additional nuclei.

As a general rule, all fresh material which is added to the fibre before the original nuclei separate, is attracted independently of fresh nuclei, but that which is added after the original nuclei have separated or become disintegrated, is by means of the additional nuclei which are attached to the exterior of the fibre. The exceptions occur in those fibres in which the lengthening appears delayed much beyond the usual time, and until after the majority of the original nuclei have disappeared. (See Plate XI. fig. 13.) In these cases nuclei in great abundance are often seen attached to the surface of the fibre. They are frequently so abundant as to be absolutely in contact, as if the same number of nuclei which would have attached themselves to the fibre had it elongated, are now crowded together into the smaller space*.

From the period of its first formation, the substance of the fibre gradually increases in strength and firmness as development advances. This fact is well illustrated in fibres which have been preserved some time in different fluids. The more advanced the development of the fibre, the less readily is its texture destroyed; therefore it is much more difficult to preserve the fibres in their earlier period than in the later stages of development. If fibres which are elongating, and in which the nuclei are separating, are kept for some time in a preservative liquid, and by-and-by examined, it will be noticed, that while the structure of those fibres in which the nuclei have separated to a considerable extent is still perfect and distinct, the substance of those in which the nuclei are still in contact is broken up and confused; and it will be observed that there is a close correspondence between the extent to which the nuclei are separated and the integrity of the fibre.

The rate of development of different fibres in the same muscle is by no means uniform, and some fibres are doubtless formed at a later period than others. If, for instance, the muscular tissue of a pig, between 2 and 3 inches long, be examined, many fibres will be found in very different degrees of development. The majority are in the second, or passing from the second into the third stage, presenting the single row of closely arranged nuclei bordered by lateral bands, while others will be seen in the first stage of formation as elongated groups of nuclei, partially invested by blastema. In any specimen numerous fibres will generally be seen in various degrees of development within certain limits. Even in the same fibre in different portions of its length, this variation may often be detected (see Plates X. and XI. figs. 14, 8 and 9 *g* and *i*), and in fibres at a more advanced period of development, and even for some time subsequently to birth, a considerable difference in size may be often observed. Generally speaking, there appears to be more uniformity in the rate of development of different muscles than of different fibres of the same muscle.

Of the development of the sarcolemma I have little or nothing to say, except that according to my observation it is not formed in the manner originally described by SCHWANN and more recently by KÖLLIKER.

I have never been able to determine satisfactorily the exact period of its first appearance, nor do I imagine that it is possible to do so. It is probably formed gradually, and only attains its more perfect characters at an advanced period of development.

To obtain a clear idea of the structure of fœtal fibres, and of the changes that occur at different periods of their development, specimens should be examined both

* Perhaps this was the case in the instance which Mr. BOWMAN has alluded to and represented. It was a specimen taken from the chrysalis of a tiger-moth.—Phil. Trans. 1840.

from perfectly fresh embryos and from others which have been kept for some hours. The changes which occur in the appearance of the fibres during the earlier periods of development, after the embryo is removed from the parent, are very remarkable, and these changes are hastened by the presence of water. The blastema in which the fibres are imbedded, and from which they are formed, is clear, transparent, and apparently structureless, but the material which is recently added to the exterior of the fibre is rather opake and obscure; and the obscurity is increased by the roughness of the surface which refracts the light irregularly, and very often gives a glistening aspect to the fibre. As this blastema is developed into the substance of the fibre it clears up, it grows much more transparent, and its general characters and arrangement can be readily investigated. Now the blastema, when recently added to the exterior of the fibre, and which has not yet assumed the structure of the fibre, adheres but slightly and is readily detached, so that the fibres, which, when fresh, are quite obscure, by simple preservation for a short time, and more especially if placed in water, part with their more recent investment of blastema, and perhaps nuclei, and become clear and transparent. Hence, during the first stage of development, by simple preservation, and still more rapidly and effectually by the action of water, the fibre is altogether broken up. The delicate material investing and binding the nuclei together is easily dissolved, the nuclei separate, and no appearance of the early fibre remains. It is very common, however, in such a case, to see three, four or more nuclei attached together and in close contact, floating freely about, the recently added blastema having been detached from their surface.

At a later period of their development, the action of water not only assists in removing the recently added and undeveloped layer of blastema which obscures the structure of the fibre, but it penetrates the interior, and renders its entire substance much more clear and pellucid, and the nuclei within more transparent.

The Nuclei, which are such important agents in the development and maintenance of muscular fibre, and indeed of tissues generally, claim much more consideration than a passing notice*. These nuclei, when free as cytoblasts, may be observed in various stages of development. The younger ones are round or slightly oval, possessing a dark and distinct outline: their substance has a nebulous or faintly granular aspect. They very generally contain one or two well-marked nucleoli, which appear either as dark or as bright highly refracting spots, according to the focus at which they are viewed. The average diameter of these cytoblasts is from $\frac{1}{5000}$th to $\frac{1}{4000}$th of an inch; the smallest are less than $\frac{1}{6000}$th.

They increase in size as age advances, and at the same time they become more

* If the preceding description of the development of muscular fibre be a true one, it is another striking example of the truth and accuracy of the opinions which Mr. Paget has expressed with regard to the relations and functions of nuclei, and their extreme importance.—Lectures at the Royal College of Surgeons, May 1847. Lecture V. Surgical Pathology.

decidedly oval, generally measuring in their long axis somewhat more than $\frac{1}{2000}$th ($\frac{1}{1700}$th), and in their short axis $\frac{1}{3000}$th. Their outline becomes broader and paler, and is less distinctly defined; their contents grow more plainly granular, and between their margin and contents, that is immediately within their softened outline, a clear bright ring may be observed.

Their characters may in some respects be more easily investigated, and the changes they undergo can be more obviously traced as they lie imbedded in the substance of muscular fibre. The walls of the nuclei are firm and far more resisting than the substance of the fibre; for when the fibre is stretched and narrowed between them, the nuclei remain unaltered in shape and bulge the fibre at the part where they are situated; and it may be constantly observed that when young fibres float freely in liquid they never bend at the points where the nuclei are situated, but always at some part between them. A sudden bend or twist is often seen just beyond the extremity of a nucleus, but the nucleus itself preserves its shape, and renders that portion of the fibre which it occupies comparatively firm.

As the nuclei lie in the substance of the fibre they increase considerably in size, and become fainter in appearance. The change in their shape and outline, and the bright border immediately within their circumference, are generally distinctly traced; they seem at last to be filled with granules, and as these are more plainly developed their walls become broken and obscure, until at last their position is marked by an irregular cluster of granules, which remain very visible for a short time and then rather suddenly disappear.

These granules have many of the characters of minute oil-globules; they appear either as dark or as bright highly refracting spots, with a thick, dark and well-defined border, according to the focus at which they are viewed. When the tissue is preserved in spirit for some time, many of them fuse together into larger globules, which in aspect and other characters completely resemble globules of oil. They are not readily acted on by ether, but the granules disappear in fibres that have been preserved for a short time in it. Except at the latter periods of development, the nuclei can be readily discerned in the substance of the fœtal fibres without any previous preparation, unless the structure of the fibre is obscured by the deposit of fresh and undeveloped material upon its surface. Towards the close of fœtal life, as the tissue grows more dense, the nuclei are discerned with greater difficulty; they become obscured by the substance of the fibre; in either case, if the tissue be preserved for a day or two, or if placed for a short time in water, the muscular substance is rendered much clearer and the nuclei become distinctly visible. The same plan of simple maceration in water succeeds so well, even with muscular fibres at a far more advanced period of development, that the nuclei they contain may be thus beautifully shown. In a day or two the substance of the fibre becomes clear and transparent and the nuclei appear; the advantage of this simple plan is, that the nuclei remain unaltered: they preserve their natural appearance. The addition of weak acids, which is recommended for the purpose of bringing the nuclei into view, always affects their appearance by altering their shape to an extent proportioned to the strength of the re-agents. They shrink, their outline becomes more or less disturbed, and they appear shrivelled; hence many of the descriptions and drawings of these nuclei are unfaithful. An artificial appearance, the effect of re-agents, is described and figured as the natural one.

However much the shape and other characters of these nuclei may be affected by various re-agents, they are not easily destroyed. When muscular tissue is preserved in alcohol, they shrink, but remain for a long time; at last, however, they become indistinct, they appear like large and irregular oil-globules, and finally break up. By the prolonged action of sulphuric ether, the nuclei become irregular in outline and somewhat shrivelled, and their substance presents a uniform clear and glistening appearance.

These and similar effects appear in great measure due to time, and this ultimate disintegration of the nuclei, under almost all circumstances, is the chief obstacle to the preservation of fœtal muscular fibre; but generally, as the nuclei become altered, the whole structure of the fibre undergoes a change. The striæ, when they exist, become confused and then disappear, and the interior of the fibre is occupied by globules of different size, closely resembling globules of oil.

Explanation of the Plates.

PLATES X. and XI.

Fig. 1. Cytoblasts from the tissue of the dorsal region of a fœtal pig, 1 inch in length.

Fig. 2. Portion of muscular fibres from a fœtal pig, between 1 and 2 inches in length. The first stage in the formation of muscular fibre.

Fig. 3. Muscular fibre from a fœtal pig, between 2 and 3 inches long, showing the linear arrangement of the nuclei and narrow bands.

Fig. 4. A similar specimen. The nuclei at one extremity have not fallen into their places, and the lateral bands are separated to a corresponding extent.

Fig. 5. Fibre from a fœtal pig, $3\frac{1}{2}$ inches long. Lateral bands increasing in width. Breadth of fibre $\frac{1}{1500}$th of an inch.

Fig. 6 *a*. Fibres from the upper extremity of the leg of a *Tipula*.

Fig. 6 *b*. Fibres from the upper extremity of the leg of a blue bottle fly (*Musca vomitoria*).

Fig. 7. Fibre from a fœtal pig, 3 inches long, showing separation of the nuclei.

Fig. 8 *a*. Fibre from a fœtal pig, $3\frac{1}{2}$ inches long, showing the progress of development in different portions. Breadth of fibre, where the nuclei are in contact, $\frac{1}{1800}$th of an inch; where nuclei are $\frac{1}{1000}$th of an inch apart, breadth of fibre $\frac{1}{3500}$th of an inch.

This fibre floated freely in the field.

Fig. 8 *b*. A smaller specimen from a fœtal pig, $2\frac{1}{2}$ inches long.

Fig. 9 *a*. Fibre from a fœtal pig, 4 inches long. Nuclei in progress of dissolution. Breadth of fibre $\frac{1}{1500}$th of an inch.

Fig. 9 *b*. Fibre from the same pig, extending; remaining nuclei and granules separating. Breadth of fibre $\frac{1}{2000}$th of an inch.

Fig. 9 *c*. Fibre from a fœtal pig, 5 inches long. Nuclei not separated, but perishing in their places. Breadth of fibre $\frac{1}{1100}$th of an inch; of lateral bands $\frac{1}{3100}$th of an inch.

Fig. 9 *d*. Fibre from a fœtal pig, $5\frac{1}{2}$ inches long. Nuclei broken up into clusters of granules.

Fig. 9 *e*. Fibre from the same pig, extending. Breadth of fibre $\frac{1}{1500}$th of an inch. Clusters of granules $\frac{1}{4000}$th of an inch apart.

Fig. 9 *f*. Fibre from the same pig, still further extended. Clusters of granules separating and elongating. Breadth of fibre $\frac{1}{2000}$th of an inch.

Fig. 9 *g*. Fibres from the same pig, showing different progress of development in different parts. Nuclei breaking up into granules.

Fig. 9 *h*. Fibre from a fœtal pig, $3\frac{1}{2}$ inches long. Distinction between lateral bands and centre well marked, faint appearance of striæ in bands. Breadth of fibre $\frac{1}{2000}$th of an inch. Nuclei round, $\frac{1}{4500}$th of an inch, separating, and about $\frac{1}{1500}$th of an inch apart. Breadth of bands $\frac{1}{9000}$th of an inch.

Fig. 9 *i*. Fibre from a fœtal pig, 4 inches long. Shows unequal rate of development in different portions.

Fig. 10. Fibre from a fœtal pig, $3\frac{1}{2}$ inches long. Nuclei separated; striæ visible; breadth of fibre $\frac{1}{3000}$th of an inch.

Fig. 11 *a*. Fibre from a fœtal pig, 8 inches long; showing the method of increase by external nuclei in various stages.

Fig. 11 *b*. Another fibre from the same pig.

Fig. 11 *c*. Another fibre from the same specimen. Striæ well marked. These fibres vary in diameter from $\frac{1}{5000}$th to $\frac{1}{3000}$th of an inch.

Fig. 11 *d*. Fibres from the same pig, after the addition of citric acid.

Fig. 11 *e*. Free nuclei from the same specimen.

Fig. 12. Fibres from a pig at the period of birth.

Fig. 13 *a*. Fibre from a fœtal pig, 5 inches long. Primary nuclei separating. Increase by external nuclei. Breadth of fibre $\frac{1}{2000}$th of an inch.

Fig. 13 *b*. Fibre from a fœtal pig, 4 inches long, increasing by means of external nuclei. Breadth of fibre from $\frac{1}{2000}$th to $\frac{1}{5000}$th of an inch.

Fig. 14. Fibre from fœtal pig, $2\frac{1}{2}$ inches long, showing irregular rate of development. At one extremity the nuclei have scarcely become arranged in a linear series; while at the other the nuclei have separated, and the striæ are faintly visible.

The figures just described have been drawn from the fibres of the fœtal pig.

Now with regard to the comparative dimensions of many of these fibres, it must be observed that the size of the fœtus did not always correspond to the degree of its development, and this for two reasons. First, growth and development do not always proceed at an equal or uniform rate. Secondly and chiefly, it was impossible to obtain a sufficient supply of fœtal pigs from parents of the same size. I had no means of choosing in this respect, and received specimens both from small and large sows. Moreover, I could not generally ascertain the exact age of the fœtus examined, and have, therefore, to avoid error, only spoken of its length.

These facts will explain the results of some measurements, which might otherwise appear to be contradictory.

St. Bartholomew's Hospital,
November 1854.

FIG. 1.

FIG. 2.

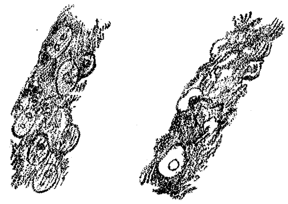


FIG. 3.

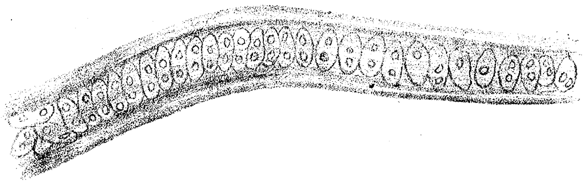


FIG. 4.

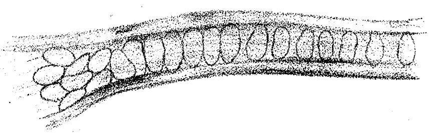


FIG. 5.

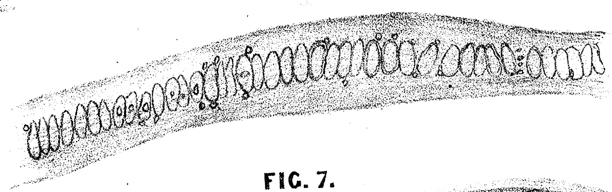


FIG. 6.

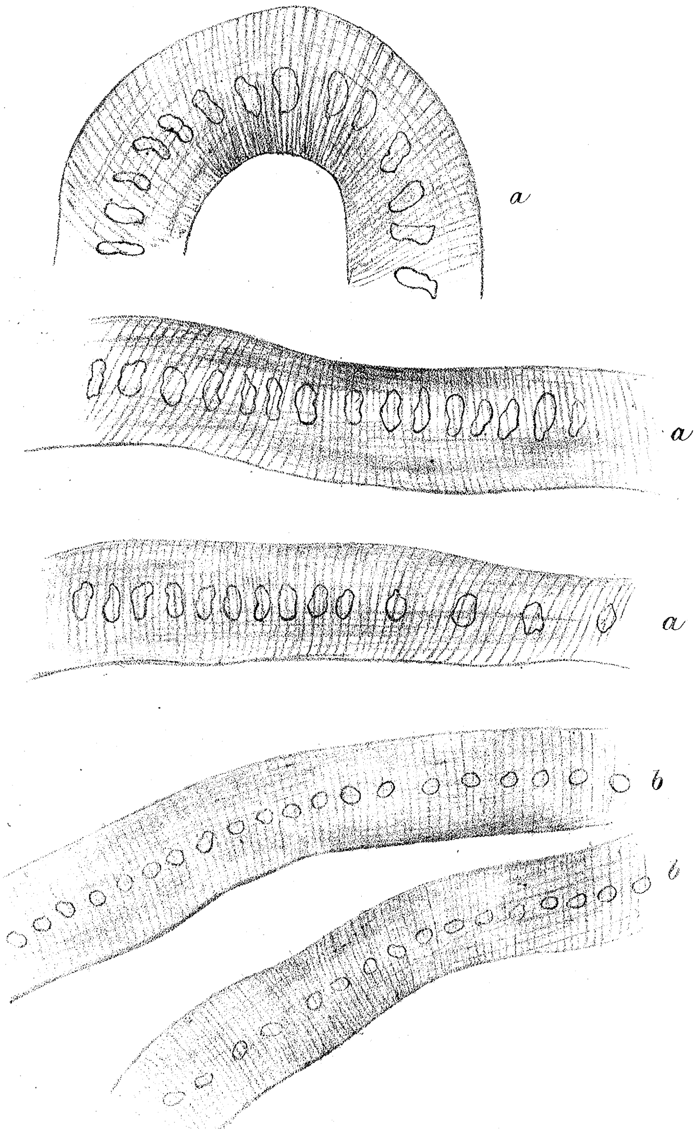


FIG. 7.

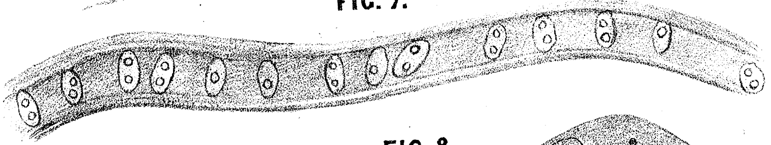


FIG. 8.

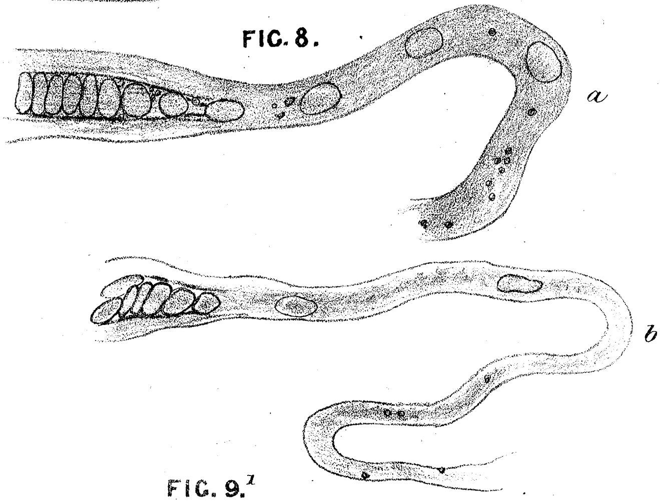
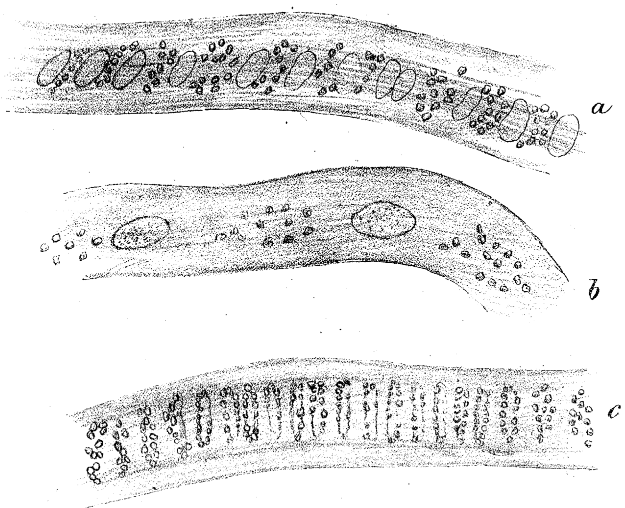
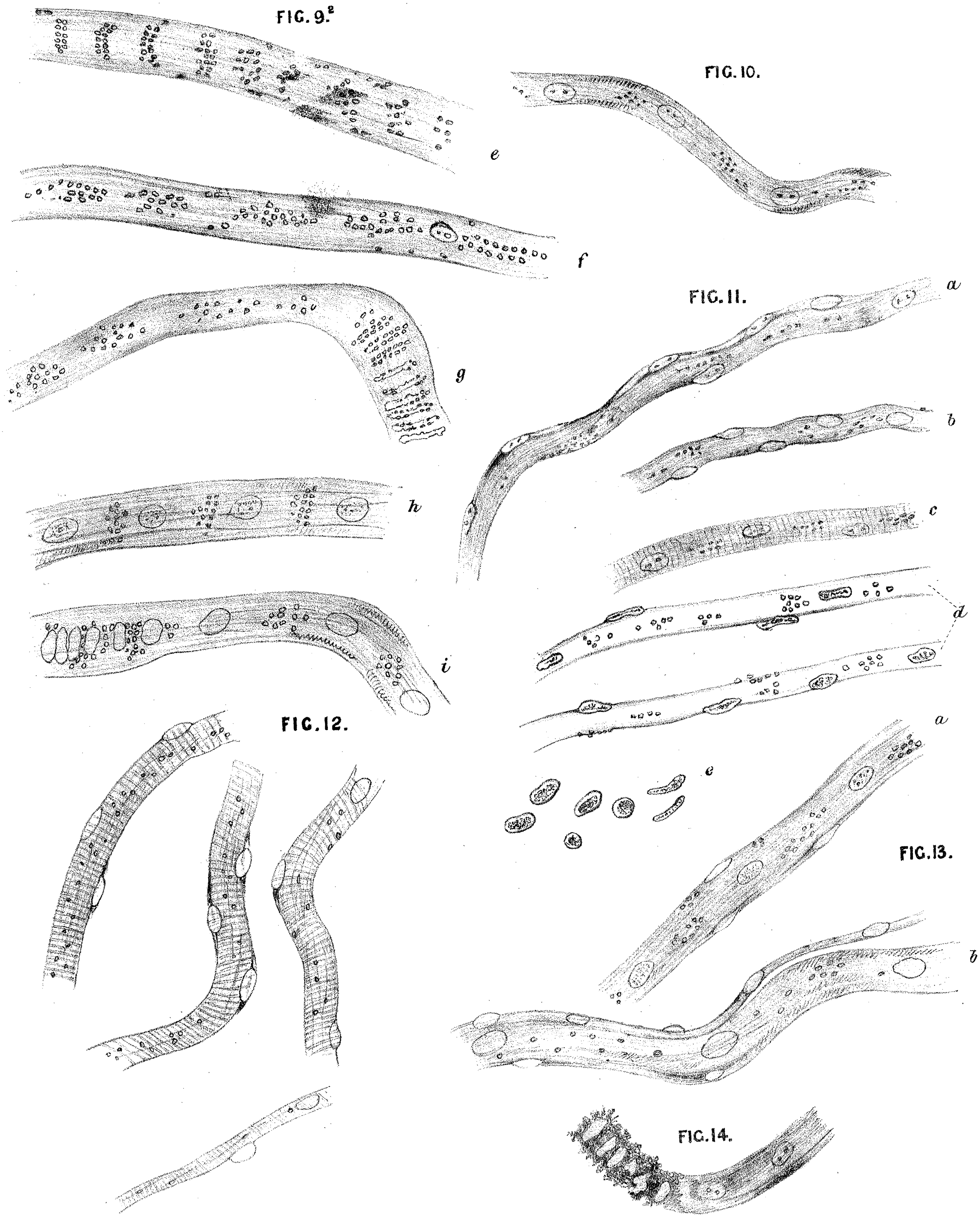


FIG. 9.



S. Savery del.t

J. Basire, lith.



W. S. Savory, delᵗ. J. Basire, lith.