auscultation. If telephone and stethoscope are applied to the same ear, one sound only is heard. Exner has shown that any two sounds which are as much as $\frac{1}{500}$ of a second apart are audible as distinct sounds. Bernstein therefore concludes that, inasmuch as contraction begins nearly $\frac{1}{100}$ second after excitation, and the electrical change culminates at $\frac{1}{200}$ second, the mechanical thud must, as well as the electrical, be molecular, and concludes that the two sounds are coincident. In the second of these conclusions, Professor Bernstein appears to be justified, but not in the first. It having been shown by the photographic records that the two responses, the electrical and the mechanical, are nearly coincident, it is no longer needful to seek an explanation of the fact that the electrical and mechanical sounds are indistinguishable.

III. "The Development of the Sympathetic Nervous System in Mammals." By A. M. Paterson, M.D. Communicated by A. Milnes Marshall, F.R.S. Received April 18, 1890.

(Abstract.)

The following investigations were undertaken with the object of determining the origin of the Mammalian sympathetic system, and of clearing up thereby certain points in its morphology.

Two opposite views exist at present among embryologists regarding its development. In both views the segmental formation of the sympathetic cord is upheld. According to the older view (Remak, &c.), it is mesodermal, and is formed *in situ*. According to more recent views, it is ectodermal. Balfour and Onodi, who have maintained the latter view, differ, however, as to the fundamental origin of the sympathetic system,—Balfour regarding each sympathetic ganglion as an offshoot from the spinal nerve, while Onodi considers it a direct proliferation from the spinal ganglion.

For the present research mammalian embryos were exclusively employed—rat, mouse, rabbit, and human embryos. The stage in development was first considered in which the sympathetic system was plainly visible, and from this point the earlier and later stages in the process were traced. It was only possible to determine approximately the ages of the embryos employed, as the time of impregnation varies in different instances, and two embryos from the same uterus often differ in size and extent of development.

The first event to occur is the formation of the main sympathetic cord. In very young embryos (*e.g.*, rabbit, 7 days, axial length 5 mm.), in which the spinal nerves are completely formed and the spinal ganglia clear and distinct, there is no trace of the sympathetic

ganglia or the connecting branches with the spinal nerves. The cord is first seen in transverse and sagittal sections of mouse and rat embryos of about 8 days. It arises on either side as a solid, uniform, unsegmented rod of fusiform cells, imbedded in the mesoblast surrounding the aorta, and lies in the interval between the latter and the adjacent veins. Slightly thicker anteriorly than posteriorly, it ends abruptly in front at the level of the first vertebral segment; behind it becomes indistinct posteriorly to the suprarenal body, to which it sends a considerable cellular bundle, and, tapering off, disappears at the level of the hind limbs. This cellular column is formed by the differentiation of the mesoblastic cells *in situ*; it is not connected with the spinal nerves, and it is unsegmented.

The next step consists in the junction of the spinal nerves on either side with these columns of cells. This is effected by the gradual growth of the inferior primary division of the nerve and its final division at the junction of the body wall (somato-pleure) and splanchnic area (splanchno-pleure) into *somatic* and *splanchnic* branches (rat, mouse, 8–9 days). The former passes on to be distributed in the body wall. The latter can be followed in succeeding stages in a ventral and mesial direction, until at last it meets and joins the cellular sympathetic cord (mouse, 11 days, rat, 12 days).

The origin of this splanchnic branch is from both roots of the spinal nerve, of which the ventral root contributes the greater number of fibres. At its peripheral end it terminates in one of two ways. At the anterior part of the thorax the fibres seem to end entirely in the sympathetic cord; that is, they have not been traced beyond it. In the posterior thoracic and in the lumbar regions the splanchnic branch, on reaching the sympathetic cord, divides into two parts, of which one joins the cord, the other passes over it. In both cases the fibres which join the cord are directly connected with the component cells.

In certain regions no such connexions can be made out. Behind the kidney and the bifurcation of the aorta (*i.e.*, behind the loins) the splanchnic branches cease. In front of the fore limbs (*i.e.*, in the neck) the splanchnic branches do not join the sympathetic system. In comparatively advanced embryos, distinct nerves, morphologically similar to the splanchnics, course inwards round the vertebral artery to the tissues surrounding the growing vertebræ, but at the same time occupying a position dorsal to the sympathetic cord, and altogether unconnected with it.

These splanchnic branches correspond to the white *rami communicantes.*

The formation of the ganglia on the main sympathetic cord occurs subsequently, and is subordinate to the connexions with it of the splanchnic branches of the spinal nerves. Up to the time of the for-

mation of cartilaginous vertebral *centra*, there is no constriction of the main cord (mouse, 17—18 days). Gangliation begins at and after this date, and is due, in the first place, and principally, to the junction of the splanchnic branches; this causes the accession of a large number of nerve-fibres at the point of entrance, and the consequent persistence of the component cells (which are joined by these nerves), as ganglion cells. Gangliation is caused, secondly, and to a less extent, by the anatomical relations of the sympathetic cord to the bony segments, vessels, &c., which are developed near it, and which, by their growth, cause indentation or constriction of the cord at certain points.

This view is supported by the evidence obtained from the dissection of human embryos of different ages (3rd, 4th, 5th, and 6th months), where the cord has the form of a band or strip, constricted irregularly at considerable intervals, rather than of a regularly nodulated chain; and by the evidence derived from the normal adult structure, where the "segmentation" of the sympathetic cord is apparent rather than real.

The cervical portion of the embryonic sympathetic cord is at first undifferentiated from the main column. Growing with the growth of the neck, it separates at the origin of the vertebral artery, into two unequal parts. The smaller part forms a fibro-cellular cord, which accompanies that artery, and forms the vertebral plexus. The other, or main, portion accompanies the carotid vessels. Growing rapidly, it becomes constricted off from the main sympathetic cord by the formation of a gradually elongating fibro-cellular commissure, and gives rise to the "superior cervical ganglion." This lies alongside the internal carotid artery, and gives off anteriorly a fibro-cellular bundle, which accompanies and is finally lost upon that vessel, as the carotid plexus. When the middle cervical ganglion is present, it may be looked upon as representing a mass of the original cells of the sympathetic cord, which have been included in the growth of the commissure connecting the main cord to the superior ganglion. These parts may be regarded as belonging to the collateral distribution of the sympathetic system, because (1) they are outgrowths from the main cord, and (2) they receive no splanchnic branches directly from the spinal nerves.

The caudal termination of the sympathetic system is likewise an outgrowth from the main cord. In the youngest embryos in which it is found (rat, 8 days), the cord is lost at the level of the hind limbs; at a later period of development (rat, 12 days) it reaches further, to the bifurcation of the aorta; while in still older embryos it can be traced alongside the middle sacral artery for a considerable distance. It is not joined by splanchnic branches, and it is only in an advanced stage of development (rat, 22 days) that trans-

verse cellular communications take place on the dorsal aspect of the middle sacral artery between the cords of opposite sides to produce the *ganglion impar* and the loop of connexion between the caudal ganglia.

The peripheral branches from the sympathetic cord arise as cellular buds or outgrowths which are first seen about the time when the splanchnic branches of the spinal nerves join the cord (mouse, rat, 11—12 days; human embryo 1st month). They accompany the parts of the splanchnic branches which do not join the sympathetic cord into the splanchnic area; and, especially in the hinder thoracic region, form considerable masses traceable along the main vessels, which in older embryos give rise to parts of the splanchnic nerves, as well as the medullary portions of the suprarenal bodies, as previous observers have described.

The gray *rami communicantes* may (doubtfully) be said to belong to the category of peripheral branches from the sympathetic cord. They appear to arise from the cord as cellular outgrowths which pursue a centripetal course along the splanchnic branches of the spinal nerves towards their roots; but in regions where these are absent, or are unconnected with the sympathetic cord, I have not been able to satisfy myself about their formation.

The principal conclusions derived from these investigations are that the sympathetic system in Mammals is mesoblastic, is formed *in situ* out of the cellular tissue surrounding the embryonic aorta, and is at first entirely independent of the cerebro-spinal nervous system; it is primarily uniform and unsegmented, in this respect resembling the organs in the splanchnic area—the vascular and alimentary systems—with which it is so closely related, functionally as well as structurally. It becomes secondarily connected with certain spinal nerves by the growth from the latter of the white *rami communicantes*, and in consequence becomes gangliated in an irregular manner. From the main cord cellular outgrowths arise which form peripheral, non-medullated nerves, plexuses, and ganglia, as well as the medullary portions of the suprarenal bodies.

Morphologically, the Mammalian sympathetic cord resembles the structures with which it is in structural and functional relation, in being mesoblastic, and in its development primarily unsegmented. It is a rod, fibro-cellular in structure, out of which, on the one hand, are produced certain ganglia and nerves, and which, on the other hand, becomes connected with certain cerebro-spinal fibres—the splanchnic branches of the spinal nerves. The mechanism thus produced may be regarded as providing for the guidance of these fibres (*e.g.*, vasomotor nerves) to their destinations, and as regulating their proper distribution to the vascular and alimentary systems.

In conclusion, I wish to express my indebtedness to Professor

Milnes Marshall, of Manchester, for his advice and criticism, and for many valuable suggestions made after reading the memoir of which this is a summary.

IV. "A Note on an Experimental Investigation into the Pathology of Cancer." By CHARLES A. BALLANCE and SAMUEL G. SHATTOCK. Communicated by Sir JAMES PAGET, Bart., F.R.S. Received April 15, 1890.

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