

A CONTRIBUTION TO THE HISTOGENESIS OF THE SYMPATHETIC NERVOUS SYSTEM.¹

BY

ALBERT KUNTZ.

WITH 2 FIGURES.

In studying embryos of the pig for the purpose of tracing the development of the sympathetic nervous system, the writer has been interested in the evidence for the migration of nervous elements from the neural tube along the fibers of the peripheral nerves. In a recent paper² I have described the migration of medullary cells, among which are to be recognized cells of an indifferent character and neuroblasts, into the dorsal and ventral nerve-roots. In transverse sections of embryos of the pig 6 and 7 mm. in length breaches in the external limiting membrane of the neural tube occur quite frequently in the region of the dorsal nerve-roots. Through these breaches lines of cells practically touching each other end to end may be traced from the mantle layer into the proximal part of the dorsal nerve-roots (Fig. 1, dnr). Further evidence for the migration of medullary cells into the dorsal nerve-roots is afforded by the fact that in many sections of embryos 6 and 7 mm. long, where no breaches occur, cells are found in contact with the external limiting membrane inside the neural tube in the region of the dorsal nerve-roots. In embryos 9 mm. and over in length this region, as shown in Fig. 2, dnr., is always occupied by fibers of the dorsal nerve-root and rarely are cells found among them.

In transverse sections of embryos of the pig from 9 to 13 mm. in length breaches occur in the external limiting membrane in the region

¹From the Laboratories of Animal Biology of the State University of Iowa.

²The Migration of Nervous Elements into the Dorsal and Ventral Nerve-roots of Embryos of the Pig. Proceedings of the Iowa Academy of Science, Vol. 16.

of the ventral nerve-roots. Through these breaches medullary cells may be observed migrating into the ventral nerve-roots (Fig. 2, vnr.). Migration of medullary cells into the ventral nerve roots of embryos of the pig has recently been described by Carpenter and Main ('07). I have been able to substantiate their observation that cells may be found "just inside the external limiting membrane, in an intermediate position half in and half out of the neural tube, and in the base of the ventral nerve-root just outside the external limiting membrane." But, whereas they have described only elongated cells which they recognize as the indifferent cells of Schaper, I have observed cells of a distinctly pyriform type migrating with the indifferent cells.

According to the researches of Schaper ('97) the germ cells (Keimzellen) of His (cells of epiblastic origin undergoing mitotic division near the internal limiting membrane of the neural tube) give rise to cells which he characterizes as indifferent. These indifferent cells migrate toward the mantle layer and are there transformed either into neuroblasts or into embryonic supporting cells. In the higher vertebrates some of these indifferent cells undergo further division by mitosis in the mantle layer.

The cells which migrate from the neural tube into the dorsal and ventral nerve-roots are of two general types; elongated cells which are to be regarded as the indifferent cells of Schaper, and pyriform cells which are to be regarded as the neuroblasts of Schaper. The neuroblasts are much fewer in number than the indifferent cells, but are distributed indiscriminately among them. When observed passing out of the neural tube the tapering end is usually directed peripherally. This also is in accordance with the usual position of the neuroblasts in the mantle layer.

The orientation of the cells in the neural tube is such that two general courses of migration into both dorsal and ventral nerve-roots may be recognized. In the ventral region some of the cells move directly outward from the ventral zone toward the base of the ventral nerve-root; others tend ventro-laterally from the region in which the lateral horn of the gray matter arises. In the dorsal region the chief course passes quite directly from the dorsal zone toward the proximal

part of the dorsal nerve-root, with some cells moving from the most dorsal region along the inner surface of the external limiting membrane. The other course tends dorso-laterally from regions ventral to the dorsal nerve-root. The cells of the latter course probably originate in the same region as those which move ventro-laterally toward the ventral nerve-root.

Further observation has shown that the cells which migrate from the neural tube into the spinal nerve-roots wander peripherally along the spinal nerves and visceral rami into the anlagen of the sympathetic ganglia. As the fibers of the ventral nerve-root emerge from the neural tube they are accompanied by medullary cells which may be distinguished from the mesenchymal cells by their size and form. Very often they also take a slightly deeper stain. As the fibers grow peripherally these cells wander along their course, while others emerge from the neural tube to take their places in the base of the nerve-root. Similar cells detach themselves from the distal ends of the spinal ganglia and wander down along the sensory fibers. Whether these represent cells which have migrated from the neural tube into the dorsal nerve roots could not be determined since it was not found possible to trace cells through the spinal ganglia. Beyond the point of union of the sensory and motor roots it is no longer possible to distinguish the cells which wander down from the spinal ganglion from those which migrate out from the neural tube along the fibers of the ventral nerve-root. The majority of the cells thus distributed among the growing fibers of the spinal nerves are cells of the elongated type. Frequently, however, pyriform cells are found among them.

In transverse sections from the dorsal region of embryos of the pig 7 mm. in length the spinal nerves have extended peripherally a little beyond the level of the dorsal aorta. The fibers are loosely aggregated. Numerous elongated cells and a few cells of the pyriform type are found among the fibers as well as at the surface of the bundle. Fibers are not yet present in the visceral ramus, but at a point a little above the level of the aorta, cells, either singly or in groups of two or three, are seen to bend from their course nearly at right angles and wander through the mesenchyme toward the dorso-

lateral angle of the dorsal aorta along the path later occupied by the fibers of the visceral ramus (Fig. 1 pvr.). At this stage the anlagen of the sympathetic ganglia are already present as loose aggregates of cells along the dorso-lateral angles of the dorsal aorta. Cells of the pyriform type were observed along the paths of the visceral rami and among the loosely aggregated cells along the dorso-lateral angles of the dorsal aorta (Fig. 1 nb.). Thus pyriform cells which are to be

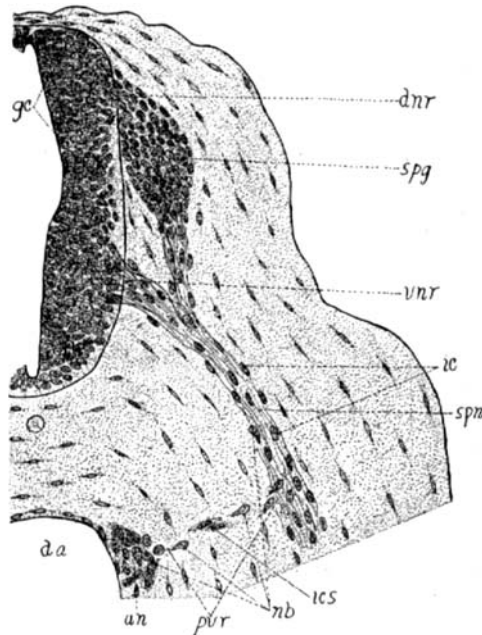


FIG. 1.—Transverse section of neural tube and sympathetic anlage of 7 mm. embryo of the pig $\times 165$. an., sympathetic anlage; da., dorsal aorta; d. n. r., dorsal nerve root; gc., germ cells of His; ic., indifferent cells; ics., indifferent cells in syncytium; nb., neuroblasts; pvr., path of visceral ramus; spg., spinal ganglion; spn., spinal nerve; vnr., ventral nerve-root.

regarded as the neuroblasts of Schaper have been traced from the neural tube along the spinal nerves and visceral rami into the anlagen of the sympathetic ganglia. It may further be observed that the elongated cells, both along the spinal nerves and visceral rami, may often be seen joined together in small groups by protoplasmic processes or in small syncytia. The pyriform cells, however, are always free.

In transverse sections of embryos 10 mm. in length fibers appear in the visceral rami but do not yet extend into the anlagen of the sympathetic ganglia, the cells of which have become more numerous and more closely aggregated. The distribution of the medullary cells along the paths of the nerve fibers remains about the same as in the preceding stage.

In embryos 12 and 13 mm. in length the embryonic nervous system has assumed more definite form. In transverse sections of 12 mm. embryos (Fig. 2) the fibers of the visceral rami are seen to extend into the anlagen of the sympathetic ganglia. These are still loosely aggregated cell columns but begin to show evidence of their future segmental character. As in the preceding stages numerous elongated cells are found among the growing nerve fibers and at the surface of the bundles, and pyriform cells may be observed all along the path from the neural tube into the anlagen of the sympathetic ganglia.

The destiny of cells which migrate out from the neural tube and spinal ganglia has already occupied the attention of not a few investigators. Harrison ('01) suggested the possibility that certain medullary cells which he observed migrating into the ventral nerve-roots of embryos of the salmon may wander farther peripherally, i. e., into the sympathetic ganglia, and there give rise to sympathetic motor neurones. Bardeen ('03) suggests that the cells which wander out from the spinal ganglia and cord along with the bundles of axis-cylinder processes may take some part in the formation of the neurilemma. He, however, believes with Vignal and Gurwitsch that in mammals the neurilemma is derived largely from mesenchyme. Kölliker ('05), though formerly of the opinion that the neurilemma is of mesoblastic origin, came to the conclusion in his later researches that the elongated cells which wander out from the spinal ganglia give rise to the neurilemma of the sensory fibers and that the neurilemma is everywhere of epiblastic origin. Dohrn and Neal have expressed the opinion that the cells which compose the neurilemma of the motor fibers have their origin in the neural tube and brain. Carpenter ('06) has shown that in embryos of the chick cells of an indifferent character migrate out from the ventral wall of the mid-

brain along the oculomotor nerve and become transformed into nerve cells of the ciliary ganglion. Carpenter and Main ('07) "feel sure" that some of the medullary cells which escape from the neural tube become cells of the neurilemma and there subserve a supporting func-

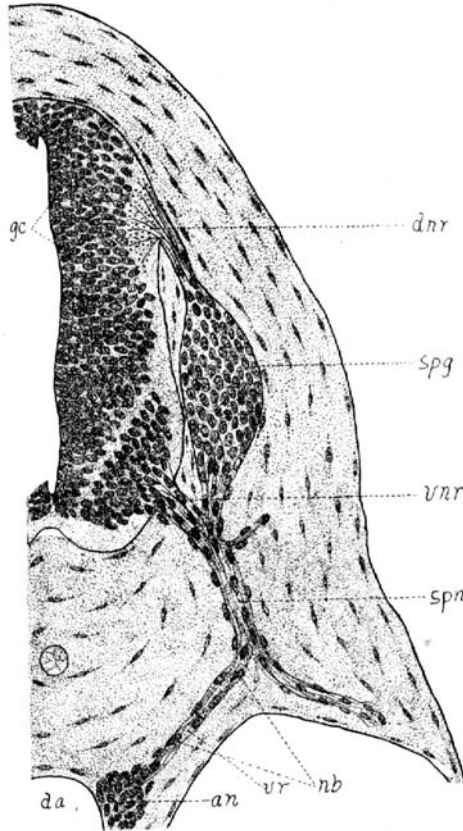


FIG 2.—Transverse section of neural tube and sympathetic anlage of 12 mm. embryo of the pig $\times 165$. an., sympathetic anlage; da., dorsal aorta; dnr., dorsal nerve root; gc., germ cells of His; nb., neuroblasts; spg., spinal ganglion; spn., spinal nerve; vnr., ventral nerve-root; vr., visceral ramus.

tion similar to that of the neuroglia cells in the central nervous system.

Thus far only cells of an indifferent character have been considered. There are, however, as shown above, two distinct types to be

recognized among the cells which migrate from the neural tube into the spinal nerve-roots. In the light of Schaper's researches we must conclude that the pyriform cells which migrate peripherally from the neural tube have already undergone differentiation and must develop into neurones. These cells having been traced along the spinal nerves and visceral rami into the anlagen of the sympathetic ganglia obviously develop into sympathetic neurones. Thus there is established a direct genetic relation between the sympathetic and the central nervous systems.

It is not the writer's purpose in this paper to discuss the fate of the elongated medullary cells found among the fibers of the peripheral nerves. Inasmuch, however, as frequent reference has been made to them they may not be passed by without brief consideration. Occasionally one of these cells is seen undergoing mitotic division. My observations do not preclude the possibility that transformations may take place along the paths of the peripheral nerves similar to those which, according to Schaper, take place inside the neural tube. However, proliferation of these cells outside the neural tube is probably not sufficient to be of any considerable importance. A large majority of the elongated cells which wander out from the neural tube and sensory ganglia probably enter into the formation of the neurilemma.

SUMMARY.

1. Medullary cells migrate from the neural tube into the dorsal and ventral nerve-roots of embryos of the pig.
2. These migrating cells are of two general types: (a) elongated cells which are to be regarded as the indifferent cells of Schaper; (b) pyriform cells which are to be regarded as the neuroblasts of Schaper.
3. These migrating cells seem to have their origin in more or less definite regions in the neural tube.
4. Both the indifferent cells and the neuroblasts wander peripherally and may be traced along the spinal nerves and visceral rami into the anlagen of the sympathetic ganglia.
5. The neuroblasts which migrate from the neural tube into the anlagen of the sympathetic ganglia develop into sympathetic neurones.

Thus, there is established a direct genetic relation between the sympathetic and the central nervous systems.

6. A large majority of the elongated cells which wander out from the neural tube and sensory ganglia probably enter into the formation of the neurilemma.

Received for publication, May 15, 1909.

LITERATURE CITED.

- BARDEEN, C. R., '03. The Growth and Histogenesis of the Cerebro-spinal Nerves in Mammals. *Amer. Jour. Anat.*, Vol. II, No. 2, p. 231.
- CARPENTER, F. W., '06. The Development of the Oculomotor Nerve, the Ciliary Ganglion, and the Adducent Nerve in the Chick. *Bull. Mus. Comp. Zoöl. Harvard College*, Vol. 48, No. 2, p. 141.
- CARPENTER, F. W., and MAIN, R. C., '07. The Migration of Medullary Cells into the Ventral Nerve-roots of Pig Embryos. *Anatomischer Anzeiger*, Vol. 31, No. 11/12, p. 303.
- GURWITSCH, A., '00. Die Histogenese der Schwann'schen Scheide. *Arch. f. Anat. u. Physiol., Anat. Abt.*, Jahrg. 1900, Heft 1-2, p. 85.
- HARRISON, R. G., '01. Ueber die Histogenese des peripheren Nervensystems bei *Salmo salar*. *Archiv. f. mikr. Anat.*, Bd. 57, p. 354.
- KÖLLIKER, A., '05. Die Entwicklung der Elemente des Nervensystems. *Zeitschrift für wissenschaftliche Zoologie, Sonderabdruck*, Vol. 82.
- SCHAPER, A., '97. Die frühesten Differenzierungsvorgänge im Centralnervensystem. *Arch. f. Entwick.-Mech.*, Bd. 5, Heft 1, p. 81. Abstract in *Science, N. S.*, Vol. 5, No. 115, p. 430.