pounds); the abducting strength of the first toe and the adducting strength of the second can be estimated at a strength of five pounds.

In the different positions of the foot in standing and walking the metatarsals and toes are severally moved to aid in balance and in the support of weight.

A certain amount of rotation at the mediotarsal articulation is normal. The strength of the toes is greatest in barefooted individuals accustomed to use extensively the front of the foot in walking.

EXPERIMENTAL STUDIES ON THE INFLUENCE OF THE CENTRAL NERVOUS SYSTEM UPON THE DEVELOPMENT OF THE EMBRYO.

ALFRED SCHAPER.

It is a pretty general conception among embryologists, as well as physiologists, that the central nervous system from a very early embryonic period has a kind of leading or controlling morphogenetic influence upon the development of the entire embryonic body, and upon the differentiation of its organs; or, morphologically expressed, every structural change in the course of development within the central nervous system is accompanied or immediately followed by a certain corresponding alteration in the rest of the organism. This exceedingly fascinating conception appears at the first glance, indeed, very plausible and very satisfactory, especially when we consider how closely the function of every part of the animal body is, later, related to certain and indeed mostly very definite areas of the central organ.

However, thus far no absolute proofs for this theory of a morphogenetic correlation between the central nervous system and the entire embryonic body have been brought forward. On the contrary, many observations in human teratology, especially upon anencephalics and amyelitics, seem scarcely to be in agreement with this conception.

A renewed careful investigation upon this subject appeared to me desirable, and led me to undertake the following *experiments*, by which method of research alone a satisfactory solution of this problem is, according to my opinion, obtainable.

As material for my experiments I selected frog larvæ, for several reasons: *first*, because they are easily procured in large quantities; *second*, they are readily raised, can be kept during development always under direct observation; and *third*, they have an enormous resistance to injuries and a great tendency towards the healing of wounds.

The aim of my experiments was to remove the entire central nervous system or certain parts of it by excision in very young larvæ where the neural tube had just closed, then to try to keep the larvæ alive, observing in the course of further development the consequences of the operation.

For this purpose I operated upon a considerable number of young tadpoles 5–6 mm. in length, by cutting off with a very sharp lancet a dorso-frontal segment of the head which (when the operation was successful) contained usually the entire brain, with the medulla oblongata, the anlage of the eyes, the olfactory and the auditory organs. The vegetative part of the head, especially the mouth cavity and the sucking disks, were always preserved.

After the operation, which was performed in small cardboard boxes with normal salt solution, the larvæ were placed in larger glass vessels with salt solution, containing, besides, some water plants. Here the brainless larvæ soon began to move again, and some even attached themselves, by means of their sucking disks, to the wall of the glass vessel or to the water plants. However, during the first, second, and third day the mortality of these larvæ was rather great; not seldom a half or more of such a set perished during this early period. Nevertheless, I succeeded, by repeated operations, in keeping a sufficient number of larvæ alive for several weeks, during which period they grew considerably and developed their outer shape, save certain defects in the head region, the direct results of the operation. As soon as the larvæ showed any signs of decreasing vitality they were preserved for microscopical examination.

From these larvæ now I wish particularly to describe one which is highly instructive, and, as I think, of especial value for answering the question at issue. This larva was, when operated upon, 6 mm. long, the eyes were visible as minute dark spots, the mouth was not yet open. By the operation, except an insignificant part of the infundibulum, the entire brain, the medulla oblongata, the eyes, the smelling and the hearing organ, were removed, while both sucking disks and the gills remained. The larva recovered very soon from the shock of operation, and regained in a few hours its full mobility and reflex irritability. Its motions were strong, but decidedly atactic, in so far as it swam now on the back, now on the side, and again in the natural position. The operation wound was completely healed after two days. The head then appeared strongly pointed in front and somewhat constricted in the region of the gills. The mouth-opening, formed meanwhile, appeared as a sagittal cleft at the front of the head.

The larva developed for seven days, and gained in volume and size. At the end of the seventh day, however, its vitality seemed to decrease, and I transferred it therefore to the preserving fluid, together with a normal larva of the same breed, for comparison. At this time the operated larva measured 8 mm. in length, being only ½ mm. behind the length of the normal larva.

Thereupon both larvæ were cut in transverse serial sections, and likewise another *normal* larva, which was preserved at that age in which the operation was performed on the other.

In describing and comparing the corresponding sections of these three larvæ I can, of course, not enter into details. I have to confine myself to calling your attention to certain principal points which are especially significant for our present purpose. Series A is made up of sections through a normal larva at the age at which our larva was operated upon.

Turning first our attention to this series, we notice that our larva at the time of operation was still in a very early stage of development. There is still a large amount of fully undifferentiated yolk, and those organs already present are found only in their most primitive state. Comparing this series with series B, representing the state of things in a normal larva at that age at which the operated larva was killed, which means seven days older than the larva of series A, we see that during this period the development has made enormous progress. We can say, indeed, that the morphological differentiation of all the organs in their rough outlines is practically finished.

This proves that our brainless larva during the time of observation has continued to develop throughout a period in which normally the most significant and most revolutionary differentiations and morphological changes in the embryonic body take place. Hence the presumption appears justified that if there exists at all a developmental correlation between the different organs, and especially between the central nervous system and the entire embryonic body, then the elimination of certain parts, or, still more, of the entire central nervous system during such a period, must produce most striking and instructive consequences.

The microscopic examination of our operated larva, therefore, should be apt to throw some light upon these very fundamental processes of development.

Directing now our attention to the illustrations of series C (sections through the operated larva), we notice first the most curious defects and distortions in the area of the operation, in the region of the head, which become still more evident by a comparison of the corresponding sections of the normal larva in series B. *We see the head entirely brainless, without eyes, smelling and hearing organs. Nowhere a trace of regeneration of these organs is to be encountered. The healing of the operation wound was brought about by a proliferation of mesenchymal tissue, which was superficially covered by a layer of ectodermal epithelium.*

Going backward in our series, we find the first traces of a central nervous system at the posterior end of the medulla oblongata in the form of an irregular accumulation of cells, which only by their continuity with the posterior parts are proved to belong to the neural tube. Still farther back, in the dorsal region of the embryo, we find finally *a spinal cord, at least in its morphological outlines. Higher magnification, however, reveals that its cellular constituents are in an extreme state of degeneration, and therefore any specific functional activity of the spinal cord is out of the question.*

These facts show that our larva lived, moved, and developed during seven days without brain and medulla, and during the second half of its life, even without a functional spinal cord, or, in other words, that we succeeded in producing by our experiment not only a living anencephalic, but at the same time an amyelitic frog larva.

Now we come to the principal point of our subject; that is, to ascertain in how far these defects of the central nervous system have influenced the organization of the entire body. Without entering into the many details which a careful microscopic study of the operated larva has furnished to us, I confine myself here to the brief and, as I think, rather surprising statement that *the absence of the central nervous system was practically of no demonstrable importance whatever in the differentiation of the embryo, at least during the period of our experiment.*

By looking over the sections of the operated larva and comparing them with the corresponding ones of the normal larva, it can be seen without difficulty that there are no fundamental differences in the organization of both. All the organs in the operated larva, except those the elements of which were directly removed by the operation, have not only developed in typical shape and correlative arrangement, but have also undergone a typical histogenetic differentiation. And still more, there have new organs and new tissues differentiated, which at the time of operation were not yet present, even in their most primitive form.

There are, indeed, some well-marked distortions of different organs in the head region, but these abnormalities have certainly nothing to do with the absence of the central nervous system; they are simply produced as direct mechanical consequences of the operation and the wound healing, together with a secondary contraction of the mesenchymal scar.

Altogether, we can say that every organ and every tissue has normally developed up to the very level of the scar.

Especial emphasis may be placed upon the fact that all the spinal ganglia, and even some of the cranial ganglia, were perfectly developed without showing the slightest traces of degeneration; that, besides, a peripheral nervous system was present, and the voluntary muscles showed the structure corresponding to that period of development.

What general conclusions, now, may be drawn from these experiments?

1. The central nervous system has, during a certain early period of development, no functional influence whatever upon the vital processes within the developing organism: it neither receives specific centripetal stimuli, nor sends any specific stimuli to the periphery; that is, it has neither sensory nor motor nor morphogenetic functions. In the same way the metabolism is independent of it; we saw the larva grow simultaneously with progressive resorption and assimilation of the yolk. All stimuli, therefore, outer as well as inner, must have met the individual cells *directly* during this period without transmission by means of a conducting nervous system.

2. The elimination of the entire brain with the foundations of the main sensory organs of the head, and the thereby produced alterations in normal topographical correlation to neighboring organs, had no demonstrable influence either upon the further development of the organs, or upon that of the entire organism. All processes of growth and differentiation took place according to typical principles.

3. According to these phenomena the development of the individual parts of an organism during a certain embryonic period takes place according to the so-called "*principle of auto-differentiation;*" which means that the power of developing in a definite direction, and into a definite end product, is from a very early period potentially inherent to the smallest parts of the germ. A correlative development of neighboring organs, or a functional control of the development of the entire organism by a central organ, is nowhere

to be proved. It is, therefore, as a kind of "*mosaic-work*" that the animal body is built up.

In applying these results obtained by experiment to *human teratology* we shall find them, I think, of some use for a rational comprehension of certain monstrosities which have been thus far more or less a puzzle to all observers. Here I have especially in mind some cases of complete anencephaly and amyely. There are cases described in which, in spite of the absence of the entire central nervous system, no fundamental disturbances in the development of the rest of the body were to be encountered. Such cases show an astonishing resemblance to our frog larva, and I think there can be no doubt that the processes which have led to such a result have been in both cases fundamentally the same.

Even the human body, during a long period of intrauterine life, cannot be considered as a functional unity; its development during this time is likewise subject to the law of *auto-differentiation* of its components, which differentiate in a definite direction without any functional or local correlations.

However, we know that after birth practically no part of the central nervous system can be removed without stopping the function of an organ, or a complex of those which are functionally related to the parts of the central organ removed; and still more, we know that these organs undergo a more or less rapid degeneration, ending in complete atrophy. That a human body can live without a central nervous system for a long time after birth is of course out of the question.

How can we bring the results gained by our experiments and the experiences of teratology into harmony with these facts? A recent theory of *Wilhelm Roux*, likewise based upon experiments, may give the desired explanation. *Roux* divides the development of every organism into an early period of what he calls "*organogenetic development*," and a later period of "*functional development*." During the first period the different organs develop by means of an inherited endogenous energy in a definite direction without influence from outer stimuli, that is, by auto-differentiation; during the second period, however, the gradually developed specific function of the individual organ, as well as the coöperative function of all the organs of the body, are the main stimuli for further growth and development, and are indispensable for the normal life of the single organs, as well as of the entire organism.

It is, therefore, during that first period of "organogenetic development" that our frog larva, as well as the human embryo, can develop in the absence of a central nervous system, without fundamental disturbances. However, with the moment they enter the second phase of functional development, that is, when the different organs develop their specific functions, the conditions of normal development become entirely changed. *It is now that the functional coöperation of all the organs of the body is absolutely necessary for further development, growth, and life in general, and therefore the absence of an important organ, and especially of the central nervous system, must be fatal and lead to the death of the organism.* This critical moment varies for different animals greatly. In mammals and in man it seems to lie near the term of birth.

STERILIZATION OF SUTURES.

CHARLES HARRINGTON.

Dr. Charles Harrington described a series of experiments conducted by him on the sterilization of catgut sutures by means of formaldehyde gas. All sizes of catgut were thoroughly sterilized, but under certain conditions they lost both strength and flexibility. Under other conditions only the smaller sizes were injuriously affected. A new series under new conditions is well under way, and thus far gives excellent results. When this is completed the detailed results obtained from all the work will be presented for publication.

DISTRIBUTION OF SUPERIOR MESENTERIC ARTERY.

T. DWIGHT.

Abstract of a paper to be published in the proceedings of the Association of American Anatomists.

It is remarkable that general descriptions of the vessels to the small intestine from this artery should exaggerate the