THE AMERICAN JOURNAL

OF

ANATOMY

VOLUME VIII

1908

PUBLISHED QUARTERLY BY
THE WISTAR INSTITUTE OF ANATOMY AND BIOLOGY
36TH STREET AND WOODLAND AVENUE
PHILADELPHIA, PA.

1224

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THE FINER ANATOMY OF THE BRAIN OF BDELLOSTOMA DOMBEYI.

I. THE ACUSTICO-LATERAL SYSTEM.

BY

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With Eight Plates.

In keeping with its position near the lower end of the vertebrate phylum, Bdellostoma possesses a brain relatively simple in its structure, yet much more complex than that of Amphioxus. It is much less complicated than that of even the lowest fishes, and represents an early and most important stage in the phylogeny of the vertebrate brain. The vertebrate brain plan, already clearly and firmly outlined in Amphioxus, is developed so much farther that all the fundamental brain organs found in higher vertebrates are present in Bdellostoma, and the fundamental divisions and fiber tracts, persistent in all other vertebrates, including man, are clearly defined. The connections between different parts of the brain are, as we would expect to find them, simpler and more direct than in higher forms. Of especial importance is the fact that the fundamental relations are not obscured by the intrusion of the many secondary tracts and centers which are present in the higher representatives of the phylum. Hence, it seemed to us that a careful study of the brain of Bdellostoma, a survey of its paths, and a charting of its relay stations, would throw much light not only on the many intricate questions of brain anatomy, but on that still more intricate and baffling problem, the origin and development of the vertebrate head.

The gross anatomy of the brain of Bdellostoma, together with the peripheral distribution of the cranial nerves, has been worked out in a previous paper (Worthington, '05), and reference will be made thereto for macroscopic relations.

We recognize two main divisions of the brain of Bdellostoma, the Hindbrain, including the medulla and cerebellum, and the Forebrain,

including the midbrain, 'tweenbrain, and forebrain. This division is fundamental and is present in Amphioxus. The Hindbrain will be described first in this and succeeding papers, each one of its component systems being studied both as a separate organ and in its relation to the other brain organs. The present paper is devoted to a study of the Acustico-lateral system, in both its internal and external relations.

Methods.

The material on which this study is based consists of embryos, the young and adult hagfish—species Bdellostoma dombeyi, Lac,—collected by the writers at various times from the Bay of Monterey. The hagfish were caught in traps and kept in healthy condition in a large tank supplied with running salt water. They were taken out as needed and the living tissue treated according to the chosen method. This course was found to be absolutely necessary, as the brain tissue deteriorates very rapidly. When the hagfish were caught by hook and line and died in consequence, brains taken from them within two hours after death uniformly failed to give the Golgi reaction. The methods found most satisfactory for the study of the relations of the fiber tracts in the adult brains were the rapid Golgi method and Cajal's absolute alcohol and ammonium-absolute alcohol silver nitrate methods, though good results along certain lines were sometimes obtained by *intra-vitam* methylene blue staining. The results obtained in these ways have been controlled by brains hardened and cut *in situ* and stained with carmine, hæmatoxyline, etc. We have not been able to obtain the characteristic reaction from experiments with the Weigert methods.

We wish here to express our thanks to Miss Elizabeth Worthington for her kindness in making the wash drawings for Figs. 47, 48 and 49.

The Acustico-lateral System.

The name acustico-lateral system is given to the group of nerves comprising the two ear nerves, the two lateral line nerves, anterior and posterior, and the acusticus nucleus with its connections to other parts of the brain. The nucleus itself is very different in Bdellostoma from what it is in higher forms, even in its nearest relative Petromyzon. In this latter form (Johnston, '02) the *tuberculum acusticum* consists of three distinct parts, a ventro-lateral nucleus, a dorso-median nucleus lying close upon it, and, dorsad to both, separated from them by an

area of fine fibers, a third nucleus, the *lobus lineæ lateralis.* In Bdellostoma, while the *lobus lineæ lateralis* is fairly well marked out, it is not entirely distinct, as in Petromyzon, and there is no differentiation of the other two parts.

The Acusticus Nucleus.—The acusticus nucleus (Figs. 1, 2, 3, 4, 26 and 30) is a long and narrow club-shaped structure, much thicker in its cephalic than in its caudal half. It is about 2.15 mm. long, .675 mm. broad just before it tapers to its cephalic end, about .6 mm. deep at its deepest part about midway of its length, and from .3 mm. to .4 mm. deep through its caudal half. This difference in depth is caused by the arrangement within the nucleus of the entering fibers. It lies in the dorso-mesial part of the dorsal column of the medulla, separated from the dorsal surface of this body by the *fasciculus communis.* It appears somewhat wedge-shaped as it lies in the medulla, its meso-ventral angle being its most ventral part, the dorso-mesial and ventro-lateral surfaces both sloping dorsad. The ventro-lateral surface is comparatively flat, but the dorso-mesial surface, although quite flat in the caudal third of the nucleus, is very convex in the cephalic part. The long axis of the nucleus runs fore and aft in its hind part, but about three-quarters of the length of the nucleus from its cephalic end it bends laterad, at an angle of about 120°, following the curvature of the dorsal column of the medulla.

There are five sets of fibers that enter the acusticus nucleus, those of *r. acusticus utricularis,* of *r. acusticus saccularis,* of *N. lateralis posterior,* and two sets for *N. lateralis anterior.* Of these entering fibers those of *r. acusticus saccularis* are the most caudal set (Figs. 26 and 30). They enter along the lateral face of the nucleus from about 1.1 mm. to 1.3 mm. from the caudal end. Immediately cephalad of the fibers of *r. saccularis,* and with only a break of about .03 mm. between the two groups, the fibers of *r. acusticus utricularis* enter.

The Auditory Fibers.—The auditory fibers of the *r. utricularis* and those of the *r. saccularis* will be considered together because their internal distribution is the same. The fibers are straight and of varying diameters when they enter the brain, some measuring 2.2 microns, while some are no more than .9 microns in thickness. They run cephalo-mesad, at an angle of about thirty degrees with the long axis of the brain until they reach the lateral border of the acusticus nucleus. After entering the nucleus the fibers divide into two branches, one running cephalad and one caudad within the nucleus (Figs. 5, 6, 26

and 30). Each of these branches may, and generally does, divide again, and sometimes a third time. After the secondary or tertiary division one branch will usually continue in the same general direction as before, the other frequently turns mesad. In many cases it could be followed no further, but in some, after reaching a more mesial part of the nucleus, it turned again and continued in the same direction as its fellow. Figs. 6 and 29 are good illustrations of the branching of these fibers. After each branching the fibers are smaller in diameter, and after the secondary branching they also become beaded; the final product in Golgi sections is a very fine fiber bearing round or oval beads (Fig. 29). These ascending and descending fibers form a large central core, extending almost the entire length of the nucleus, and we have not been able to find any direct connection between these fibers and the cells of the nucleus, *i. e.,* no end plates resting against the body of the cell. When, however, the nucleus is studied in methylene blue and Cajal preparations, it is seen to possess, in addition to cells and fibers, an exceedingly fine intercellular network, extending all through it, and composed of the finest fibers thickly beaded with tiny beads. In Cajal sections a few of the finer fibers of the entering acusticus fibers have been found to be connected with this network, and it is probable that this is the destination of all of them.

The Lateralis Posterior.—This lateral line nerve (Acusticus *b,* Worthington, '05) enters the medulla on the dorsal surface at the level of the saccularis fibers, entering the acusticus nucleus directly (Figs. 3, 8 and 10). It runs cephalo-meso-ventrad until it reaches a point about one-third of the way between the dorsal and ventral surfaces of the nucleus; here it turns latero-cephalad, and runs as a distinct bundle of fibers along the mesial edge of the nucleus (Figs. 5, 6 and 11). As it nears the cephalic end of the nucleus, the fibers separate somewhat (Fig. 32), some of them turning dorsad, some ventrad (Fig. 13), to distribute themselves in the dorso-cephalo-mesial angle of the nucleus (Figs. 8 and 14). The fibers measure between 1.8 microns and 2.7 microns in diameter before they turn cephalad, and are of quite uniform size. Afterwards, during their course cephalad, some of them become irregular in outline (Figs. 13 and 32), the thickened parts being ovoid in shape, and sometimes double the diameter of the fiber,—occasionally the irregularities are almost as sharply defined as the beads of the regular acusticus fibers, but this appearance is very seldom seen. Most of the fibers, however, maintain approximately the same thickness as

far as they can be traced. Not many of them branch, but occasionally one is found, after it has turned cephalad, that divides into two branches as in Fig. 32, both branches continuing cephalad. One Golgi slide also showed a few fibers of this nerve which, after division, sent a branch caudad, and one fiber that turned caudad without division. Branching fibers are, however, infrequent.

The Lateralis Anterior.—This nerve is not a separate and distinct trunk like the *lateralis* posterior; instead its fibers join the trunks of such nerves as give most convenient passage to their destination. The largest and most conspicuous bundle of *lateralis* anterior fibers joins the posterior sensory trunk of the *trigeminus* and runs with it to the skin of the side of the head where these *lateralis* fibers supply some if not all of the anterior group of lateral line canals. The fibers of this combined *trigeminus* and *lateralis* trunk pass over the utricular ganglion in close juxtaposition to it, and enter the brain surrounded by the fibers of the auditory utricular root (Figs. 15, 26 and 30). So closely are these fibers intertwined and so difficult are they to follow that, judging from hæmatoxylin sections, it was thought they all entered the acusticus nucleus, and the entire trunk was called *lateralis* anterior (*Acusticus a,* Worthington, '05). With Golgi and Cajal sections, however, their true relations are made plain. Figs. 16 and 17 show the greater part of the fibers of this trunk running meso-caudad in the general cutaneous nucleus, while a smaller part turns directly mesad, entering the acusticus nucleus with a bundle of utricular fibers (Fig. 16). We have not yet succeeded in disentangling this middle bundle of *lateralis* anterior fibers from its accompanying utricular fibers inside of the nucleus. This particular bundle cannot be identified in the Golgi sections at our disposal; the Cajal sections show it to run mesad and slightly caudad to the center of the nucleus, but as the fibers subdivide they are lost in the maze.

The anterior bundle of the *lateralis* anterior is smaller than the posterior bundle just described. It accompanies the anterior sensory trunk of the *trigeminus.* After this trunk has passed through the cranial capsule on its way to the brain, several small bundles of fibers separate themselves slightly from the others, and instead of entering the general cutaneous nucleus directly, like the rest of the trunk, enter the *acusticum* at its ventro-cephalic angle (Fig. 18). These bundles run caudad for a short distance through the ventral part of the *acusticum,* and then those of them that belong to the general cutaneous

system curve laterad into the general cutaneous nucleus (Fig. 18), while the *lateralis* fibers remain behind. As this extreme meso-cephalic part of the nucleus is also the part in which the fibers of the *lateralis* posterior distribute themselves, as previously stated, it may be called the representative of the *lobus lineæ lateralis* of higher forms. This anterior division of the *lateralis* anterior supplies certain neuromasts in the tentacles.

There is a probability that there is still a third division of the *lateralis* anterior which accompanies the *facialis*. After the latter nerve has passed through the cranial capsule on its way to the brain a very small bundle of fibers is given off that runs dorsad. Having penetrated about to the middle level of the utricular ganglion, the bundle appears to divide, sending some of its fibers dorsad with the utricular auditory root, and the rest mesad with the utricular general cutaneous fibers. This bundle is difficult to trace; it is almost impossible to follow it from the *facialis* unless the angle at which the sections are cut is favorable. We have not been able to trace its fibers with absolute surety to their entry into the brain; nor have we succeeded as yet in tracing the *facialis* to its endings in the skin, and consequently cannot state that any of its fibers innervate *lateralis* neuromasts. Lacking this confirmation, we do not care to state positively that this small bundle contains *lateralis* fibers, but can only say that the probabilities are all in favor of this conclusion. If these probabilities should prove to be actualities, then all three of the divisions of the *lateralis* anterior as found in the higher forms, the two that compose the "Dorsal VII" of the Amphibian facial nerve, and the hyomandibular branch, are represented in Bdellostoma.

The Cells of the Nucleus.—When the acusticus nucleus is studied in sections, it is found that the entering fibers form a central core, running fore and aft throughout its entire extent. Cells are interspersed among these fibers, but the great majority of the cells lie outside of the core as a surrounding cortex, and they are massed in particular dorsad and ventrad of the core. The cells may be divided roughly into two classes, large and small.

The Small Cells.—The small cells are in overwhelming majority, and are found all through the nucleus. They measure from 5.9 microns to 8.5 microns in diameter, and the cell body may be round, pear-shaped, or spindle-shaped. They have large round nuclei occupying nearly the entire body of the cell, and one or more prominent nucleoli. In some

Cajal sections fine fibers running towards these cells divide, on reaching them, into two or more fibrils which apply themselves closely to the surface of the cell.

We have not been able as yet to identify these fibers. In the sections where they appear they are impregnated in a somewhat different manner from the ends of the entering fibers, and as yet we have not succeeded in tracing them into definite bundles.

When the small cells are studied in Golgi sections they are seen to belong to both the spindle and multipolar types of cells. Fig. 31 shows two small cells lying in the dorso-cephalic part of the nucleus. The left cell is the more mesial of the two and belongs to the spindle-shaped variety. The fiber running mesad is cut off close to the cell; the other, running latero-ventrad, forks a little beyond the cell, giving rise to three others, all of which run more or less laterad. The one that runs farthest forks again, one of its subdivisions being a fine-beaded fiber. None of the prolongations of this cell run beyond the acusticus nucleus. The other cell is of the multipolar variety, giving off two very fine and two heavy prolongations. The two fine fibers run laterad and mesad. Of the two heavy ones the shorter runs ventrad, the longer dorsad; this latter, about half way of its length from the cell, becomes very fine and beaded with round or oval beads. It penetrates among the fibers of the *fasciculus communis* that overlie the *acusticum*. Figs. 33 and 35 show small cells lying in the ventro-mesial part of the nucleus about midway of its length, close to the fibers of the great ventral commissure. Fig. 33, which likewise sends its axone into the ventral motor column of its own side, is a tri-polar cell, having, beside the axone, one short fine fiber, and one stout one that subdivides later into two fine ones. Fig. 35 is a spindle cell whose mesial prolongation bifurcates, sending one branch dorsad, the other ventrad. The dorsal fiber is cut off close to its starting point, the ventral one divides again, giving off a fine-beaded fiber running mesad, and the axone that runs ventrad, and pierces through the ventral commissure to end in the ventral motor column of its own side.

The Large Cells.—The large cells are few in number compared to the small ones. Occasional ones are found all through the nucleus and a large group of them occurs in the ventral part caudad of the middle. These large cells are generally elongated in shape with large nuclei. Sometimes they are spindle-shaped, as in Fig. 34, sometimes tri- or multipolar (Figs. 36 and 37). These cells, whatever their form, usually

give out very thick protoplasmic processes. Sometimes the axone is found to arise from one of these processes at a little distance from the body of the cell; in other cases, however, it is impossible to distinguish the axone from the other processes.

The connections established by these large cells are quite various. Some of them send their axones ventrad into the ventral motor column of the same side of the brain; some send them across the brain through the ventral raphé. Sometimes they apparently serve to establish connection between different parts of the nucleus. The cell in Fig. 34 lies about in the center of the nucleus and sends one process dorsad and the other ventrad, where it divides in the extreme ventral part. It is possible that the cell processes, though not to be followed in this section, really penetrate beyond the *acusticum* into the general cutaneous nucleus. In some horizontal sections large cells lying in the dorsal part of the nucleus near the middle send axones caudad into the dorso-caudal part. In one section a fiber was seen that, though it could not be traced to a cell, resembled in every particular the axones of the large cells in the same locality; this fiber, first seen in the dorsal part of the *acusticum* of the left side of the brain, slightly cephalad of the middle, crossed to the dorso-caudal part of the nucleus of the right side.

Many of these cells lie on or near the borders of the nucleus and send their processes into adjacent parts of the brain. In Fig. 37 the cell lies on the ventral border of the acusticus nucleus; processes 1, 2 and 3 go into the upper layers of the *acusticum*, while process 4 divides into branches that penetrate into the general cutaneous nucleus. Fig. 38 shows a cell lying in the lateral part of the nucleus that sends process *a* into the nucleus, and processes d^1 and d^2 into the general cutaneous nucleus. In this cell *a* appears to be the axone. Fig. 43 is a similar cell in the cephalic end of the acusticus nucleus which sends its axone into the nucleus, processes d^1 and d^2 into the general cutaneous nucleus, and d^3 among the fibers of the *fasciculus communis*. On the other hand, cells are sometimes found that lie in the general cutaneous nucleus close to the *acusticum* that send some of their processes into the *acusticum* while their axones remain in the general cutaneous nucleus (Fig. 40). Thus the connection is established in both directions between these two important centers of the medulla.

The Secondary Fiber Tracts of the Acusticum.—Thus far we have considered the connection of the acusticus nucleus with other parts of the brain by means of individual cells located in various parts of the

nucleus. We will now describe the outgoing fiber tracts. First are the fibers that cross in the ventral raphé. These fibers come from all parts of the nucleus, run ventro-mesad to its ventro-mesial angle, and cross to the other side of the brain in the raphé without forming a distinct bundle (Figs. 26 and 30). All of the fibers of the raphé distribute themselves in the ventral part of the brain of the opposite side, and it is impossible to differentiate those derived from the *acusticum* from the fibers of a different origin. All that can be said is that by this means a motor connection is established with the opposite side of the brain. A motor connection is also established between the acusticus nucleus and its own side of the brain by means of a large tract that forms about the level of the entering auditory fibers, and crosses the raphé to run directly to the ventral motor tract of its own side of the brain (Figs. 1, 2 and 26). Arrived there, many of its fibers turn caudad, running with the other fibers of this tract. How far they continue cannot at present be stated. Individual cells, both large and small, taking part in the formation of this tract have already been mentioned, and are shown in Figs. 33, 35, 36 and 39.

Another important outgoing tract may be called the *tr. acustico-funiculi.* This tract is forked in the *acusticum.* The dorsal fork arises at the level of the entering auditory fibers and lies on the lateral border of the *acusticum.* It receives many fibers from the interior of the nucleus, fibers that run laterad or caudo-laterad until they reach this tract, but which, upon reaching it, turn caudad and form part of it. Toward the hind part of the *acusticum* this division joins the ventral fork of the *tr. acustico-funiculi.* This ventral division arises in the extreme cephalic part of the nucleus and runs caudad along its lateral border until it nears its hind end. Here, turning dorso-meso-caudad, it rises to the dorsal part of the nucleus, receiving on its way the dorsal division of the tract (Fig. 26). The combined tract leaves the nucleus at its dorso-caudal angle and runs caudad, immediately ventrad of the nucleus *fasciculus communis,* some of whose cells send processes into it, into the nucleus funiculi (Figs. 1, 2, 3, 4, 26 and 30). There is also a small *tractus acustico-cerebellaris.* This tract arises near the cephalic end of the acusticum along the mesial border, near the mid dorso-ventral plane. It runs caudo-mesad close to the mesial surface for about 1.2 mm.; then it turns mesad into the cerebellum, runs slightly dorso-mesad, and crosses to the other side. After crossing its fibers separate and turn cephalad. They run dorso-latero-cephalad in small

bundles for varying distances, and are eventually distributed in the cerebellum (Figs. 26 and 30, *tr. a. c.*). In addition to this definite cerebellar tract an occasional fiber may be seen that leaves the central part of the acusticum and runs cephalad into the cerebellum. There is no indication that these fibers cross.

The Auditory Nerves.

In Bdellostoma there are two distinct auditory nerves, each with its own ganglion, one for each of the two main divisions of the auditory sac. These nerves are the *ramus acusticus utricularis,* and the *ramus acusticus saccularis.*

The Auditory Ganglia.—These two ganglia lie laterad of the medulla between it and the cranial wall (Figs. 15, 21, 22, 23 and 24); they are closely apposed to each other, and the two are wrapped together in a common connective tissue sheath, so that when dissected out they appear as one body, and it requires microscopic study to show their histological separateness. The utricular ganglion (Fig. 47) lies the more cephalad, and is also the larger of the two. It is cone shaped, with its apex directed dorsally. The long axis of its ovoid base runs parallel to the long axis of the lateral face of the medulla. The plane of the base is inclined at an angle of about 15° to the plane of the long axis of the brain. The extreme length of the base of the cone is about 1.37 mm. and its height about 1.25 mm. The caudal face of the cone is not uninterrupted in its slope from apex to base like the other faces. About .9 mm. ventrad of the apex it leaves the *saccularis* ganglion, to which it has been applied, and its face runs ventro-cephalad from this point of division for about .4 mm. It then makes an angle of 18° and runs ventro-caudad for about .4 mm. At this point there is a space of about .2 mm. between the dorsal and ventral limits of the ganglion, and across this entire face the *ramus utricularis* is given off (Fig. 47, VIIIu). Through the indentation mentioned above the *facialis* passes between the cranial wall and the brain (Figs. 21 and 47).

The utricular fibers pass from the ganglion to the brain in two distinct roots (Fig. 47), a dorsal root, whose emergence is confined to the dorsal third of the ganglion (this root consists exclusively of acusticus fibers), and a ventral root emerging along the mesial face from the indentation dorsad about .3 mm., consisting of general cutaneous fibers.

In histological structure the utricular ganglion is found to consist of

two distinct sizes of nerve cells, large ones measuring from 46 microns to 66 microns and small ones measuring from 16 microns to 26 microns. The large cells are found in all parts of the utricular ganglion, but the small cells are largely confined to its ventral portion, although a fairly large number are found in its dorso-caudal part (Fig. 15). They are particularly numerous in its ventro-caudal part (Fig. 21 and 23), but comparatively few are found in the ventro-cephalic part of the ganglion. The large cells are the ganglion cells of the general cutaneous fibers, which innervate the lining epithelium of the ear apart from the sense organs (Fig. 19); the small cells belong to the acusticus fibers. Fig. 23 shows how these two sets of fibers cross in the ganglion to reach their proper paths of entry to the brain.

The general cutaneous fibers enter the brain in numerous bundles arranged in a series along the lateral surface of the medulla and penetrate directly into the general cutaneous nucleus. In Worthington, '05, this is described as an acusticus root, as it was thought at that time that its fibers penetrated to the acusticus nucleus. Golgi sections, which had not been obtained at that time, disprove this completely, as they show that these ventral fibers turn and run cephalo-caudad in the general cutaneous nucleus (Fig. 24). This is not the ventral root mentioned by Sanders, '94, the group of fibers that he calls the ventral root of the *acusticus* being in reality the motor root of the *trigeminus*. Holm, '01, probably saw the root, but did not attach any significance to it, for he speaks of it as "a few fibers that leave the ganglion here and there and enter the medulla."

The *sacculars* ganglion, when stripped of its nerves, may also be considered as a cone, this time an inverted one, its apex directed ventrad, and having the base cut away at its caudal end (Fig. 47). It is about .37 mm. from the base to the apex of the cone, and its greatest cephalo-caudal length is also about .37 mm. The fibers of *ramus sacculars* leave the ganglion in two distinct sets, those of *ramus sacculars* anterior (Fig. 47, VIIIs. a.), leaving from the apex of the cone, and those of *ramus sacculars* posterior (Fig. 47, VIIIs. p.), leaving from the middle portion of the caudal surface. The cells of the *sacculars* ganglion are similar in size and character to the acusticus cells of the utricular ganglion.

The *ramus sacculars* has but one root, a dorsal one that leaves the ganglion at its dorso-cephalic end and enters the brain caudad and dorsad of the dorsal root of the *ramus utricularis*. The saccular nerve does not, apparently, carry any general cutaneous fibers.

The Lateralis Nerves.

The *lateralis* system is but slightly developed in Bdellostoma when compared with its condition as found in higher fishes and the Amphibia. Its peripheral nerves are distributed exclusively to the head, but both anterior and posterior *lateralis* nerves are represented, and the sense organ canals and isolated lateral line organs, neuromasts, are also present. The *N. lateralis* posterior leaves the brain as a distinct cranial nerve, while the fibers of the *lateralis* anterior are bound up with and accompany both trunks of the *trigeminus*. There are indications that a few of them may also accompany the *facialis*.

There are two groups of lateral line canals in the head of Bdellostoma, an anterior group, innervated by the *lateralis* anterior, and a posterior group, innervated by the *lateralis* posterior. The anterior group is composed of four, occasionally three, or five short canals, nearly equidistant from each other, and located on the side of the head in front of the eye of its side of the body (Fig. 48). The posterior group lies on the dorsal surface of the head and consists of two divisions; the three (occasionally two) inner canals run meso-laterad, and the outer ones run at a slight angle to the long axis of the body (Fig. 49). These canals are almost impossible to find in the full grown adult, but in young hagfish, about eleven inches long, they are easily seen on heads that have been hardened in chromic acid. A description of their structure and of the effect of different hardening agents upon the underlying tissue has already been given in a previous paper (Ayers and Worthington, '07).

The *lateralis* components in the nerves of Bdellostoma, owing probably to their inferior bulk and the intimate association of the anterior fibers with those of other systems, have been overlooked by most of the previous workers in Myxinoid anatomy, not only by those who were working principally by dissection and dealing with the entire head, but also by those who were working with sections and making a special study of the brain. Sanders, '94, makes no mention of them whatever, not having detected their presence even in the second *trigeminus* trunk, and apparently not having seen that part of the *lateralis* posterior that lies between the cranial capsule and the brain. He seems to have included a description of the peripheral part of the *lateralis* posterior in his "upper division of the *trigeminus*," but his account of the distribution is so brief and vague that it is difficult to tell what he really

does mean. Max Fürbringer, '97, calls the *lateralis* posterior the first spino-occipital nerve. Holm, '01, who has done very good work on the internal structure of the brain of Myxine, and who has produced some beautiful plates, unfortunately follows Sanders in this matter, as in several others of equal importance, and considers the second trunk of the *trigeminus* to be composed entirely of general cutaneous fibers, though he recognizes that its root is distinct from the rest of that nerve. The *lateralis* posterior he has apparently failed to find. None of these writers, even those who have dealt with the internal anatomy of the brain, have shown a true conception of the complex nature of these *trigeminus* trunks; Allis, '03, comes nearest, when he calls the second *trigeminus* trunk *r. buccalis lateralis n. trigeminus II.* He has not found the larger *trigeminus* component of this trunk, but considers it to be solely *lateralis* in character, and declares it to be homologous with the *buccalis facialis* of the higher fishes. In addition to this, Allis finds *lateralis* fibers in the first trunk of the *trigeminus,* and finds also the *lateralis* posterior, which he interprets correctly as a lateral nerve, and, while not feeling sure of its homology, is inclined to call it the *lineæ lateralis vagi.*

Summary.

We find that the several parts of the acusticus nucleus are connected with each other by individual cells and their processes. The *acusticum* is connected with its fellow of the opposite side of the brain and with the general cutaneous nucleus of its own side by individual cells. The connections between the acusticus and general cutaneous nuclei are both numerous and intimate, as shown by the very considerable number of cells lying on either side of the boundary that send out interpenetrating fibers between the two. This close connection tends to support Johnson's theory that the *tuberculum acusticum* and the general cutaneous nucleus have developed concomitantly from the same fundamental part, the dorsal horn of the spinal cord,—the morphological differentiation being due to a division of labor with a specialization of function. Certain cells of the acusticus nucleus send fibers into the *tractus fasciculus communis* just as they do into the general cutaneous nucleus. Whether this is reciprocated by the cells of the *communis* nucleus has not yet been ascertained. The acusticus nucleus is connected with the lobe of the cerebellum of its own side of the brain by individual fibers.

It is connected with the cerebellar lobe of the opposite side by a fiber tract. It is also connected by a fiber tract with the ventral motor column of its own side of the brain, and with the ventral motor column of the opposite side by the great number of fibers that cross in the ventral raphé. It is connected with the nucleus *funiculi,* and hence with the spinal cord, by a tract into which cells of the *communis* nucleus also send processes.

Neither the *trigeminus,* the *facialis,* nor the auditory nerves of Bdellostoma are mono-functional nerves. Each carries at least two, and probably more, sets of functionally distinct fibers. The auditory nerve consists in reality of two distinct nerves, *N. utricularis* and *N. sacccularis. N. utricularis* carries a large general cutaneous component that innervates the lining membrane of the ear apart from the sense organs. The *N. lateralis* anterior runs with both trunks of the *trigeminus* and probably with the *facialis* also. The *N. lateralis* posterior, instead of being associated with the *NN. glosso-pharyngeus* and *vagus,* has a trunk to itself. We have found no trace of lateral nerves or organs in the region of the trunk, consequently a lateral line and nerve *sensu strictu* is not formed in Bdellostoma.

Cincinnati, June, 1907.

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ABBREVIATIONS.

a. = axone.
ac. c. = acusticus cells in the utricular ganglion.
ac. f. = acusticus fibers.
ac. n. = acusticus nucleus.
c. = cerebellum.
d^1, d^2, d^3 = processes of nerve cells.
e. = cavity of the ear.
f. c. = *fasciculus communis.*
g. c. c. = general cutaneous cells in the utricular ganglion.
g. c. f. = general cutaneous fibers of the ear.
g. c. n. = general cutaneous nucleus.
m. = medulla.
s. g. = saccular ganglion.
tr. a. c. = *tractus acustico-cerebellaris.*
tr. a. f. = *tractus acustico-funiculi.*
tr. a. v. = tract from the acusticus nucleus to the ventral motor column of the same side.
u. g. = utricular ganglion.
v. c. = ventral motor column.
v. r. = ventral raphé.
x. = support on which the model of the acusticus nucleus rests.
V_1 = fibers of anterior root of *N. trigeminus.*
V_2 = fibers of posterior root of *N. trigeminus.*
VII = *N. facialis.*
VIII l. a. a = Anterior branch of *N. lateralis* anterior.
VIII l. a. p. = posterior branch of *N. lateralis* anterior.
VIII l. p. = *N. lateralis* posterior.
VIII s. = *r. saccularis N. acustici.*
VIII u. = *r. utricularis N. acustici.*

PLATES.

PLATE I.

FIG. 1. Model of acusticus nucleus, dorso-lateral angle. × 18⅓.

FIG. 2. Model of acusticus nucleus, cephalo-ventral angle. × 18.2.

FIG. 3. Model of acusticus nucleus, mesial surface. × 14¼.

FIG. 4. Model of acusticus nucleus, dorsal surface. × 18.2.

FIG. 5. Ascending and descending acusticus fibers in acusticus nucleus. × 41⅔.

FIG. 6. Branching acusticus fibers in acusticus nucleus. × 41⅔.

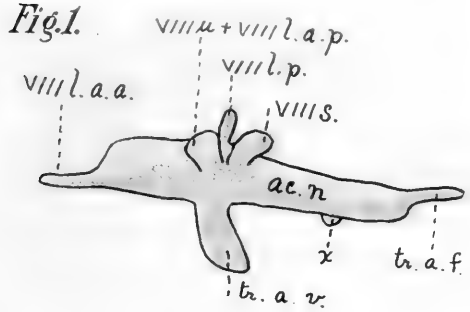
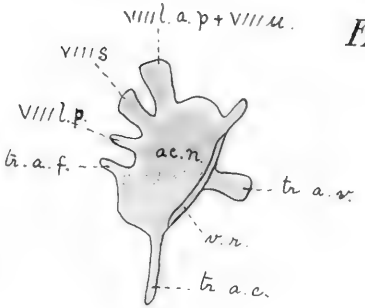


Fig.1.
VIIIm + VIIIl.a.p.
VIIIl.p.
VIIIl.a.a.
VIIIs.
ac.n
x
tr.a.f
tr.a.v.


VIIIl.a.p + VIIIm.
Fig2.
VIIIs
VIIIl.p.
tr.a.f.
ac.n
tr a.v.
v.r.
tr a.c.

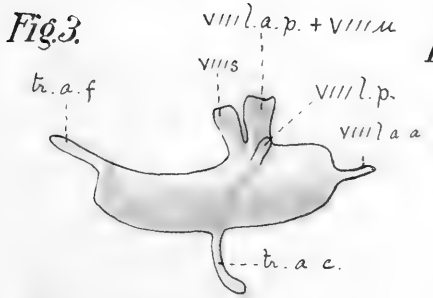


Fig.3.
VIIIl.a.p. + VIIIm
VIIIs
tr.a.f
VIIIl.p.
VIIIl a a
tr.a c.

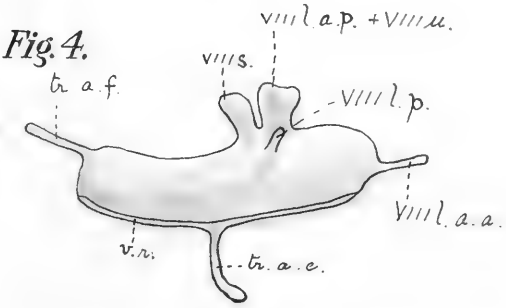


Fig.4.
VIIIl.a.p. + VIIIm.
VIIIs.
tr a.f.
VIIIl.p.
VIIIl.a.a.
v.r.
tr.a.c.

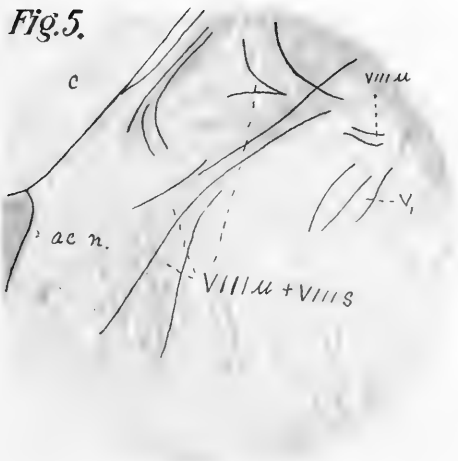


Fig.5.
c
VIIIm
V1
ac n.
VIIIm + VIIIs

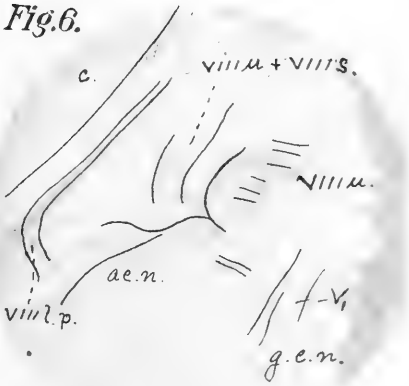


Fig.6.
c.
VIIIm + VIIIs.
VIIIm.
ae.n.
V1
VIIIl.p.
g.e.n.

Fig. 1.

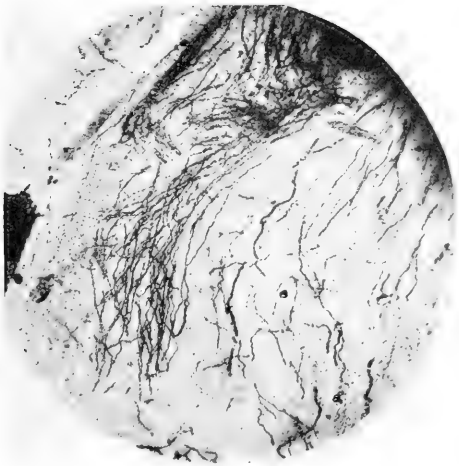
Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.



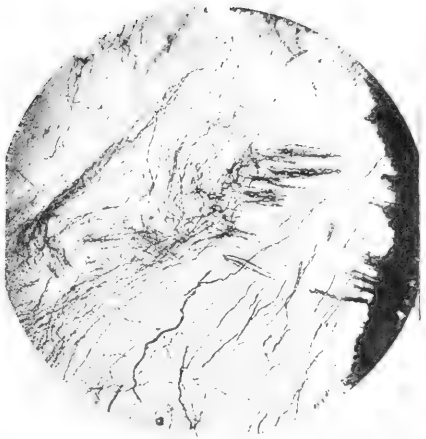


PLATE II.

FIG. 7. Descending acusticus fibers in acusticus nucleus. × 41⅔.

FIG. 8. Entrance of *N. lateralis* posterior into acusticus nucleus (sagittal section). × 66⅔.

FIG. 9. Fibers of *N. lateralis* posterior and *N. acusticus, rr. utricularis et sacculares*. × 66⅔.

FIG. 10. Entrance of *N. lateralis* posterior into acusticus nucleus (cross section). × 66⅔.

FIG. 11. Acusticus nucleus through entering fibers. × 41⅔.

FIG. 12. Acusticus nucleus through entering fibers. × 66⅔.

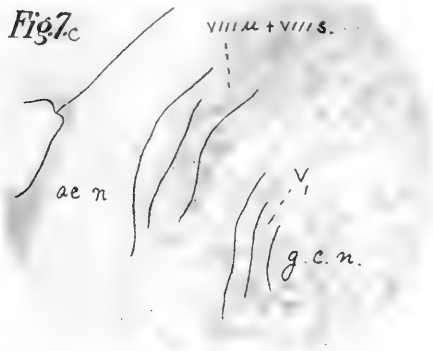


Fig.7.
VIIIm + VIIIs.
ae n
V
g.c.n.

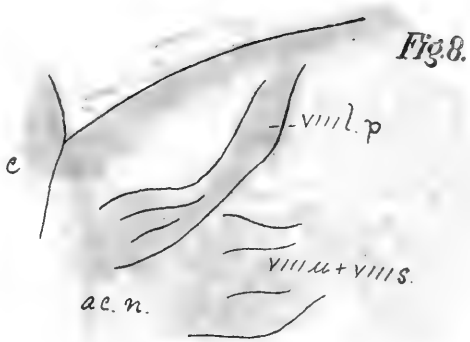


Fig.8.
c
VIIIl.p
VIIIm + VIIIs.
ae.n.


Fig.9.
VIIIl.p
VIIIm + VIIIs.

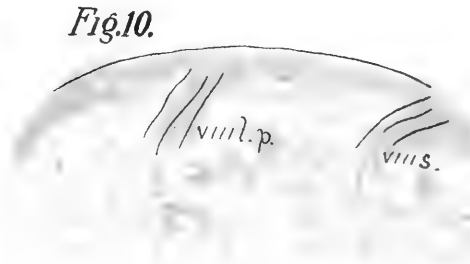
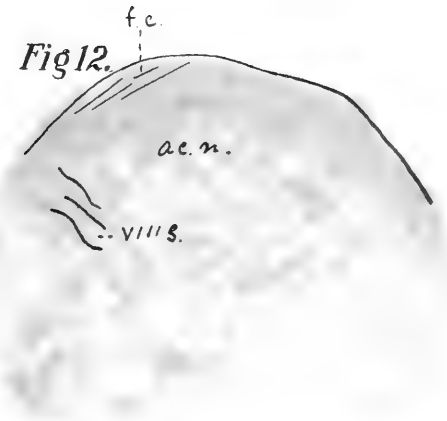
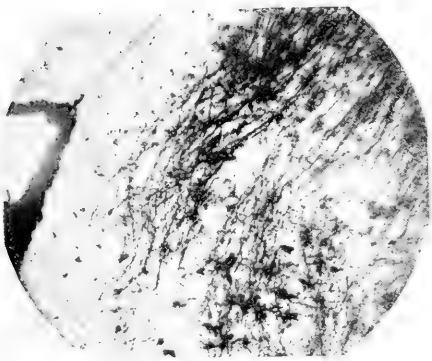
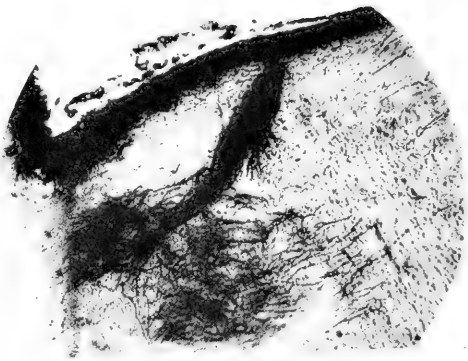
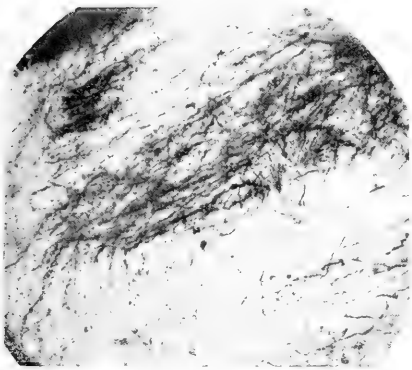
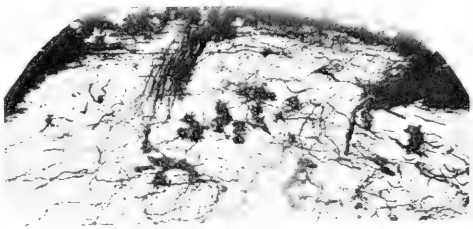


Fig.10.
VIIIl.p.
VIIIs.


Fig.11.
VIIIl.p.
ae n
VIIIs+VIIIm.
VIIIm.
v.n.
v.c.
V
g.c.n.


f.c.
Fig.12.
ae.n.
VIIIs.

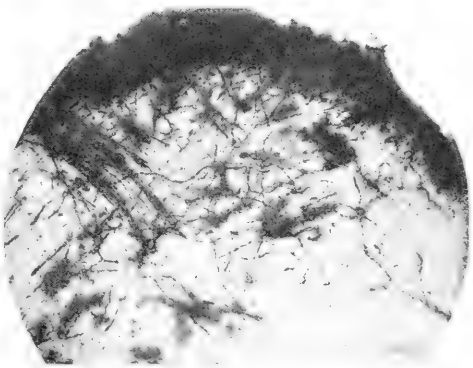


PLATE III.

FIG. 13. Fibers of *N. lateralis* posterior. × 150.

FIG. 14. Cross section of dorsal columns of medulla, near the cephalic end. × 41⅔.

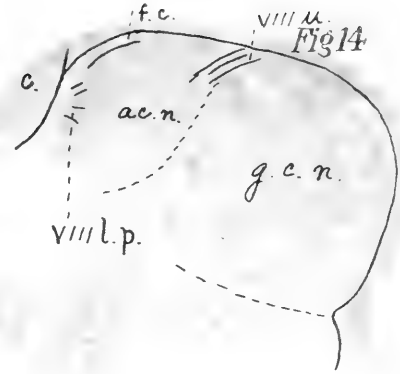
FIG. 15. Utricular and saccular ganglia and root of *N. trigeminus II* (horizontal section). × 66⅔.

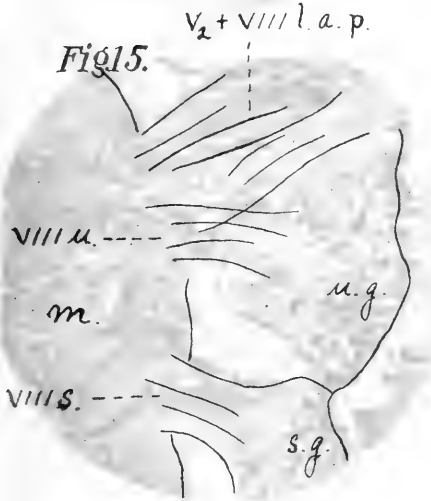
FIG. 16. Entrance of posterior branch of *N. lateralis* anterior with *N. trigeminus II* into the medulla. × 108⅓.

FIG. 17. *N. trigeminus II* within the medulla. × 41⅔.

FIG. 18. Entrance of anterior branch of *N. lateralis* anterior with *N. trigeminus I* into the medulla. × 66⅔.


Fig.13.
VIII l.p.


f.c.
VIII m.
Fig14
c.
ac.n.
g.c.n.
VIII l.p.


V2 + VIII l.a.p.
Fig15.
VIII m.
m.
m.g.
VIII s.
s.g.

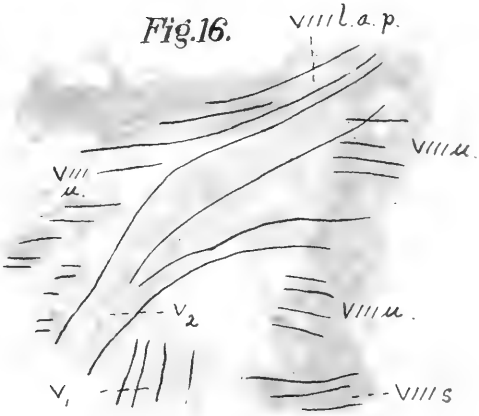


Fig.16.
VIII l.a.p.
VIII m.
VIII m.
V2
VIII m.
V1
VIII s

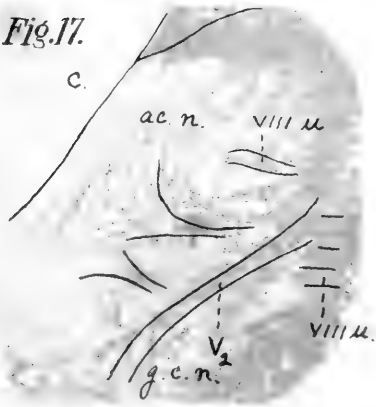


Fig.17.
c.
ac.n.
VIII m
V2
VIII m.
g.c.n.

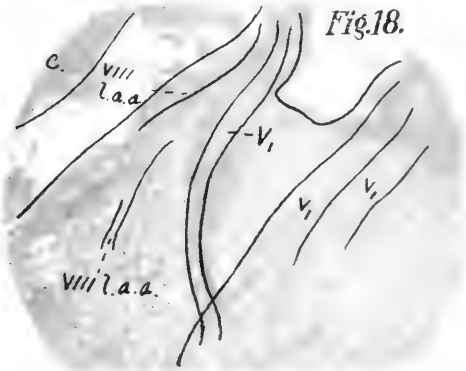


Fig.18.
c.
VIII l.a.a.
V1
V1
V1
VIII l.a.a.

PLATE III.

Fig. 13. [illegible] *N. lateralis* posterior. × 150.

Fig. 14. Cross section of dorsal columns of medulla, near the cephalic end.

Fig. 15. Utricular and saccular ganglia and [illegible] of *N. lateralis* anterior.

Fig. 16. [illegible] posterior branch of *N. lateralis* anterior.

Fig. 17. [illegible] medulla.

Fig. 18. [illegible] of *N. lateralis* anterior.

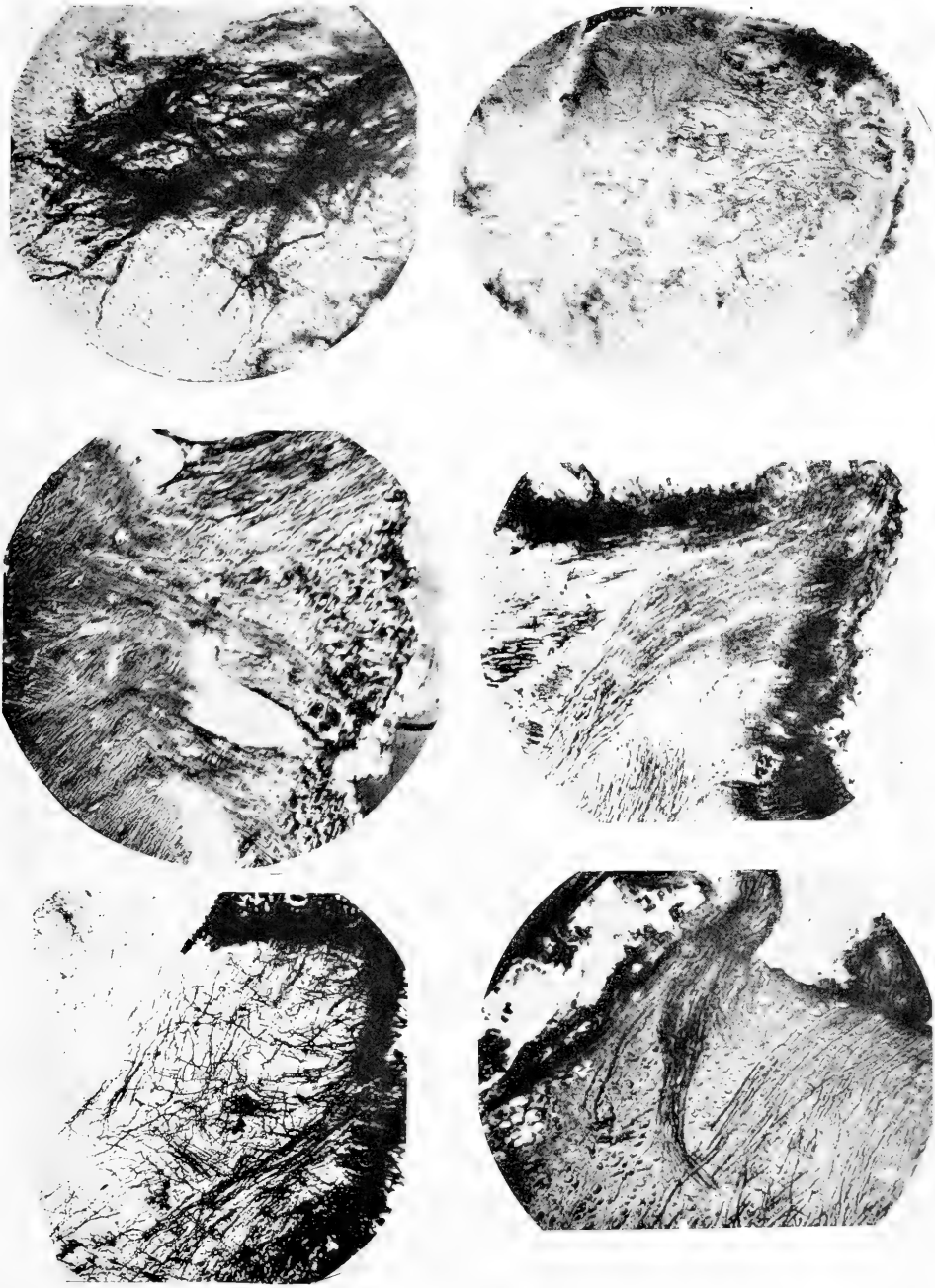


PLATE IV.

FIG. 19. General cutaneous fibers in the ear. × 66⅔.

FIG. 20. Cells lying in acusticus nucleus that send processes into the general cutaneous nucleus. × 66⅔.

FIG. 21. Utricular ganglion and *N. facialis* (horizontal section). × 66⅔.

FIG. 22. Utricular and saccular ganglia near their dorsal surface (horizontal section). × 41⅔.

FIG. 23. Cross section of the utricular ganglion. × 66⅔.

FIG. 24. Entry of general cutaneous fibers from the utricular ganglion into the medulla (horizontal section). × 66⅔.

FIG. 25. Entry of general cutaneous fibers from the utricular ganglion into the medulla (cross section). × 66⅔.

Fig.19.

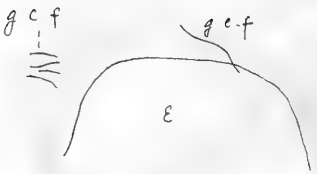


Fig.20.

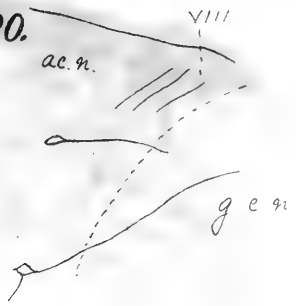


Fig.21

Fig.22.

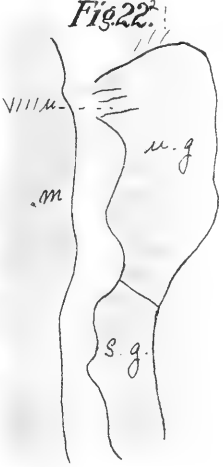


Fig23

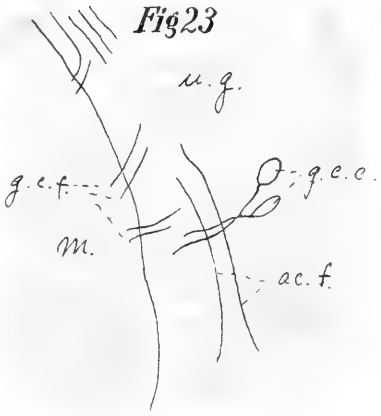


Fig.24.

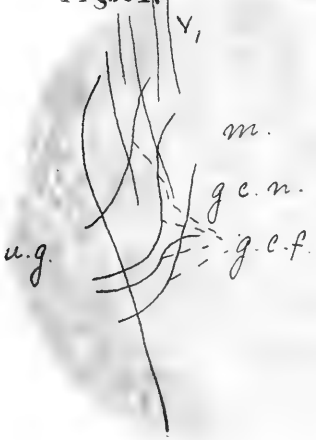


Fig.25.

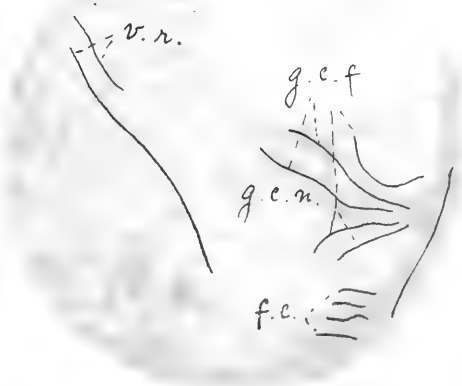


Fig. 25. Entry of general cutaneous fibers into the medulla (cross section). × 66⅔.

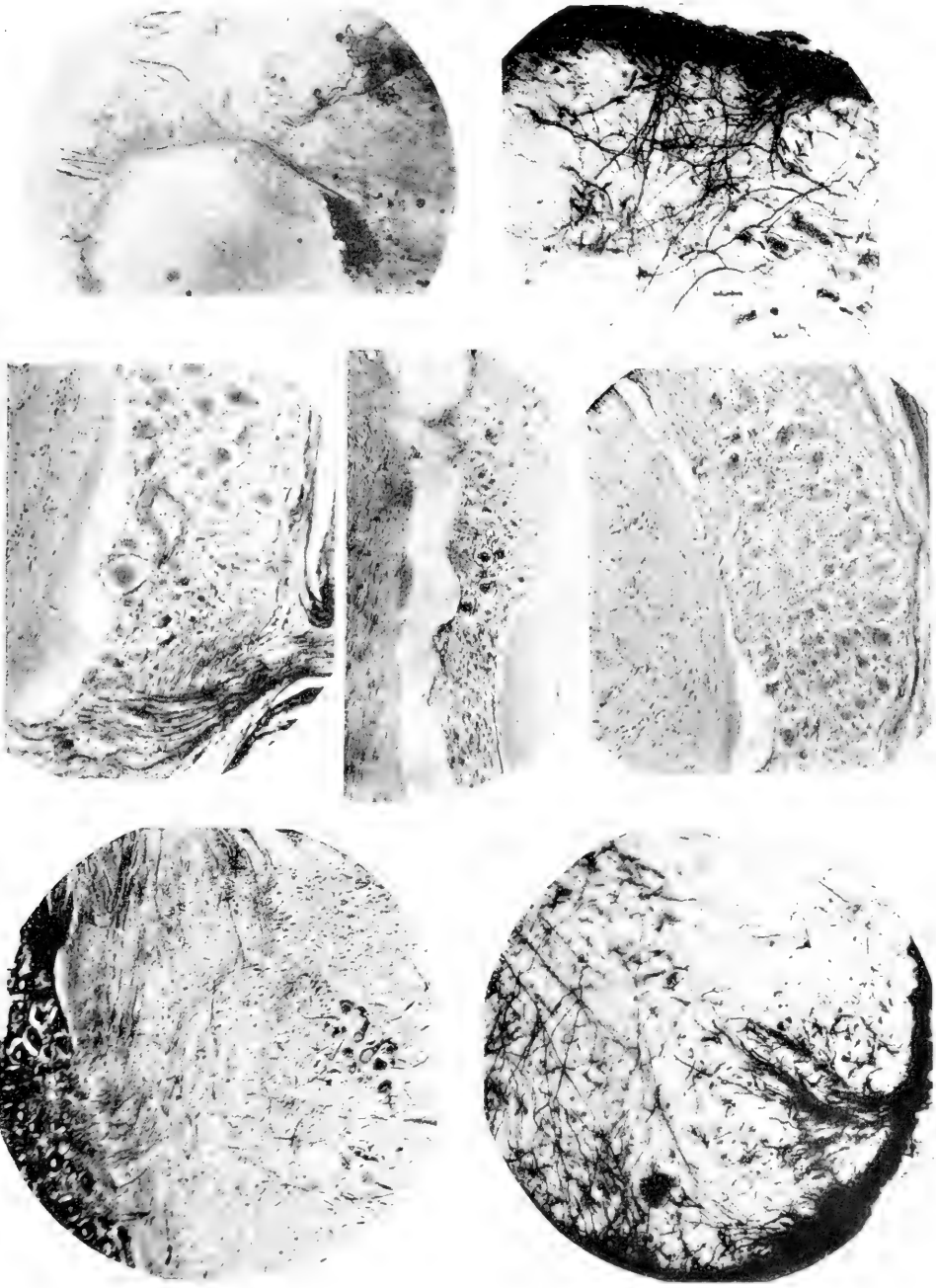


PLATE V.

FIG. 26. Diagram of acusticus nucleus (sagittal). × 24.

FIG. 27. Large cell of acusticus nucleus that sends axone into the ventral raphé.

FIG. 28. Cell of acusticus nucleus. × 250.

FIG. 29. Branching acusticus fibers. × 125.

FIG. 30. Diagram of acusticus nucleus (horizontal). × 24.

FIG. 31. Small cells of acusticus nucleus. × 250.

FIG. 32. Fibers of *N. lateralis* posterior where they begin to separate. × 250.

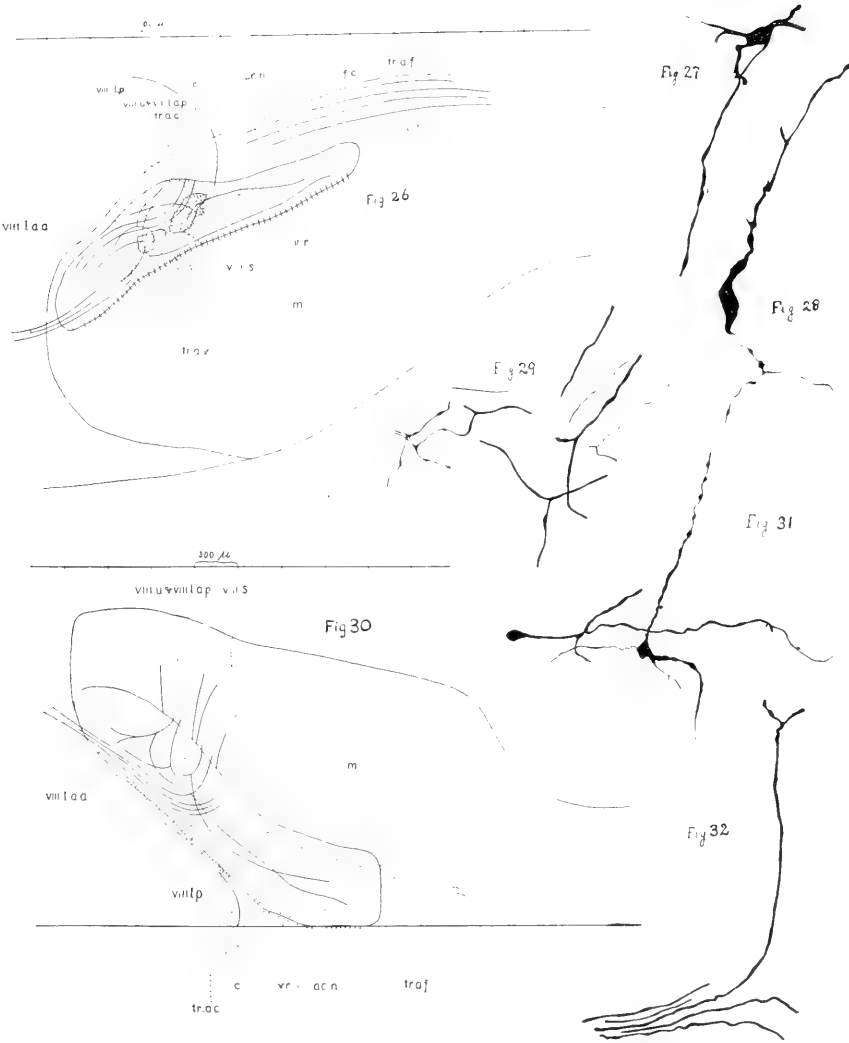


Fig 26
Fig 27
Fig 28
Fig 29
Fig 30
Fig 31
Fig 32
traf
trac
viiitaa
m
trav
300 μ
viiitp
acn

PLATE VI.

FIG. 33. Small cell in acusticus nucleus. *a* runs to ventral motor column. × 250.

FIG. 34. Large cell in acusticus nucleus. *d* ramifies in ventral part, near the general cutaneous nucleus. × 458.

FIG. 35. Small cell in acusticus nucleus. *a* runs to ventral motor column. × 250.

FIG. 36. Large cell in caudal end of acusticus nucleus. *a* runs to ventral motor column. × 125.

FIG. 37. Large cell on ventral border of acusticus nucleus. Processes 1, 2 and 3 go into acusticus nucleus, process 4 into the general cutaneous nucleus. × 458.

FIG. 38. Cell lying near the lateral border of acusticus nucleus. *a* runs into the nucleus, d^1 and d^2 into the general cutaneous nucleus. × 250.

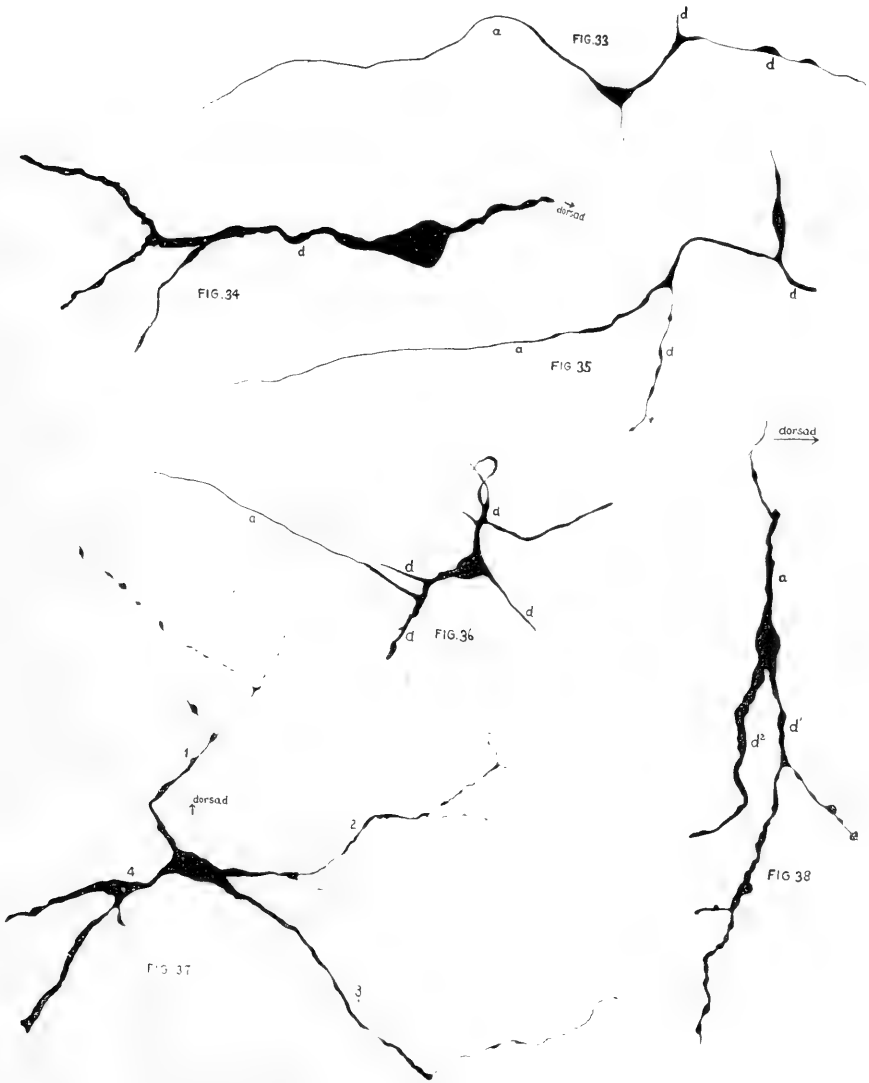

a
d
d
FIG. 33
dorsad
d
FIG. 34
d
a
FIG. 35
d
dorsad
a
d
d
d
d
FIG. 36
dorsad
a
d'
d²
FIG. 38
1
dorsad
2
4
3
FIG. 37

PLATE VII.

FIG. 39. Cell in acusticus nucleus.

FIG. 40. Cell in general cutaneous nucleus. d^1 and d^2 branch in the acusticus nucleus. × 458.

FIG. 41. Large cell in the ventro-lateral part of the acusticus nucleus. d^1 and d^2 reach just outside the nucleus. × 333.

FIG. 42. Spindle cell in acusticus nucleus. It lies at the level of the entry of *r. sacccularis*, and its axis is parallel to the entering fibers. × 250.

FIG. 43. Large cell in the cephalic end of acusticus nucleus. *a* is cut off, d^1 runs to the fasciculus communis, d^2 and d^3 stop among the trigeminus tracts. × 125.

FIG. 44. Group of large cells in the cephalic half of acusticus nucleus. Cell 3 lies just within the lateral border. *d* of cell 3 extends into the general cutaneous nucleus. *a* of cell 4 runs into the ventral raphé. × 125.

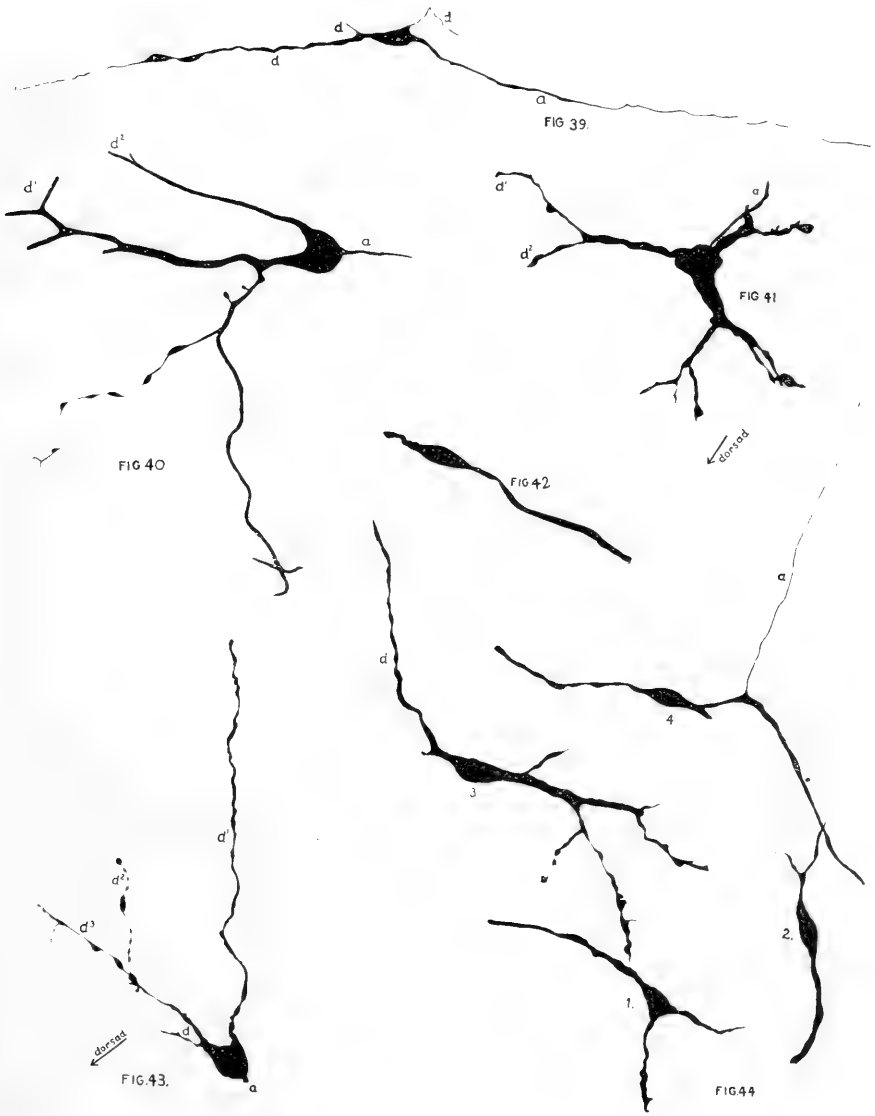


FIG 39.

FIG 40

FIG 41

FIG 42

FIG 43.

FIG 44

PLATE VIII.

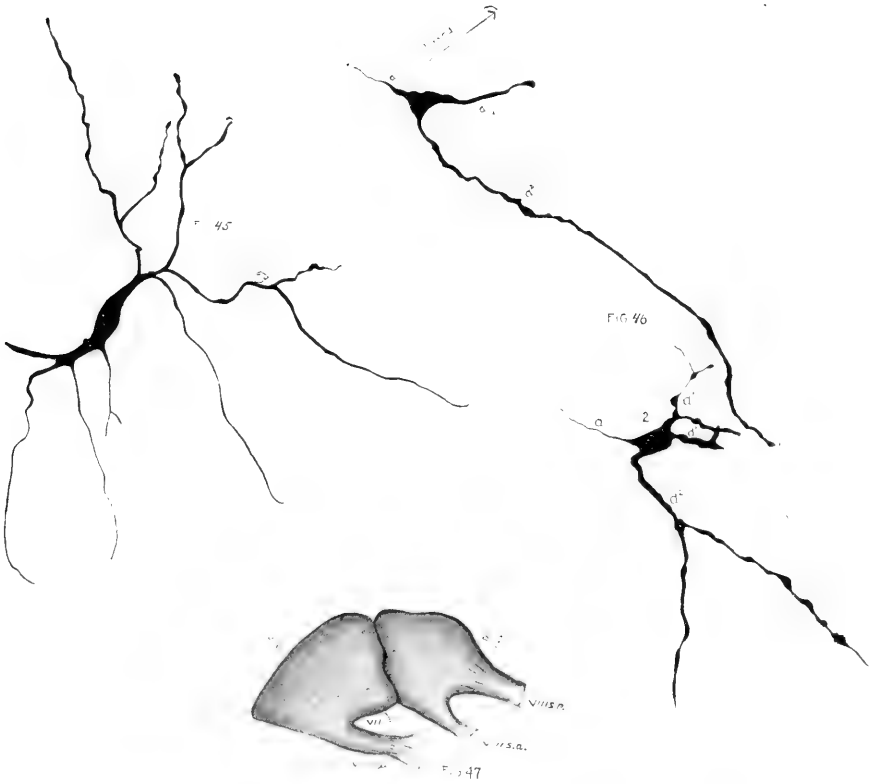
FIG. 45. Large cell in acusticus nucleus.

FIG. 46. Two large cells in acusticus nucleus. d^2 of cell 2 reaches the general cutaneous nucleus.

FIG. 47. The utricular and saccular ganglia. × 24.16.

FIG. 48. Head of a young hagfish eleven inches long, lateral view. × 1⅔.

FIG. 49. Head of a young hagfish eleven inches long, dorsal view. × 1⅔.



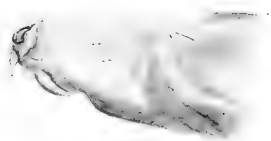


FIG. 48


FIG. 49

A CONTRIBUTION TO THE KNOWLEDGE OF THE OLFACTORY APPARATUS IN DOG, CAT AND MAN.[1]

BY

EFFIE A. READ, PH.D.

From the Laboratory of Histology and Embryology, Cornell University.

WITH 17 PLATES AND 1 FIGURE.

CONTENTS.

STATEMENT OF THE PROBLEM.

1. Position, extent and character of the olfactory epithelium in (*a*) dog; (*b*) cat; (*c*) man.
2. The position and nature of the olfactory cells.

[1]This paper was submitted to the Faculty of Cornell University as a thesis for the degree of Doctor of Philosophy, June, 1907. I wish to express my grateful appreciation to Professor S. H. Gage, whose aid and encouragement made this work possible, and also to acknowledge the abundant material put at my disposal by the Departments of Physiology and Anatomy.

3. The olfactory nerve fibers as central prolongations of the olfactory cells and the character of their termination in the olfactory bulb.
4. The relations of the olfactory nerve fibers in their passage from the sensory epithelium to the olfactory bulb.
5. The position of the vomeronasal or Jacobson's organ and its sensory epithelium and nerves.
6. The relations and terminations of the branches of the trigeminus in the nasal mucosa.

As will be more fully stated in the body of the paper, I have employed in this work the methods necessary for showing clearly the gross anatomy, and for the fine anatomy the three standard histological methods: (1) Gold chloride; (2) chrome silver or Golgi method, and (3) the methylene blue method.

Except where otherwise stated, the results given depend upon repeated gross dissections and upon clear demonstrations by each of the histological methods. That is, no statement has been made which has not been abundantly verified.

Naturally the quality of the human material available did not make all the histological demonstrations and verifications so extensive as for the dog and cat.

1-3. I have demonstrated in the clearest possible manner that the olfactory sensory cells are present in the slightly pigmented mucosa on the conchæ and septum usually designated as olfactory, and that the sensory cells are true nerve cells and their central prolongations are the olfactory nerves, which extend to the olfactory glomeruli in the olfactory bulb. This work is confirmatory of the published results briefly summarized in the historical part of this paper.

My results as to the extent of the Olfactory Region in man differ considerably from those of von Brunn, the latest and most quoted authority upon this point. He shows only a small area upon the septum and superior concha as olfactory (Figs. 28, 29). My dissection shows that the olfactory nerves extend over a much larger area, about one-third of the septum and nearly the whole of the superior concha (Figs. 30, 31).

4. With regard to the relation of the olfactory nerves in their passage from the olfactory cells to the olfactory bulb, the results of my work are strikingly different from the published statements of human and comparative anatomists from the time of Scarpa to the present.

Naturally the conditions are more completely described for man than for the lower animals. The figures of Leveillé have been and still are

frequently copied into text-books (E. G. Barker's Laboratory Manual of Anatomy, 1904; Quain's Organs of the Senses, 1906) and represent pictorially the opinion of anatomists as to the true relation.

Instead of a plexus of the olfactory nerves I have found that the nerves extend in non-anastomosing bundles to the olfactory bulb. All appearance of anastomosis being due (*a*) to a crossing of the bundle of nerves or (*b*) to a net-like arrangement of the connective tissue or blood vessels.

5-6. The position of the vomeronasal organ and its innervation by the olfactory and 5th nerves have been shown in gross preparations of dog and cat. In histological preparations the sensory cells of this organ with their nerves have been demonstrated in the cat and mouse. Branches of the anterior ethmoidal nerve have been traced among the olfactory nerves of the conchæ in dog and cat; their terminations among the folds were not found in gross specimens.

The naso-palatine nerve was found on the septum in all gross preparations. Nerves with free terminations were seen in histological specimens, both on the nasal septum and in the conchæ; it is thought that these are the endings of the 5th nerve.

These facts are in agreement with the results of other workers.

Historical Summary.

The olfactory region has been a subject of special investigation for many years. Various opinions concerning the endings of the olfactory nerves have been published. Some views have been disproven, but as early as 1856 Max Schultze had established with considerable certainty the true conditions of the endings of the olfactory nerves in the nasal mucosa. A review of the literature will give the present standpoint.

Eckhard, 1855, found that the olfactory epithelium of the frog was formed of two kinds of cells, a cylindrical cell and a fusiform cell. These were morphologically and physiologically distinct. The cylindrical cell, an epithelial cell, had a central bifurcating end which terminated in the subjacent layer. The fusiform cell was entirely different from the epithelial cell. He suspected a difference in function, and thought, without doubt, that one was the true termination of a nerve fibril; but he did not say which one.

Ecker, 1855, published his observations on the olfactory mucosa of man and some mammals. He saw two kinds of cells, a cylindrical cell

and a fusiform cell. The cylindrical cells reached the free surface and were connected, according to Ecker, by the central prolongations with the olfactory fibrils. These he called the true olfactory cells. The fusiform cells, replacement cells, situated at the base of the epithelium never reached the free surface. These replacement cells were simply stages in the development of the olfactory cells. Thus there was, according to Ecker, only one kind of cell, but in different developmental stages.

Schultze, 1856, worked on man, mammals, birds and amphibia. He found three kinds of cells, olfactory cells, epithelial cells and stellate cells. The epithelial cell was long, with a prismatic peripheral end. The central end was a short process and was connected with neighboring epithelial cells through side processes. These cells were pigmented but not ciliated. Between the epithelial cells he found cells of a peculiar chemical reaction. The cell bodies were round and had two processes, one reaching the free surface of the epithelial cells and the other passing to the connective tissue. This central process was the finer and could be recognized by the enlargements. The peripheral process was wide, at first, but tapered quickly and was then the same width to the surface. It bore at the end six to ten long brush-like hairs which were free in the air current of the nose. He describes each epithelial cell as surrounded by at least four to six of these hair cells.

In a comparison of these peculiar fiber cells of the olfactory region with other known cell forms, he first emphasizes the fact that in no other epithelial layer, either in the nose outward from the olfactory region, or back in the air tubes, is a trace of such varicose fiber cell found. The stellate cells, which lie under and between the surface cells, do not have the form, length or nature of the other cells of the olfactory region.

He believes the nerve cells of the retina to be the most favorable for comparison with these cells. By a comparison of these with the bipolar cells and by a comparison of the chemical reaction of the two cells, it is highly probable, according to Schultze, that these cells are also ganglion cells. He adds that comparative researches have made it as good as certain that the varicose fiber cells of the olfactory region are nerve cells. It, however, lacks proof of a direct connection with the fiber of the olfactory nerve. He concludes by saying that it is highly probable that the varicose fiber cells are the peripheral ends of the olfactory nerves. It is to these cells, and not to the epithelial cells, as Ecker thought, that the name olfactory cell should be given. These cilia-

bearing cells serve both to collect the molecules of odorous substance and to serve directly in their perception.

In 1862 he still had never seen the olfactory fibers connected with the bipolar cells, but believed there was no ground to doubt this, and says: "The future will prove this view through observation."

Exner, 1872, alone disagreed. In his work on amphibia, birds and mammals, he could find all intermediate stages between epithelial and olfactory cells; the epithelial cells had all the characters attributed to olfactory cells. He believed that the olfactory nerve fibers reached the superficial connective tissue and terminated in a special greatly reticulated layer, the subepithelial network. From this network pass two kinds of fibers, one of epithelial cells, one of olfactory cells. This network forms, with the two kinds of cells, the terminal apparatus of the olfactory nerve. Exner says: "It would be difficult to say whether all parts of this apparatus serve in the same degree in the olfactory perception."

Cisoff, 1874. By use of isolation methods, Cisoff claims to have seen the nerve cell with a long central varicose process, and also to have seen the connection of these cells with nerve bundles. His work, however, seems not to be credited.

von Brunn, 1875, worked on cat, dog, rabbit and sheep. He found the epithelial cells and the olfactory cells. The olfactory cells were pear-shaped with a round nucleus. Beneath the epithelium the central process joined with other processes to form a network in which stellate cells were found. The olfactory nerves were broken up in the same manner in the upper part of the mucous membrane. He did not see the direct connection of these fibers with the central processes of the olfactory cells, and says, "I can only declare such a connection as possible." Both these and the retinal cells are, according to von Brunn, bipolar sense cells with similar function. For mammals, he describes a membrana limitans olfactoria, which covers the epithelial cells as a whole. The peripheral processes of the olfactory cells project through pore-like openings in the membrane.

In 1880 von Brunn modifies his views concerning this membrana limitans, and thinks it lies underneath the "rudimentary cilia" of the epithelial cells.

Ehrlich, 1886, by methylene blue established with certainty the direct connection of the olfactory fibers and the bipolar cells of the mucosa. This stain is very transitory and lasts only a short time, so the work was not credited until confirmed by the Golgi method.

Arnstein, 1887, confirms Ehrlich's work. He saw the olfactory cells with the central thread-like processes passing into the nerve bundle of the submucosa. He claims also to have seen the same thing in the gold chloride preparations of Cisoff and in the isolated osmium preparations of Dogiel. He, like Ehrlich, used methylene blue.

Ranvier, 1889, found three kinds of cells in batrachians. His general descriptions of these do not differ from those of other investigators. In the frog, salamander, triton, dog and rabbit, Ranvier found a plexus formed from the olfactory fibrils. The central prolongations of the olfactory cells appeared to connect with this plexus. Ranvier claims that the subepithelial plexus described by Exner was above the basal membrane, while the one he found was beyond the basal membrane and hence in the connective tissue. Ranvier does not believe that the fibrils of the olfactory nerve continue directly with the central prolongations of the olfactory cells. He adds that all histologists who pretend to have seen this are victims of a delusion.

Grassi and Castronovo, 1889, worked on dogs from two to six years old. They demonstrated by the Golgi method an olfactory cell with the peripheral process and with the central end connected with a varicose nerve fiber. This fiber is shown as dividing and subdividing in the connective tissue. In one figure two neighboring cells joined. They were undecided whether the supporting cells were such or whether they were also connected with the nerve, but they state "the connection of these cells with the nerve fiber has never been seen," nor have they seen a connection between this supporting cell and the olfactory cell. In the "limiting zone," at the boundary between the respiratory and olfactory epithelium, they find many varicose nerve fibers which are described as ramifying in the deeper and middle layers of the epithelium. From the many horizontal branches there are some which pass up close to the surface of the epithelium and some which end in the cylindrical olfactory cells. The former may end free, but "this is still not determined." They consider it probable that these fibers are olfactory fibers, but they cannot prove it.

They also describe for the cylindrical cells of this zone a varicose central process which appears like the nerve fiber. In some cases these have unmistakable signs of nerve fibers, and one figure shows cylindrical cells joined by these branching processes.

Van Gehuchten, 1890, by his work on the rabbit, has confirmed Cajal's work, and says that Cajal's figures are an almost exact representation

of his preparations. The olfactory fibers unite into thick bundles, but, according to Van Gehuchten, the individual fibers do not vary in size during their entire length.

They are rarely varicose; the varicosity is probably due to an incomplete reduction of the stain. At the base of the epithelium the fibers may turn abruptly or may pass to the olfactory cell directly in a more or less undulating course. The olfactory cell is bipolar, its peripheral end is the longer and reaches the free surface, in some cases where there is no deposit of silver, ending by a cilia-like projection as described by Ranvier for the frog. The central process may be followed for some distance in the connective tissue. Van Gehuchten concludes thus: by methylene blue and by the Golgi method it has been proven that there is a direct continuity of the olfactory fiber and the bipolar cell. There is no plexus, as thought by Exner and Ranvier, no free intraepithelial terminations, nor a connection of the nerve fibers with the cylindrical cells in the limiting zone, as described by Grassi and Castronovo.

von Brunn, 1892, finds the membrana limitans and the olfactory hairs; these are on a bud-like swelling of the olfactory cell. He is not certain whether or not the enlargements are due to reagents. The olfactory hairs come out of holes in the membrana limitans; this limitans is comparable to the homogeneous border which is penetrated by cilia or ciliated cells, and he considers it comparable to a cuticular border.

He has seen the nerves join the olfactory cells and seen them join with other threads, but has never seen free endings which were olfactory fibers. He has seen fibers on the border of the olfactory and ciliated epithelium which pass up into the epithelium, but these did not join with any cell and were therefore free ending fibers.

Retzius, 1892, worked on mouse, cat, dog and rabbit, using the rapid Golgi method. He found two kinds of cells: the supporting cells and the olfactory cells. The supporting cells had a nucleus in the outer third of the cell body. The inner part of the cells had two, three or more wing-like processes which reached to the inner surface of the epithelium. These did not form a fiber. Between these supporting cells were found the olfactory cells. They were bipolar; the cell body was oval or spindle shape with two processes. The outer, thicker process passed to the surface between the supporting cells and bore cilia-like hairs. The inner one was much finer and often varicose. There were several layers of cells, so that the processes were of varying

lengths. The central process had a straight or undulating course. It often passed just under the epithelial layer for some distance and then entered the mucosa to join the olfactory bundle which passed through the foramina of the cribriform plate to the olfactory bulb. The fiber remained often the same width from the olfactory cell to the olfactory bulb; it did not anastomose or divide, at least not before its entrance into the olfactory bulb.

In *mouse* at the transition point between respiratory and olfactory epithelium, Retzius has seen free nerve endings reaching nearly to the surface of the epithelium. He describes them as very fine and varicose, only here and there were small end knots seen, and these did not differ from the varicosities found on the nerve fiber and were not true end knots. He suspects that they are the endings of the 5th nerve, but is not willing to give this verdict.

Cajal, 1894, speaks of his results thus: Our observations prove not only the continuation of a fiber of the olfactory nerves with a bipolar cell of the mucosa, but also the unity and independence of this fiber in all its course as far as the bulb, where it ends by means of a free arborization. The network and the ramification described in the intra or extra epithelial course of these nerves he has not confirmed by the new methods of coloration.

Morrill, 1898, investigated the olfactory organ of dog-fish, using Ehrlich's method. He found continuity of the nerve fiber and cell, and also found free nerve endings. He describes three types of olfactory cells, cylindrical, spindle-shaped and conical; whether the difference in shape is due to function or to mechanical causes has not been determined.

With Reference to the Gross Anatomy of the Olfactory Nerves.—Up to a comparatively short period the olfactory tracts were called olfactory nerves; and further, in speaking of the filaments in the nasal mucosa it was always assumed that they extended *from* the olfactory bulb. In the newer literature, the nerves are described as extending from the olfactory epithelium *to* the olfactory bulb. They are so considered in this paper.

Relation of the Olfactory Fibers and Bundles to the Olfactory Mucosa.—In the newest and most reliable works on anatomy of the present time the authors describe, in their explanations of the olfactory regions of man both for the nasal septum and lateral wall of the nose, a plexus of the large nerve bundles before they pass through the cribriform plate of the ethmoid bone. In many cases the figures of Leveillé

have been used to represent this condition. In cases where the figures used are original, they lack distinctness, which is, no doubt, due to the uncertainty of knowledge of this region.

The idea of a plexus of the nerve bundles is of earlier origin than the work of Leveillé, as will be shown by Figs. 10 and 12. These are copies of the figures of Scarpa, 1785. The ideas of Leveillé did not differ esentially from those of Scarpa, and were, no doubt, strongly influenced by them. Our knowledge at the present day concerning the plexiform arrangement of the olfactory nerve bundles is practically that of Scarpa. Much credit is due Scarpa for his excellent work, the facts of which have formed a basis for the knowledge of that region to the present time, as will be seen by the following résumé of a part of the second book of his Anatomicarum Annotationum.

A series of nerve bundles varying in number with the subject come from the apex of the bulb. These, covered by the meninges, pass through the foramina of the cribriform plate and are spread out as nerves of olfaction within the nose. The principal branches are arranged in an internal and an external series. The internal send out filaments to the nasal septum. When the nasal membrane is turned back from the septum it is found to be filled with filaments of nerves running down in series. They differ in length, some often so long as to reach the lowest base of the septum and almost touch the floor of the nasal cavity. Others descend only half way. Some pass perpendicularly, while others are arched, as the posterior ones (Fig. 10).

The external series is distributed far and wide through the upper turbinal bones. The longest branches reach from the upper nares to the lowest edge of the middle turbinated bones. These are perpendicular at first and then recurved to the posterior. The posterior ones are arched (Fig. 12). These nerves in their course from the cribriform plate to the pituitary membrane form anastomosing plexiform connections. The plexiform nerve bundles are found in canals of the turbinated bones of the nose, as is admirably shown in the figures of Scarpa (Figs. 11, 12). Not many olfactory filaments go to the lower turbinals, and he questions whether they are of much importance.

There are no olfactory nerves to the membranes of the pituitary sinuses, and hence these are not olfactory in function.

His descriptions of the 5th nerve to the nose are practically those of to-day.

The following are Scarpa's own words concerning the olfactory nerves:

"Rami porro isti copiosiora mox emittunt filamenta, quorum magna pars nudo oculo conspicua, inter membranam pituitariam, & periosteum septi narium a summo ad imum septum decurrunt. . . . Maiores vero rami non intermisso per cribriformem laminam itinere continuos canaliculos superiorum turbinatorum ingrediuntur, intra quos iterum, ac saepe divisi, & ramosi porro pergunt late per turbinata ossa superiora distribuendi. Quo in itinere, utpote canaliculorum quamplures communicationem inter se alunt, crebrisque orificiis ad narium cavitatem hiant; ita nervorum, de quibus loquimur, rami intra hos canaliculos adhuc reconditi anastomosim, & plexuosas copulationes (t) inter descendendum in vicem constituunt, frequentesque propagines extus per patula canaliculorum orificia membranae pituitariae turbinata ossa superiora vestienti largiuntur. . . . Medio modo se habent, qui per mediam turbinatorum superiorum regionem feruntur: nempe quo ad numerum, crassitiem, & incessus rationem; in eo autem discrepant, quod omnium huius provinciae longissimi sunt (x) quippe a summis naribus ad imam usque oram turbinati medii pertingunt. . . . Sed neque ad turbinatum inferius paris primi filamenta deduci plura sunt, quae sin minus suadent, saltem dubitationi locum praebent vehementer. . . . Neque enim ad organi olfactus sedem adscribendi sunt finus pituitarii, quoniam olfactilis nervus membranae eas caveas vestienti filamenta nullatenus tribuit."

For Comparative Anatomy the statements of Milne-Edwards, Cheveau and Owen agree very closely with those in the works on human anatomy.

The following is a generalized statement by Owen:

"The nerves are grouped in all Mammals into a set for the septum and a second for the upper or ethmo-turbinals, a third or middle short set being, in some, distinguished for the labyrinth or roof of the nasal chamber. The branches of the second set, after expanding on the ethmo-turbinals, usually converge to become connected with the lateral nasal branch of the 'fifth.' Their mode of distribution is best seen on the ethmo-turbinal: here they divide, subdivide, expand and anastomose with each other, forming a reticular nervous expanse, with long and narrow meshes, and becoming impacted in the central, or inner, layer of the olfactory membrane."

For the true relation of these nerve bundles see the body of this paper, page 33 and Figs. 24-27.

Methods for Gross Dissection.

The nitric acid method was used for gross dissection. The head was placed in 20 per cent nitric acid for 6-12 hours, depending upon the size; the decalcification had then proceeded so far that the bone could be easily cut.

The bones were removed from the nose and orbit, thus exposing the olfactory bulb, the nasal mucosa and the lining of the maxillary, frontal and sphenoidal sinuses.

As the bone was removed from the mucosa the deepest or attached surface of mucosa was exposed (Figs. 5, 6). It is this surface which must be exposed to view them.

In dog and cat the ethmo-turbinal bones were easily removed, as they are not perforated by the nerve bundles. In man, however, this is not so easily accomplished. The turbinated bones are filled with small canals through which the nerve bundles pass (Fig. 11). There is, therefore, an interweaving of bone and nerve. Much care is necessary to free these bundles without injury. If the specimen is favorable there is a marked contrast between the white nerves and the darker mucosa. This differentiation is destroyed if the material is left too long in nitric acid. The olfactory nerves are very prominent and are spread out in a fan-shaped manner upon the olfactory folds. They stand out with remarkable sharpness as white cords against the darker background of the nasal mucosa (Figs. 5, 6). This is also true of the branches of the 5th nerve which innervate the nose. It is this differentiation and the fact that the nerves lie in the deeper layers of the mucosa next to the bone which made this dissection of the fine terminal branches of the 5th nerve possible. Even under these favorable circumstances it was necessary to dissect under water and in brilliant light (sunlight or electric light) with a magnifier giving 8-12 diameters.

Material prepared by the nitric acid method may be preserved during the dissection in 2 per cent formalin without markedly changing color. This does not hinder the dissection and material will not deteriorate in it. Five per cent formalin is recommended for permanent preservation.

If material preserved in formalin is used, further decalcification may not be necessary. There will, however, be no differentiation in color between the mucosa and the nerves, and the material, therefore, does not give as satisfactory results.

Histological Methods.

Four methods have been used: the rapid Golgi, the mixed Golgi, gold chloride, methylene blue and dissociation methods.

The Rapid Golgi Method.—Fresh tissue was put into osmium-bichromate mixture for 3-4 days and kept in the dark.

3 per cent potassium bichromate.....2 parts.
1 per cent osmic acid .....1 part.

This was changed at least once. The material was then placed in ¾ per cent silver nitrate for 3 to 4 days, being changed several times in the first half hour until no precipitate formed. Dehydration was as rapid as possible, 1½ per cent, 3 per cent and 8 per cent collodion was used for infiltration. Tissue was left in 8 per cent collodion ½ day without harm and was imbedded in 8 per cent collodion. It was hardened in chloroform vapor for 2 to 12 hours. The knife and block were flooded with 95 per cent alcohol during the cutting; sections were 60 to 80 microns.

The results were very good both in the dog and in the cat. Olfactory cells, with their axones, peripheral processes and the olfactory hairs, could be seen. Sensory cells were found in the vomeronasal organ of the cat. In man the results were less satisfactory, due to the lack of fresh material, but positive verification was obtained.

The Mixed Golgi Method.—Good results were obtained in the dog and the mouse from the mixed Golgi method. (The tissue was treated as for the rapid method, except that it had been previously fixed in Müller's fluid.) The nasal conchæ and the septum of this dog were still cartilagenous, so it was possible to make sections through the entire nose and olfactory bulb. Nerves could be traced for a long distance even through the cribriform plate to the olfactory bulb. Olfactory cells were obtained and also sensory cells in the vomeronasal organ of the mouse.

The Gold Chloride Method.—Both Ranvier's formic acid method and Hardesty's modification of the gold chloride method were used. The difficulty in the use of the former method is due to the fact that the epithelium is very easily exfoliated in fresh material. Good results, however, were obtained from human material by this method. Hardesty's modification of the method[2] gave good results with dog and cat. The dog material had been in 10 per cent formalin for eight years, the cat only a few weeks. Sections were made from 1 to 20 microns. The sustentacular cells were stained as well as the olfactory cells; in fact, the

[2]Hardesty, Neurological Technique.

whole mucosa was stained. The thicker sections proved valueless for the olfactory cell. Sections 1 to 3 microns showed the olfactory cells and in some cases a very small part of the axone. Its course is undulating and can be followed only in thick sections. The peripheral process was easily found.

The Methylene Blue Method.—Huber's modification method was used.[3] Olfactory cells with their two processes were found in dog and cat. The same difficulty was encountered here as with the gold chloride material, much of the epithelium had been exfoliated.

Dissociation Method.—The gold chloride material and fresh tissue were placed in formaldehyde dissociator (2 cc. formaldehyde and 1 liter of normal salt solution) for forty minutes. Olfactory cells with their two processes were obtained in dog and cat.

Gross Anatomy of the Nose.[4]

The cavity of the nose (cavum nasi) is divided into two lateral halves by the nasal septum (septum nasi) (Figs. 15-23). This septum is formed of two parts, the septum cartilagineum or cephalic part and the septum nasi osseum which joins the cribriform plate (Lamina cribrosa). In the dog and cat the septum is extended dorsally by the median parts of the os frontale and os nasale.

In this paper the term septum does not include this area. When referred to, it is designated as the turbinated part of the septum.

The lateral halves of the nose consist of the turbinated bones (conchæ nasales) (Figs. 15-23). In the dog and cat these conchæ may be divided into two parts. The ethmo-turbinals (Figs. 16, 17, 19, 20) and the maxillo-turbinals or concha nasalis inferior (Figs. 15, 18). The ethmo-turbinals are thin plicated bones which are attached to the cribriform plate. In the dog these extend about $^1/_3$ and in the cat about $\frac{1}{2}$ the length of the nose. Figs. 1 and 3 show the mucosa of the ethmo-turbinals (mucosa nasi), but the bones have been removed.

The maxillo-turbinal is also a plicated bone situated cephalad of the ethmo-turbinals. This is a larger bone and much more plicated in dog than in cat.

In man the condition is much different. There are three turbinal bones (conchæ nasales), concha nasalis superior, media and inferior

[3] *Journal of Applied Microscopy*, April, 1898, p. 64. The Methylene Blue Method for staining Nerve Tissue, G. Carl Huber.

[4] The B. N. A. terms are introduced as far as possible.

(Fig. 23). These are plate-like bones and are roughened and perforated (Fig. 11), but not plicated, as in dog and cat (Figs. 17, 20).

The superior turbinated bone is attached to the cribriform plate and is more or less united to the median one which lies ventrad to it (Figs. 11, 23). The inferior is just dorsad of the palate (Figs. 11, 23). The extent of the turbinated bones is relatively much less in man.

The nasal cavity is divided into three regions according to the nature of the epithelial lining.

The vestibule or cephalic part of the nose is lined with stratified epithelium which is continuous with the epidermis. In the respiratory region (regio respiratoria) the epithelium is replaced by the columnar ciliated type (Fig. 43).

The olfactory region (regio olfactoria), with which this paper deals, is adjacent to the cribriform plate. In fresh material the mucosa is slightly yellow, due to the pigment in the sustentacular cells. The extent of this area is relatively much greater in dog and cat than in man. In dog and cat it comprises about ½ of the numerous ethmo-turbinals (Figs. 1, 3, 5), and from $^1/_3$ to ½ of the nasal septum (Figs. 2, 4, 7, 8). With reference to the three sinuses opening into the nasal cavity, viz., the sphenoidal, the maxillary and the frontal, only branches of the 5th nerve could be traced to the mucosa of the sphenoidal and maxillary. This is in agreement with previous workers. In works on human anatomy (Quain, Piersol) only the 5th is given as innervating the mucosa of the frontal sinus.

In the dog and cat there is one scroll (Jayne) of the ethmo-turbinal extending for a short distance into the funnel-like opening of the frontal sinus. This may be in the form of a somewhat curved leaf, the free margin dividing the funnel-like outlet in part or the scroll may be rolled up more completely so that the free end in the frontal sinus is curved and looks like the open mouth of a snail shell. Olfactory nerves ramify in this scroll. In the dog they extend also for some distance into the mesal mucosa covering the bony wall of the sinus opposite the cribriform plate. In the cat the scroll-like projection is more lateral and the mucosa lining the sinus opposite the orbit has the greater number of olfactory nerves. That is, in the dog the olfactory nerves of the mouth of the frontal sinus are toward the middle line, while those in the cat are lateral in position. The brown coloration of the epithelium in the olfactory part of the sinus is marked. From the position of the olfactory nerves in the cephalic part of the sinus and its

opening into the nose, any movement of the air back and forth through the narrow outlet would be likely to bring the odorous particles in contact with the olfactory epithelium. There is a variation of opinion concerning the extent of the olfactory area in man. According to Scarpa, this is very extended. It includes the entire area of the upper turbinated zones (a few filaments going to the inferior turbinal). Some of the nerves of the septum are pictured as reaching the floor of the nasal cavity (Fig. 10). Sappey's pictures show a less extended distribution of these nerves a little less than ½ of the septum; the superior ½ of the middle turbinated bones. According to von Brunn only a small portion of the superior turbinals and a corresponding area of the septum are olfactory in function (Figs. 28, 29). My results are midway between those of Sappey and von Brunn. Figs. 30, 31 were made from dissections and show that the olfactory nerves reach nearly to the free edge of the superior turbinated bone and about ¾ the width of the lateral wall and occupy about $^1/_3$ of the septum.

The Histological Structure of the Olfactory Epithelium.

The epithelium of the olfactory region consists of three kinds of cells: the supporting or sustentacular cells, the olfactory cells and the small stellate basal cells (Figs. 39, 42). In the submucosa serous glands are found; these are known as Bowman's glands and are well pictured in all the books. The ducts of these glands are stained by the Golgi method and pictured in Fig. 41.

The supporting cells are elongated and cylindrical; they have an oval nucleus and a thin cuticular border (Figs. 40, 42). The central end has wing-like processes, often irregular in outline, which project toward the basement membrane between the olfactory cells. This cell was distinguished from the olfactory cell by Eckhard in 1855; but he and other early writers were doubtful as to its true nature. These cells occupy the superficial border of the epithelium and contain pigment. Stellate cells lie near the basement membrane among the processes of the epithelial cells.

The olfactory cells have been studied by four different methods: the Golgi, gold chloride, methylene blue, and dissociation (Figs. 32-38). In all, their position appeared the same. They lie in the middle and deeper layers of the epithelium and send their process between the supporting cells. They are fusiform in shape, with a spherical nucleus

in the central end. The peripheral process is often irregular and reaches the surface of the epithelium. Its outer edge is bulbous and has numerous cilia-like appendages, the olfactory hairs (Fig. 34). These extend beyond the outer border of the epithelium, free in the nasal cavity. The central process is the axone or olfactory nerve fiber. It is very fine and extends in an undulating course into the underlying connective tissue. Only in thick sections could this be followed. These were best seen in the Golgi preparations and in methylene blue material (Figs. 32-34). The sections of gold chloride material showed the axone for a slight distance (Figs. 35, 36). In the dissociated material the axone was generally broken off, but in some preparations axones were found (Figs. 37, 38).

My work agrees with the results of Van Gehuchten as to the shape of these olfactory cells. He believes the varicosities are due to imperfect impregnation. I found both varicose fibers and those which were uniform in outline.

With Max Schultze, I consider these the true olfactory cells. The peripheral process bears the olfactory hairs. The central process is the axone. Early writers described a network for these olfactory axones directly beneath the epithelium as they enter the connective tissue. Recent work has disproven this, and it is now believed that the axone or olfactory fiber "keeps its unity and independence from the olfactory cell to the olfactory bulb," branching only when it reaches the glomerulus of the bulb. In none of my work was the branching or anastomosis of an olfactory fiber seen except at this place. Upon reaching the deepest layers of the connective tissue next to the bone these axones or fibers collect into bundles of various sizes and as olfactory nerve bundles extend to and pass through the cribriform plate to the olfactory bulb.

As has been stated in an earlier part of this paper, almost all authors describe a nerve plexus for these olfactory bundles. This has nothing to do with the network just mentioned, as it concerns only the large nerve trunks and not the individual axones. From the time of Scarpa, 1785, to that of Barker, 1904, and Quain, 1906, the olfactory bundles are pictured and described as forming a plexus on the septum and lateral wall of the nose of man.

If the bone is removed from the orbit and side of the nose (Figs. 13, 14), there is certainly a plexiform appearance of the tissue in which the nerve bundles extend. With a consideration of the gross specimen

only, Scarpa and subsequent authors were justified in their conclusions that the nerve bundles form a plexus in this region. But upon a microscopical examination after differential staining, it is found that the nerve bundles do not anastomose.

This plexiform appearance is due, not to a joining of nerve bundles, but rather to the ramification of the blood vessels and to the arrangement and abundance of the connective tissue which surrounds these vessels and nerves (Figs. 24, 27). The nerves have been traced in these cords of connective tissue. As shown in the drawing and photograph, they pass almost vertically through this to the foramina of the cribriform plate without anastomosis or the formation of a plexus (Figs. 24, 27).

There is but little appearance of a plexus upon the nasal septum (Figs. 25, 26), and the picture of Scarpa (Fig. 10) is much more accurate than are those of Leveillé. Figs. 13, 14, 24 to 27 show strikingly that there is a marked difference in the plexiform appearance of the lateral wall and septum. In both cases, especially upon the septum, there is a crossing and recrossing of nerves, but focusing shows that these do not join. There is, however, some slight joining of the smaller nerve bundles near their origin (Figs. 25, 26).

All authorities on comparative anatomy, wherever the subject is discussed, speak of a plexus of the olfactory bundles. But there is no such marked appearance of this in dog and cat as that found in man. It looks as if the conditions in man had been interpreted for mammals without adequate investigation. Whenever there is an appearance of a plexus, it has been found to be merely a crossing of nerve bundles.

The Olfactory Bulb.

The olfactory bulb has been described by various workers as consisting of from two to seven layers, according to the subdivisions made by these investigators.

Golgi, 1875, describes three layers, olfactory fibers, mitral cells and nerve bundles of the olfactory tract. Van Gehuchten and Martin, 1891, also describe three main layers. In this paper we are concerned only with the olfactory fibers, the glomeruli and mitral cells; we will not enter into the discussion beyond this.

Van Gehuchten and Martin, 1891, worked on the dog and the cat, both adult and young animals, also the rabbit, rat, and mouse. The

rapid Golgi method was used, with results as follows: The olfactory fibrils collect into bundles which go to the glomeruli; these fibers form the outermost layer of the bulb.

Retzius, 1892, says that the nerve fibers divide either at a short distance from the glomerulus or oftener near it. After a repeated and profuse dichotomous branching the fibers weave through the glomerulus, but do not form a network.

Van Gehuchten and Martin, 1891, have seen these fibers bifurcate in the cat and form fibrils of equal thickness, which pass to a single glomerulus, or each may pass to a different glomerulus. Some fibers bifurcate more than once. Thus a single olfactory cell would be connected with two or more glomeruli. "This bifurcation cannot be said to be constant but it is frequent."

The olfactory glomerulus is formed by an interlacing of the terminations of the olfactory cells and the dendrites of the mitral cells. These are independent of each other, that is, there is no anastomosis as was thought by Golgi, 1875. Olfactory fibrils were free in the glomerulus of the cat, the dog, the rabbit, the rat and the mouse, and a number of olfactory fibrils go to each glomerulus.

In the dog they believe the glomeruli to receive dendrites from a great number of mitral cells. In all mammals studied, each mitral cell is connected with a great number of bipolar cells, but each olfactory cell of the mucosa is connected with one, rarely two, mitral cells; at the glomerulus each olfactory fibril terminates generally with only one mitral cell.

In all animals where the olfactory sense is greatest, each bipolar cell may be in contact with several mitral cells, not because the fiber bifurcates and goes to different cells, but because in the same glomerulus may be found the dendrites of several mitral cells.

Personal Observations.

The following are the results which were obtained from the olfactory bulb of the dog and cat. The olfactory bulb was studied in gross preparations and in sections; in the gross dissection the olfactory nerves were traced from the mucosa through the foramina of the cribriform plate to the olfactory bulb. They could be plainly seen lying irregularly upon the bulb (Fig. 4). This was also seen in the transections and sagittal sections of the olfactory bulb and mucosa. Individual

fibers could be traced for a considerable distance, and in some cases fibers were traced nearly through the cribriform plate. The nerves were not seen to bifurcate in the layer as described by Van Gehuchten and Martin, but remained as individual fibers until near the glomerulus. At their entrance into the glomerulus they divide and subdivide to form many branches which interlace but do not anastomose with the other fibers found there. In some cases four or five of these axones were traced into the same glomerulus (Fig. 47).

The glomerulus of the olfactory bulb is formed by the interlacing of branches from the axones of olfactory cells and the dendrites of the mitral cells of the olfactory bulb (Figs. 48-53). (For clearness these have been shown in separate drawings, that is, axones of nerve cells and dendrites of mitral cells are not shown in the same figure.) A glomerulus may be formed by the interlacing fibers from one axone (Fig. 46), and from one dendrite (Fig. 50), or from several axones (Fig. 47), and several dendrites (Fig. 52). While each axone comes from an individual olfactory cell, the dendrites may come from a single or several mitral cells.

In the cat three dendrites from different mitral cells were found in one glomerulus (Fig. 52). Fig. 51 shows three dendrites from at least two different cells. Fig. 53, two dendrites from the same mitral cell. The branching of a single dendrite to different glomeruli was not seen.

In the dog, dendrites from several different mitral cells were traced to a glomerulus (Fig. 49), and a single dendrite was seen to branch to three different glomeruli (Fig. 48).

In man the olfactory bulb has been studied only in gross preparations. The olfactory nerves were traced through the cribriform plate to the outer layer of the bulb. The histology of the olfactory bulb was not studied, but is given by all authors. The glomeruli are formed by an interlacing of the axones of the olfactory cells and the dendrites of the mitral cells, as in lower animals.

Distribution of the 5th Nerve to the Nose.

The nose is innervated by branches of two divisions of the 5th nerve. The anterior ethmoidal (nervus ethmoidalis) of the ophthalmic and the spheno-palatine (nervii spheno-palatini) of the maxillary division.

In the orbit the anterior ethmoidal nerve passes between the muscles of the eye and enters the cranial cavity through the anterior ethmoidal

foramen (foramen ethmoidale) into the cranial cavity. It passes along the olfactory bulb (bulbus olfactorius) (Fig. 3) cephalad through an opening on the cribriform plate and passes along the upper part of the nasal septum (septum nasi) (Figs. 2, 4, 7, 13, 14), where it divides into the external nasal nerve (nervus nasalis externus) and the internal nasal nerves (nervii nasales internii). The external nasal nerve passes along the sulcus ethmoidalis of the nasal bone (os nasale) and passes out to innervate the skin of the nose (Figs. 13, 14). The internal nasal nerve divides into the median nasal (ramus nasalis medialis), which supplies the septum, and the lateral nasal nerve (ramus nasalis lateralis), which innervates the mucosa of the lateral wall.

The remaining part of the mucosa is innervated by the sphenopalatine nerves (Figs. 1, 3). The naso-palatine branch of this nerve (n. palatinus) was traced along the septum to the canal of the incisors (canalis incisivus). It sends several branches into the middle of the septum (Figs. 2, 4). In dog and cat this was traced into the vomeronasal organ (Figs. 2, 4). This nerve was also dissected in man and was traced almost into the organ. The terminal branches were so fine that their complete dissection was not successful.

Free Terminations of the 5th Nerve Within the Nasal Mucosa.

von Brunn, 1892, saw free nerve terminations within the nasal epithelium at the border of the respiratory region. According to him these fibers could not be the olfactory axones, as they were much thicker than those. He, therefore, concludes that they are the endings of the Trigeminus. He quotes Cajal as supporting his decision.

von Lenhossek, 1892, has seen the fibers described by von Brunn, but instead of being thick, as described by that author, those seen by him are finer than the olfactory fibers, varicose and with terminal endings; these did not always reach the free surface of the epithelium. The nerves which are pictured and described by von Lenhossek are like those pictured by Cajal and not of the ordinary much branched appearance of a sensory nerve in epithelium. von Lenhossek did not commit himself as to the origin of these fibers.

Retzius, 1892, pictures in the nasal epithelium of the mouse and cat, both in the respiratory and olfactory regions, fine, much-branched nerve fibers, which end free in the epithelium like other sensory nerves. These are varicose, but not always with an end knot. Retzius wishes to confirm

the appearance of these nerve fibers within the nasal epithelium, but does not wish to give his verdict as to their origin, he adds that it is plausible that these are of a sensory nature. In his work on Fishes he does not find any structures comparable with the "Geruchsknospen" of Blaue. Retzius considers as false the theory of Blaue that there are such structures which have sense cells in direct connection with the olfactory nerve.

Cajal, 1894, in his Système Nerveux denies having committed himself upon the character of these nerves, but ascribes their discovery to von Brunn. According to his work, the endings of the 5th nerve are found only in the submucosa and do not extend into the epithelium. He finds in man fibers which end free at the surface of the epithelium, but these are nearly vertical and end in a conical projection at the top, as is shown by von Lenhossek. He withholds his verdict as to the origin of the fibers thus ending until work then in progress was complete. He has seen them only in the embryo, but never in new-born animals or those several days old.

Disse, 1896, found in the nasal mucosa of some mammals "Epithelknospen" which resemble the taste buds in appearance. These buds are of two kinds, the large buds in the olfactory epithelium and the small buds in the respiratory epithelium. These consist of supporting cells and sense cells, (the sense cells are not ganglion cells). By the Golgi method he traced nerve fibers into the large buds. He considers these fibers as belonging to the 5th nerve. Disse does not credit Blaue's theory that these buds are in connection with the olfactory nerves, but thinks that they have to do especially with the sweet and sour sense of taste in the nose.

Kallius, 1905, has seen the free endings of the 5th nerve in the respiratory and olfactory epithelium of calf. He finds nothing in his preparations, except possibly nests of mucous cells, which in any way resemble the "Epithelknospen" of Disse, nor have any such structures been found in the nasal epithelium of man.

Personal Observations.

I have seen in the nasal epithelium of the kitten a few days old, both in the respiratory and olfactory regions, many much-branched nerve fibers. These were varicose and often ended with a varicosity (Figs. 44, 45). From the gross dissection, fibers from the 5th nerve

pass to the olfactory folds (Fig. 3), and to the lateral wall and septum (Figs. 1-4). It would, therefore, seem probable that the nerves described above are the free terminations of the 5th nerve. My preparations agree very closely in appearance with those of Retzius for the mouse and cat. I find no structure in the nasal epithelium of dog, cat or man which resembles the "Geruchsknospen" of Blaue or the "Epithelknospen" described by Disse.

Organon Vomeronasale.

This organ has been the subject of various investigations; a detailed account is given by Kölliker, 1877, 1883, and Harvey, 1882; von Brunn, 1892; von Lenhossek, 1892; Merkel, 1892; Mihalkovics, 1898. Klein worked on the guinea pig, the rabbit and the dog; von Lenhossek on the rabbit; Harvey on the mouse and the cat; von Brunn on the sheep; Kölliker, Merkel and Mihalkovics on man.

The gross structure, briefly stated, is as follows:

The vomeronasal organ of the dog and the cat is a bilateral tubular organ situated in the ventral part of the septum in the region of the pre-maxillary and maxillary bones. It is either entirely or partially surrounded by a capsule of hyaline cartilage (Figs. 15, 18, 54, 55). At the cephalic end of the nose there are two prominent folds on each side of the nasal septum. The dorsal one is due to a solid fold of the mucosa and to the presence of glands. This is the smaller and passes dorsad of the incisors. The cartilaginous capsule is complete in the cephalic part of the vomeronasal organ of the cat. In the remaining portion in the cat and through its entire extent in the dog this capsule is only partial. As stated above, the vomeronasal organ is tubular and is flattened laterally. It is blind at the caudal end, but opens at the cephalic end into the ductus nasopalatinus. In man the vomeronasal organ is much less developed than in dog and cat. It is a bilateral organ situated in the mucous membrane of the ventral part of the nasal septum (Fig. 21). It is a short blind tube only a few millimeters in length which opens anteriorly into the nasal cavity by a small pore-like opening just above the incisors. This opening was seen both in child and adult. The cartilage of this organ is much reduced and lies entirely below the organ (Fig. 21). The shape of the tube in the dog and the cat varies in the different regions; near the cephalic opening it is circular in transection and lined with stratified epithelium; in the

median and caudal parts it is kidney-shaped and the epithelium is columnar. The median and lateral epithelia differ in thickness; the median is sometimes two or three times thicker than the lateral. In the human which were examined the vomeronasal organ of a 6-7 weeks embryo was flattened as described for the dog and the cat and man, and the epithelium of the median wall was the thicker. In a four months human fetus it seemed to be circular in outline for its entire length, with a uniform thickness of epithelium.

The epithelium, like that of the nasal cavity, consists of sustentacular cells and are longer and narrower than those of the nasal mucosa; the sensory cells found in cat had a process which passed to the surface of the epithelium (Figs. 54A, 55A). These cells have not been found in man, according to Mihalkovics, 1898, and Quain, 1906. According to Klein, the sensory cells are found only in the thick median epithelium. von Lenhossek found olfactory cells in the median and lateral epithelium of an embryo kitten. The central process undivided and unbranched passes into the submucosa as a fine varicose nerve fiber. No olfactory hairs were found by von Lenhossek, 1892, as a precipitate was present. He saw in the deeper layers of the epithelium of the vomeronasal organ free nerve endings. An end knot was always present, but a little rod often projected beyond this; according to him, these were either free endings of the 5th nerve or of olfactory nerves whose cells were somewhere in the olfactory course.

von Brunn in Golgi preparations of the vomeronasal organ of the sheep saw the connection of the olfactory cell and nerve. He also found olfactory hairs.

Personal Observations.

Gross Anatomy.

The gross anatomy of the organon vomeronasale, or Jacobson's organ, has been carefully worked out. As has been previously stated, the large nerves of the nose lie in the deepest layers of the mucosa next to the bone. In order to see these, it is necessary to remove the bone and thus to expose the back or deepest parts of this mucosa. The nitric acid method described above made this possible. The mucosa was freed from the cartilaginous septum, being careful not to tear the nerves which lie almost on the bone. Figs. 2, 4, 8, 9 show such a dissection. In the dog and the cat the vomeronasal organ was also intimately con-

nected with the palate, and this was divided in the median suture. The most successful dissection of this organ in those cases was obtained by sawing the entire head in two from front to back, including both the nose and the brain; the entire septum being on one side. The cartilage and the bone were then removed from the mucosa. The vomeronasal organ was found as an elongated flattened fold at the cephalic end of the nose, just above the palate (Figs. 2, 4, 8, 9). Its small cephalic end passes ventrad to the incisors and opens into the ductus naso-palatinus, which leads from the oral to the nasal cavity. In man the position of this organ is somewhat different (Fig. 21). It is found some distance above the palate and not in intimate relation with it as in the dog and the cat. It opens directly into the nasal cavity. The vomeronasal cartilage is represented by only a small piece of cartilage which lies some distance ventrad of the organ and not enclosing it as in the lower animals (Fig. 21).

I wish to emphasize what has been stated before. It is the deepest layers of the mucosa next to the bone and not the nasal side with which we are at present concerned. There are many nerves in this septal mucosa. These nerves are from two distinct sources: the olfactory nerves, which are connected with the olfactory cells and which can be seen to pass through the foramina of the cribriform plate, and the anterior ethmoidal and spheno-palatine branch of the 5th nerve. The olfactory nerves are found near the cribriform plate (Figs. 2, 4, 7, 9); the branches of the 5th nerve innervate the middle and cephalic parts of the nose (Figs. 2, 4, 7).

There are still several prominent nerves which we have not described (Figs. 2, 4, 8, 9). These are olfactory nerves. They were traced from the olfactory bulb obliquely across the septal mucosa into the vomeronasal organ. In the dog, the cat and man they branch many times just before their distribution in this organ. The vomeronasal organ in dog and cat is also innervated by several branches from the naso-palatine nerve; thus we see that this organ contains nerves from two distinct sources. In man, according to von Kölliker, these olfactory nerves are present only up to the third month of development and atrophy directly after that. Mihalkovics did not find them at all in a three months human fetus. Long olfactory nerves resembling in every way those of the dog and the cat were seen on the septum of a child. These were traced to the vomeronasal organ. The naso-palatine branches were traced nearly to this organ, but the nerve was so fine that further dissection was not successful.

Histology of the Organon Vomeronasale.

Fig. 18 is a transection of the head of an embryo kitten in the region of Jacobson's organ. This shows the position of the organ, the cartilaginous capsule and the thickness of the epithelium. Figs. 54 and 55 will show the complete and partial capsule in the kitten. The fine structure is described by several investigators. I have been chiefly concerned with the sensory cells. In the kitten (Figs. 54A, 55A) sense cells were found. These agreed in every way with the olfactory cells of the nasal mucosa. There are two processes: the thicker, peripheral one, and the fine, somewhat varicose, central fiber. The axone was followed for a considerable distance in the submucosa. No olfactory hairs were found, but in Fig. 54A indications of these are seen in the spike-like process.

I have no hesitation in calling these sense cells nerve cells, apparently identical with those of the olfactory mucosa. Free terminations mentioned by von Lenhossek, 1892, and Cajal, 1894, were not found, but we should consider those, from the gross dissection, to be the endings of the 5th nerve, as several branches of this nerve were traced into the organ. I believe, then, with others, that the vomeronasal organ is intimately connected with the olfactory sense.

Results.

DOG AND CAT.

1. The olfactory nerves are large and numerous in the dog and the cat, relatively less in the cat.

2. About one-half of the ethmo-turbinal folds are olfactory. This is a large distribution as compared with man.

3. All the folds of mucosa adjoining the cribriform plate are olfactory.

4. The mucosa is thick in the olfactory region; thin beyond this; the transition is sharply marked.

5. The mucosa of the septum is in two parts. The upper part is lined by the dorsal turbinated folds; the lower part is lined by a continuation of the mucosa of the cephalic part of the nose. About one-third to one-half is olfactory.

6. The anterior ethmoidal nerve innervates the olfactory folds and septum; its branches extend from the cribriform plate to the tip of the nose; it also innervates the roof and upper lateral wall of the nose. Small branches pass among the olfactory folds.

7. The spheno-palatine nerve innervates the mucosa, cephalad of the ethmo-turbinal folds, the maxillary sinus, the lateral wall of the nose and the maxillo-turbinal folds, also the vomeronasal organ.

8. The vomeronasal organ is a tubular organ found on either side of the septum. It is innervated by olfactory and naso-palatine nerves.

9. The outer layer of the olfactory bulb is formed from the axones of the olfactory cells.

10. The glomeruli of the olfactory bulb are formed by the interlacing of the axones of the olfactory cells and the dendrites of the mitral cells. The number of mitral cells represented in a glomerulus varies in different animals.

MAN.

11. The olfactory nerves are relatively less in number in man than in the dog and cat.

12. They are distributed to the upper third of the septum and to nearly the whole of the superior concha (Figs. 30, 31).

13. The nose is innervated by two divisions of the 5th nerve, the anterior ethmoidal which innervates the anterior part of the septum and lateral wall, and a branch is also sent to the skin of the tip of the nose.

14. The spheno-palatine nerve innervates the lateral wall, the conchæ and the ventral part of the septum.

15. The vomeronasal organ is much less developed in man than in the lower animals. A branch of the olfactory nerve passes to it, at least at the time of birth.

16. The axones of the olfactory cells form the outer layer of the olfactory bulb.

Conclusions.

DOG, CAT AND MAN.

1. The fusiform cells of the olfactory mucosa are true olfactory cells and true nerve cells. They lie in the deeper parts of the epithelium of the olfactory region.

2. The peripheral process is long and cylindrical and reaches the free surface of the epithelium, passing between the sustentacular cells. It bears the olfactory hairs.

3. The olfactory fiber is the axone of the olfactory cell; these collect to form olfactory nerve bundles and pass through the cribriform plate to end in the glomeruli of the olfactory bulb. These nerve bundles do not anastomose to form a plexus.

4. The supporting cells are cylindrical and the inner process is often divided. Stellate cells are found at the base of the supporting cells.

5. The development of the sense of smell in the dog and the cat may be due to the large number of the olfactory nerves and to the extent of their distribution, and, according to Van Gehuchten, to the number of mitral cells with which each olfactory cell is associated.

6. The vomeronasal organ is intimately connected with the sense of smell. It contains, at least in the cat, sensory cells apparently identical with those of the olfactory mucosa.

7. There are free nerve terminations in the olfactory epithelium. These are the endings of the 5th nerve.

In the position of the olfactory nerve cell we apparently have a primitive condition. This is the only case in vertebrates where the nerve cells are within the epithelium, as are those for the tactile sense in many invertebrate forms. In the other organs of sense there is a gradual recession of the ganglion cell until, in the ganglion of the dorsal root of the spinal cord, the central nervous system is approximated. The branches for the tactile sense end freely either in special organs (tactile corpuscles) or in the free end-knots within the epithelium, but do not reach to the surface of it; while the branches of the nerves of other sense organs end freely *among* special cells, but do not reach the free surface of the epithelium. In the olfactory region the olfactory hairs are above the free surface of the epithelium and in direct contact with the air.

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TERMS AND THEIR ABBREVIATIONS IN THE EXPLANATION OF FIGURES IN PLATES I-XVII.

Ax., axone.
Bo., bulbus oculi.
B. olf., bulbus olfactorius.
Crt. v-n.,cartilago vomeronasalis.
Cv. n., cavum nasi.
Cc. eth., cellulæ ethmoidales.
Cbl., cerebellum.
Cbrm., cerebrum.
Ch. n. i., concha nasalis inferior.
Ch. n. m., concha nasalis media.
Ch. n. s., concha nasalis superior.
Ch. n., conchæ nasales.
Cranium, cranium.
D. i., dens inferior.
D. s., dens superior.
Os., developing bone.
Dct. n-l., ductus nasolacrimalis.
F. l. cr., foramen laminæ cribrosæ.
L. cr., lamina cribrosa ossis ethmoidalis.
Lingua, lingua.
Mnd., mandibula.
Mt. n. i., meatus nasi inferior.
Mt. n. m., meatus nasi medius.
Mt. n. s., meatus nasi superior.
Md. sp., medulla spinalis.
M. n., mucosa nasi.
M. s. n., mucosa septi nasi.
M. sn. f., mucosa sini frontalis.
M. sn. mx., mucosa sini maxillaris.
M. c., Meckel's cartilage.
Nn. olf., nervii olfactorii.
Nn. org. v-n., nervii organi vomeronasalis.

N. eth. a., nervus ethmoidalis anterior.
N. mnd., nervus mandibularis.
N. mx., nervus maxillaris.
N. nph., nervus nasopalatinus.
N. sph., nervus sphenopalatinus.
N. org. v-n., nervus organi vomeronasalis.
Orbita, orbita.
Olf. c., olfactory cell.
Olf. h., olfactory hairs.
Org. v-n., organon vomeronasale.
Zyg., os zygomaticum.
Palatinum, palatinum.
R. n. ext., ramus nasalis externus.
R. n. lat., ramus nasalis lateralis.
Rg. olf., regio olfactoria.
Sen. c., sensory cells of the vomeronasal organ.
S. n., septum nasi.
Sn. f., sinus frontalis.
Sn. mx., sinus maxillaris.
Sn. sph., sinus sphenoidalis.
St. c., stellate cell.
Sust. c., sustentacular cell.

PLATE Ia ($\times$ 1.14).

Same as Plate I. To show the lining of the maxillary sinus and its innervation by the 5th nerve.

PLATE Ia ($\times$ 1.14).

Same as Plate I. To show the lining of the maxillary sinus and its innervation by the 5th nerve.

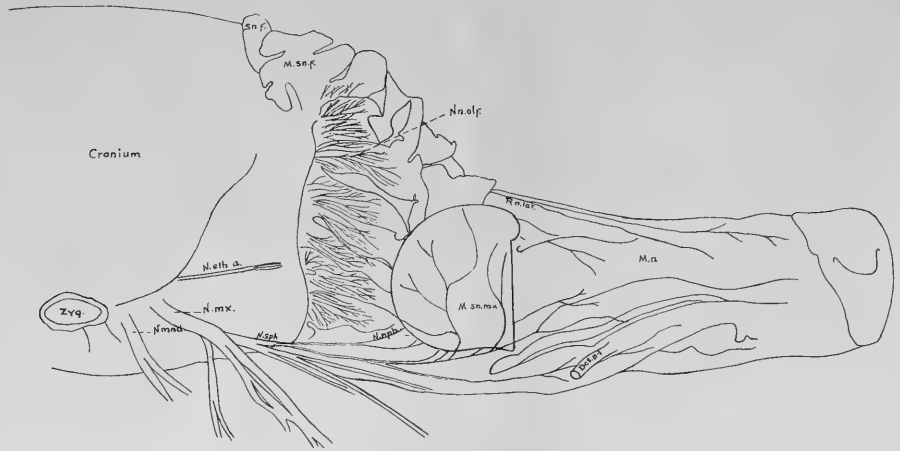

Sn.f.
M.sn.f.
Nn.olf.
Cranium
N.m.lat.
M.r.
N.oth.a.
N.mx.
Zyg.
N.mnd.
N.SPh.
N.opth.
M.sn.mx.
Oesoph.

PLATE I.

FIG. 1 ($\times$ 1.14).

Head of a dog, the bone has been removed from the lateral aspect of the nose and part of the orbit, exposing the deeper layers of the mucosa in which lie the olfactory nerve bundles and their branches.

Note the divisions of the 5th nerve and their distribution to the mucosa of the lateral wall of the nose and to the maxillary sinus.

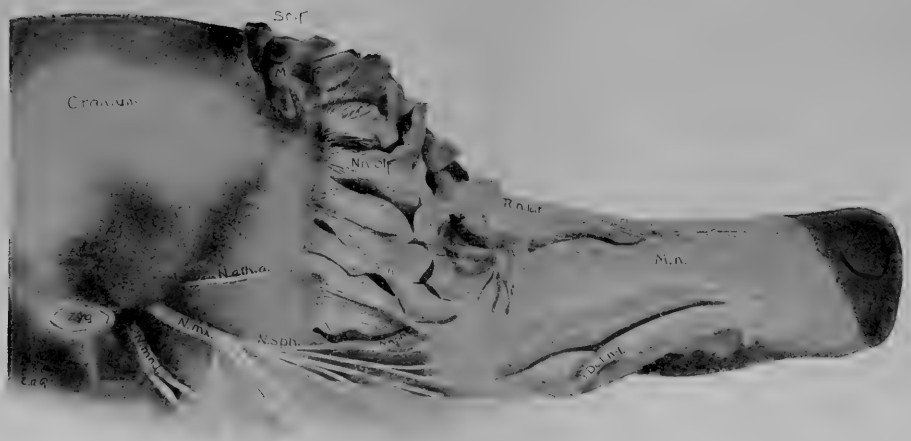

Scl.f
Cranium
N.olf
Rol.f
N.n.
Nath.a.
N.mx.
N.spn.
Ect.f
Ent.f
Ect.g
Ent.g

PLATE II.

FIG. 2 ($\times$ 1).

Median section of the head of a dog, with the mandible and bony septum removed, to show the septal mucosa and its olfactory nerves; the turbinated part of the septum and its olfactory nerves; the vomeronasal organ and its innervation by the olfactory and naso-palatine nerves.

Note the anterior ethmoidal branch of the 5th nerve along the dorsal wall of the septum and its distribution to the septal mucosa.

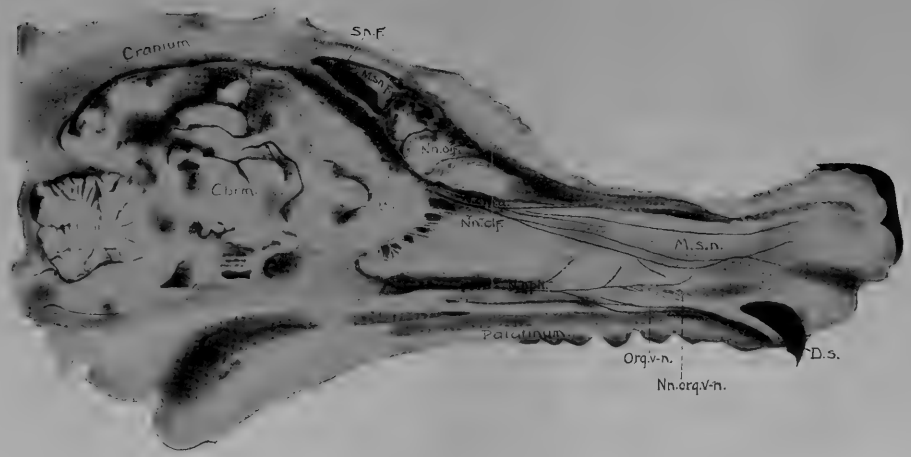

Cranium
Sp.F
Nn.olf.
Cbrm.
M.s.n.
Palatinum
Orq.v-n.
D.s.
Nn.orq.v-n.

PLATE III.

FIG. 3 ($\times$ 1.4).

Head of a cat, except the mandible.

The bone has been removed from the nose, orbit, and a part of the cerebrum, exposing the attached surface of the nasal mucosa. This shows especially the olfactory folds with their nerves, the divisions of the 5th nerve, and their distribution to the lateral wall and mucosa of the maxillary sinus.

Note the small branches of the anterior ethmoidal nerve to the olfactory folds.

FIG. 4 ($\times$ 1.4).

Median section of the head of a cat, without the mandible; the bony septum has been removed to show the deep or attached surface of the mucosa. This is to illustrate the mucosa of the septum and its olfactory nerves; the turbinated part of the septum and its olfactory nerves; the vomeronasal organ and its innervation by the olfactory and naso-palatine nerves.

The anterior ethmoidal branch of the 5th nerve passes along the dorsal part of the septum and is distributed to the septal mucosa.

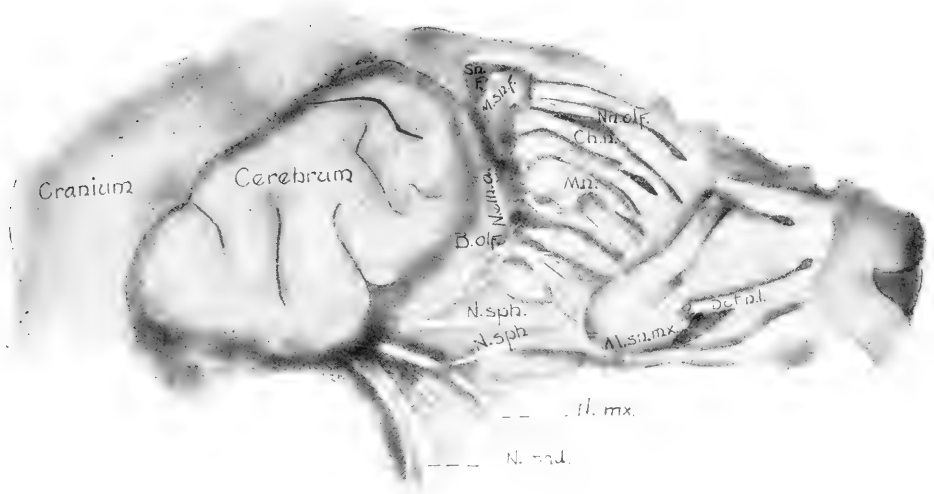

Cranium
Cerebrum
Sn. F.
M.spf.
Nn.olf.
Ch.n.
M.n.
N.lam.a
B.olf.
N.sph.
N.sph
M.s.n.mx.
Pal.n.
__ M. mx.
___ N. pal.

FIG. 3

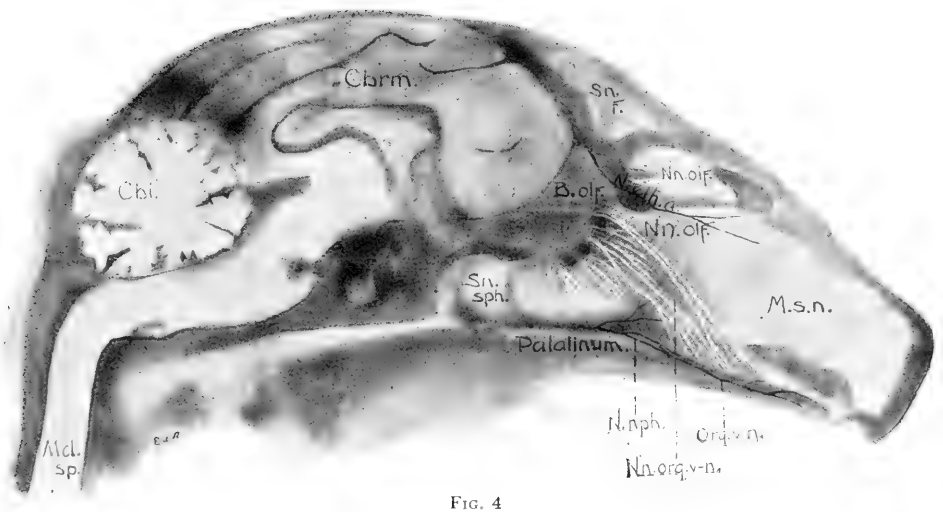

Cbrm.
Cbl.
Sn. F.
Nn.olf.
B.olf.
N.lam.a
Nn.olf.
Sn. sph.
M.s.n.
Palatinum.
N.nph.
Org.v-n.
Nn.org.v-n.
Md. sp.

FIG. 4

PLATE IV.

FIG. 5 (× 1.28).

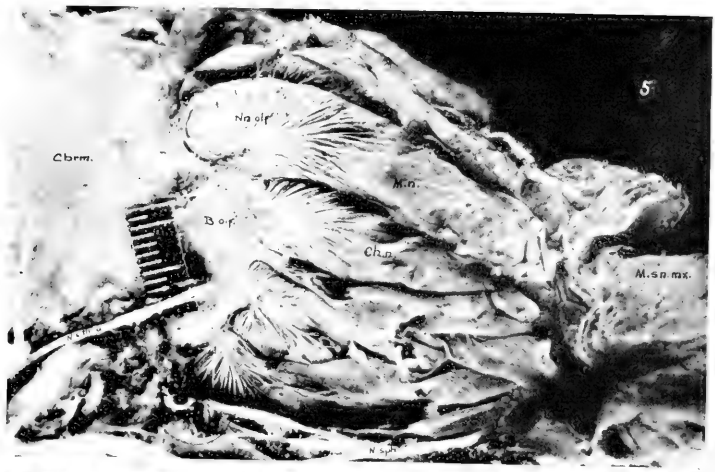
The ethmo-turbinals of a dog, showing olfactory nerves in the deeper layers of the mucosa and the branching of the nerves which lie upon each other. The lining of the maxillary sinus is turned forward to show the thinner part of the folds; these are thick in the region supplied by the olfactory nerves; the thin part is not olfactory. The anterior ethmoidal nerve is shown entering the skull through the ethmoidal foramen.

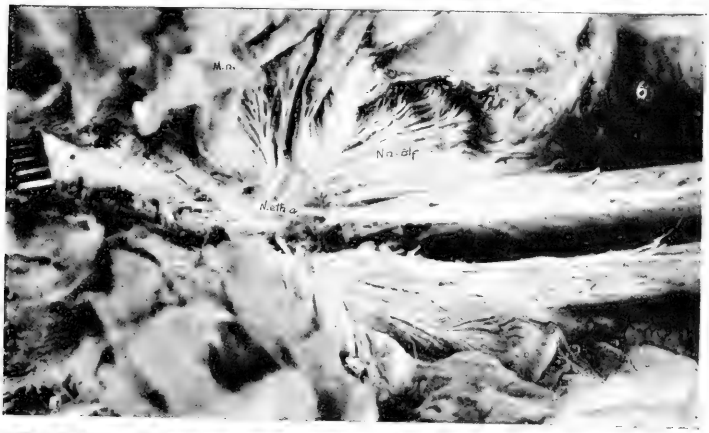
FIG. 6 (× 1.8).

Same animal as shown in Fig. 5. Dorsal view of the ethmo-turbinals to show the olfactory nerves. Note the anterior ethmoidal branch of the 5th nerve to the septal mucosa.

FIG. 7 (× 1.2).

Median section of the head of a dog with the bony septum removed to show the turbinal part of the septum and its olfactory nerves; the septum and its olfactory nerves, the anterior ethmoidal and the naso-palatine nerves.


5
Na olf
Cbrm.
M.n.
B olf
Ch.n.
M.sp.mx.


6
M.n.
Na olf
N.eth.a


7
Na.olf
Cbrm.
B.olf
M.s.a.
Na.olf
Palatinum.

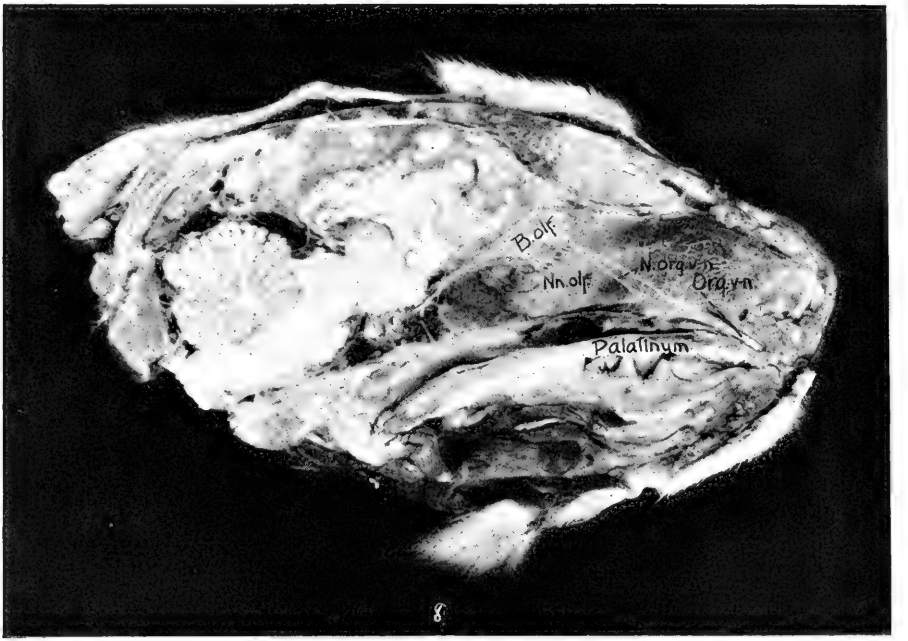
PLATE V.

FIG. 8 ($\times$ 1.07).

Median section of the head of a cat with the bony septum removed, to show especially the olfactory nerves to the septal mucosa and the vomeronasal organ. Note the arterial plexus.

FIG. 9 ($\times$ 3.6).

The septal mucosa of a cat, with the blood vessels injected. To show especially the vomeronasal organ and its olfactory nerves, and the olfactory nerves of the septum. Note the numerous blood vessels. The thicker part of the mucosa is light, the thinner dark.


B.olf.
Nn.olf.
N.org.v-n.
Org.v-n.
Palatinum
8

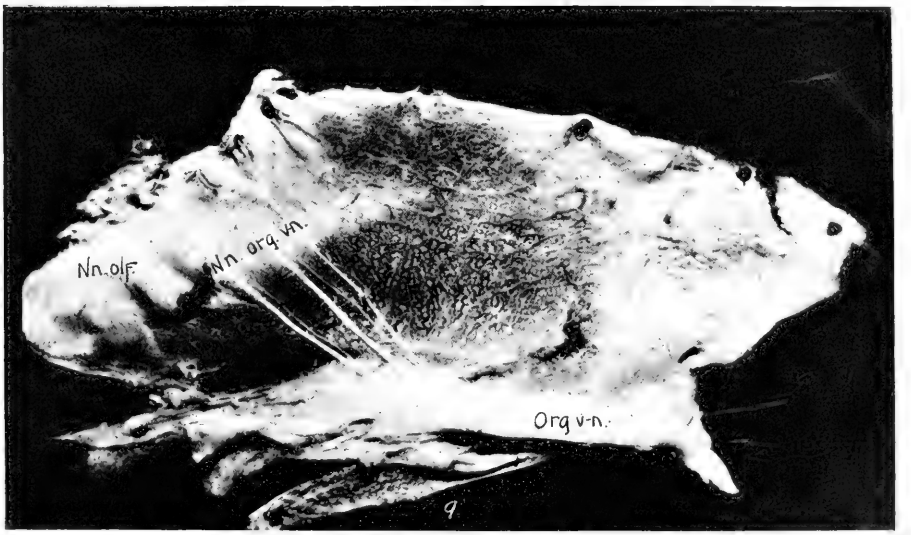

Nn.olf.
Nn. org.vn.
Org.v-n.
9

PLATE VI.

FIGS. 10-12.

Photographs of the drawings by Antonio Scarpa of the nose of man.

FIG. 10.

Median section of the nose of man with the bony septum removed to show the septal mucosa. Note the very large distribution of olfactory nerves. The naso-palatine nerve is also shown.

FIG. 11.

A median section through the skull, septum removed, to show the superior, median and inferior conchæ of the nose. Note the perforated appearance of these bones. The olfactory nerve bundles pass through these canals and within them form an apparent anastomosis. To demonstrate the nerves the bony walls of these canals must be removed piece by piece.

FIG. 12.

Septal mucosa removed to show the superior, median and inferior conchæ. Note the apparent anastomosis of the olfactory nerves and their extent; also the distribution of the 5th nerve.

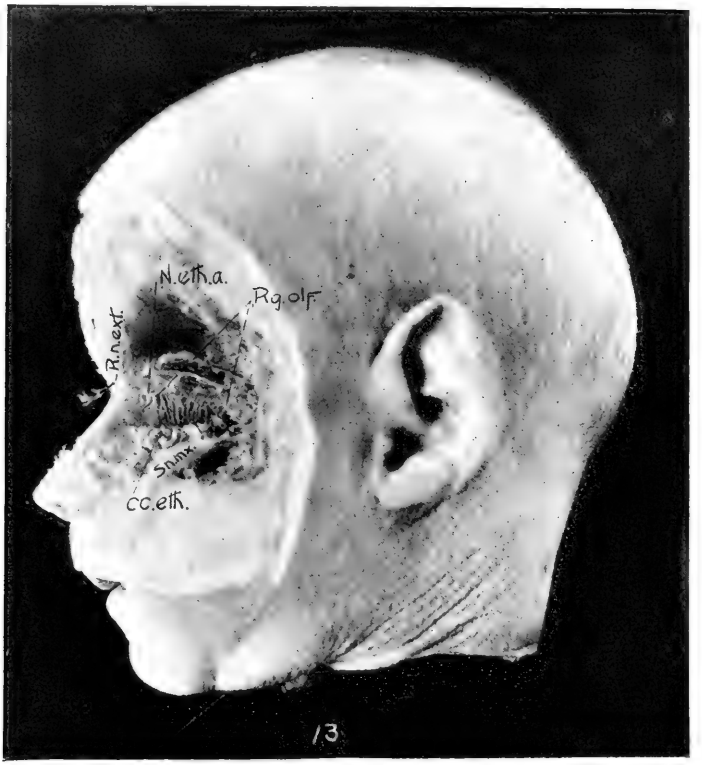
PLATE VII.

FIG. 13 ($\times$ .64).

Head of a child, about one year. The lateral wall of the nose and orbit have been removed to show the deeper layers of the mucosa in which lie the nerve bundles. Note the anterior ethmoidal nerve.

FIG. 14 ($\times$ 3.75).

Lateral wall of the nose of a child about one year. Same as 13, enlarged. To show especially the plexiform appearance of the olfactory region of the lateral wall of the nose, which has been interpreted by all workers to be a plexus of olfactory nerves. These cords, however, are formed not only of olfactory nerve bundles, but also of blood vessels and connective tissue, as shown by Figs. 24, 26, 27. Note also the anterior ethmoidal nerve.


N.eth.a.
Rg.olf.
R.n.ext.
Sn.mx.
cc.eth.
13

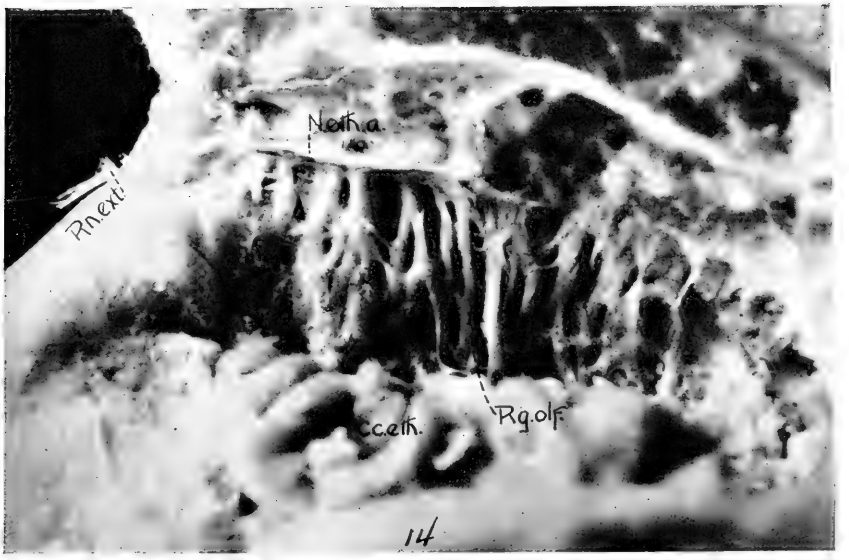

N.eth.a.
R.n.ext.
cc.eth.
Rg.olf.
14

PLATE VIII.

FIGS. 15-17 ($\times$ 5).

Transections of the head of an embryo dog.

FIG. 15.

In the region of the vomeronasal organ. Note its relation to the vomeronasal cartilage. Maxillo-turbinals are shown.

FIG. 16.

In the region of the maxillary sinus. Note the number of folds of the ethmo-turbinals.

FIG. 17.

Near the cribriform plate. Note the increased number of folds of the ethmo-turbinals and the maxillary sinus.

FIGS. 18-20 ($\times$ 5).

Transections of the head of an embryo cat.

FIG. 18.

In the region of the vomeronasal organ. Note its relation to the vomeronasal cartilage. The inferior turbinal is shown.

FIG. 19.

In the region of the maxillary sinus. Note the number of folds of the ethmo-turbinals.

FIG. 20.

Near the cribriform plate. Note the increased number of folds of the ethmo-turbinals.

FIGS. 21-23 ($\times$ 5).

Transections of the nose of a four months human fetus.

FIG. 21.

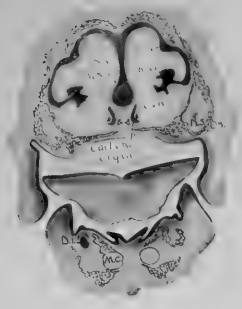
In the region of the vomeronasal organ. Note its relation to the septum and to the vomeronasal cartilage. Inferior concha is shown.

FIG. 22.

Shows the relation of the inferior and median conchæ.

FIG. 23.

Shows the relation of the superior, median and inferior conchæ. Note the olfactory bulb, the cribriform plate and a section of an olfactory bundle.



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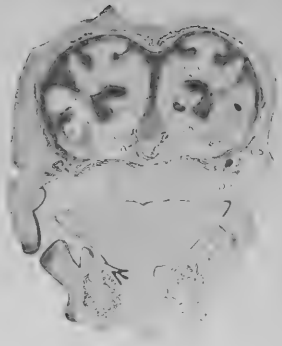
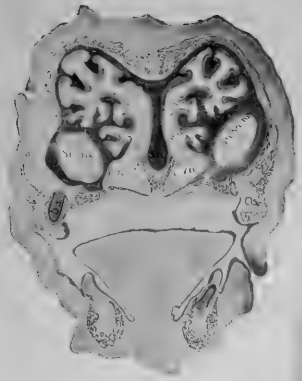


16



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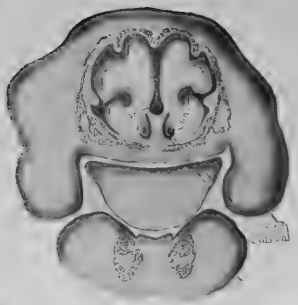

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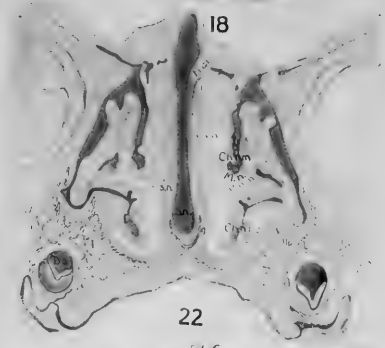
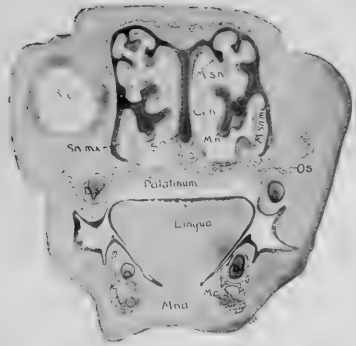


22



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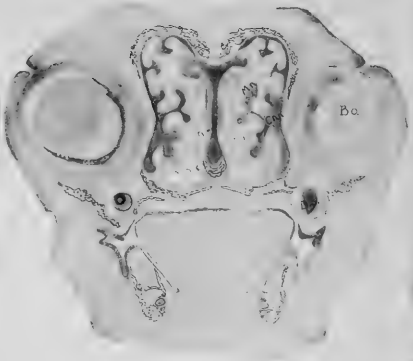

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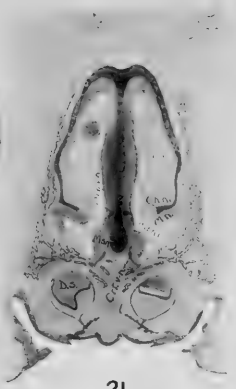

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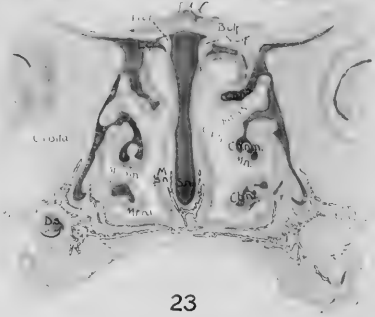


23

PLATE IX.

FIG. 24 ($\times$ 17.5).

The right lateral wall of the nose of a child about one year. This was stained with a differential stain to demonstrate that the olfactory nerves pass as dark bands within the cords of connective tissue and to show that the plexiform appearance is due, not to these olfactory nerve bundles, as has always been stated, but to the ramification of blood vessels and to the amount and arrangement of the connective tissue.

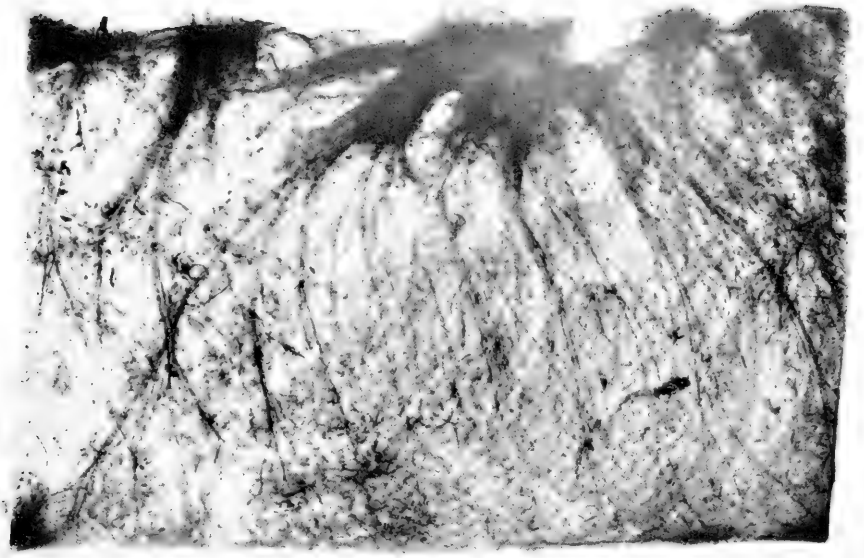
PLATE X.

FIG. 25 (× 9.2).

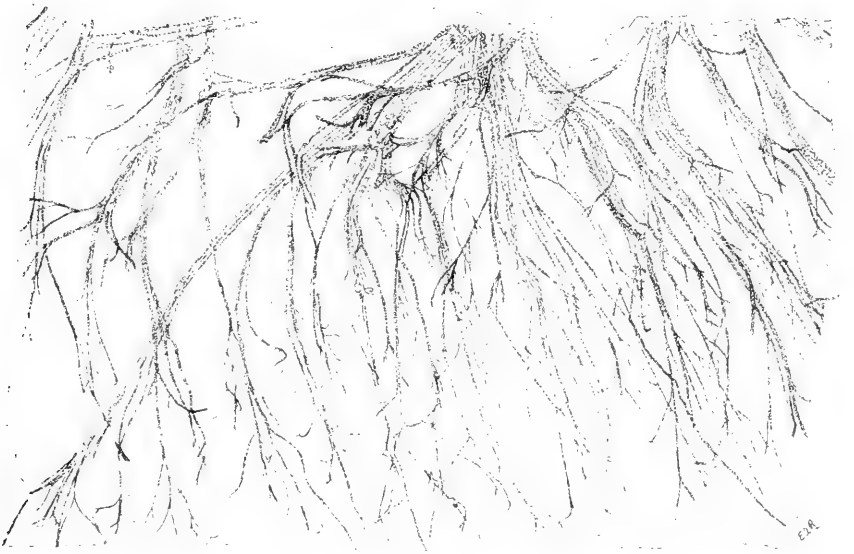
A part of the septal mucosa of the nose of a child about one year. (Same child as shown in Fig. 24.) This is stained with a differential stain to demonstrate that the large olfactory nerve bundles do not form an anastomotic plexus.

FIG. 26 (× 9.2).

A drawing from Fig. 25. The nerves were carefully followed out to show that any plexiform appearance is due to the crossing and recrossing of nerves. Joining was found in a few cases of the smaller nerve bundles.



25



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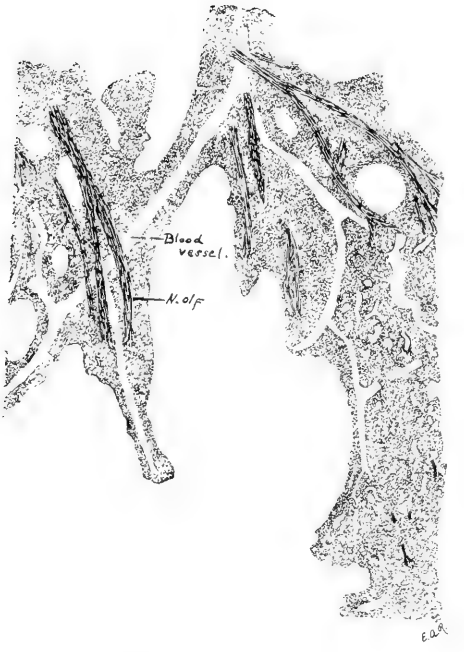


FIG. 27 (× 12.3).

Longitudinal section of the left lateral wall of the nose of a child about 1 year, same child as shown in Figs. 24 to 26. This figure shows in section what is demonstrated in Fig. 24, that is, that the plexiform appearance of this region is due to blood vessels, and not to nerves.

PLATE XI (½ natural size).

FIGS. 28, 29.

Von Brunn's 1892 diagram of nasal cavity of man to show the area of olfactory nerve distribution (blackened area).

Fig. 28 = man 40 years; Fig. 29 = man 30 years.

FIGS. 30, 31.

Diagram of olfactory nerve distribution made from my dissection.

Fig. 30 = child about 1 year.

Fig. 31 = man 30-40 years.

28

29

30

31

PLATE XII.

FIG. 32 ($\times$ 585).

Olfactory cells from the nasal mucosa of the dog (Golgi stain). Note the long axones and the olfactory hair. (Enclosing lines indicate the thickness of the epithelium.)

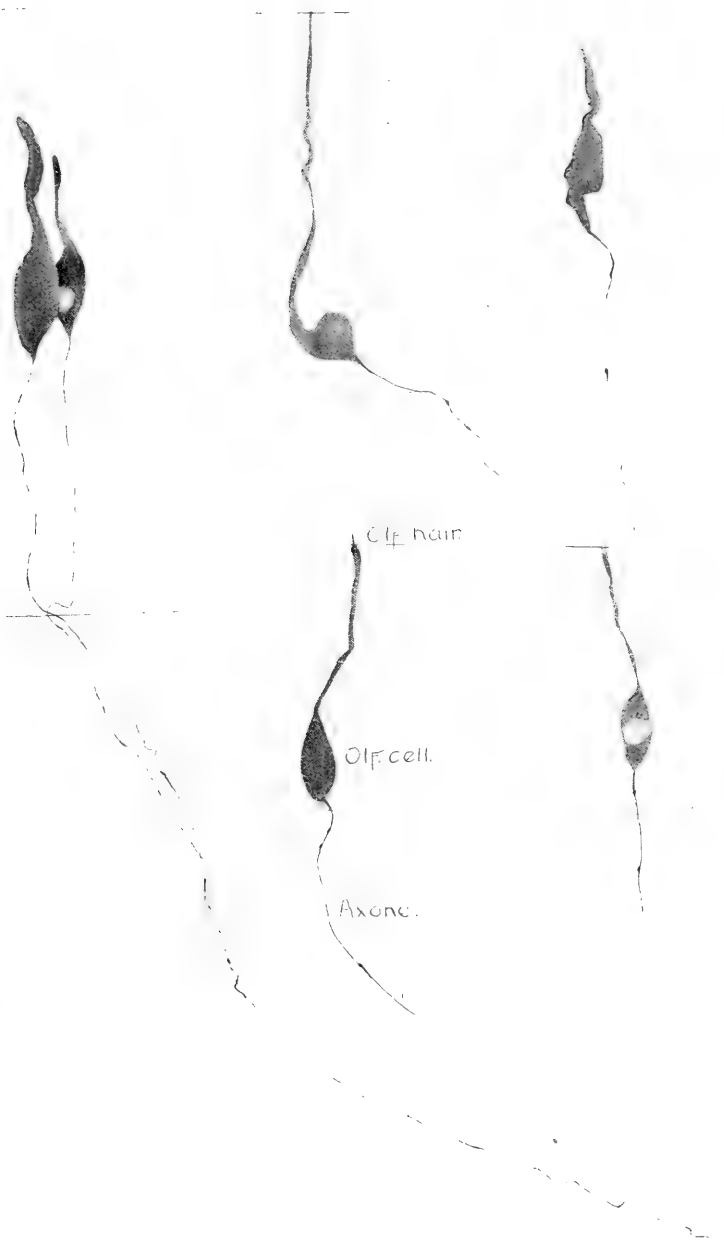

Olf hair
Olf cell
Axone

PLATE XIII.

FIGS. 33, 34.

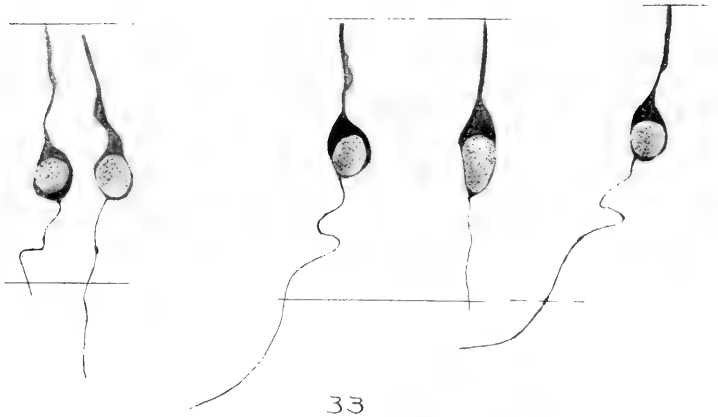
Olfactory cells from the nasal mucosa of the cat. (Enclosing lines indicate the thickness of the epithelium.)

FIG. 33 (× 833.4).

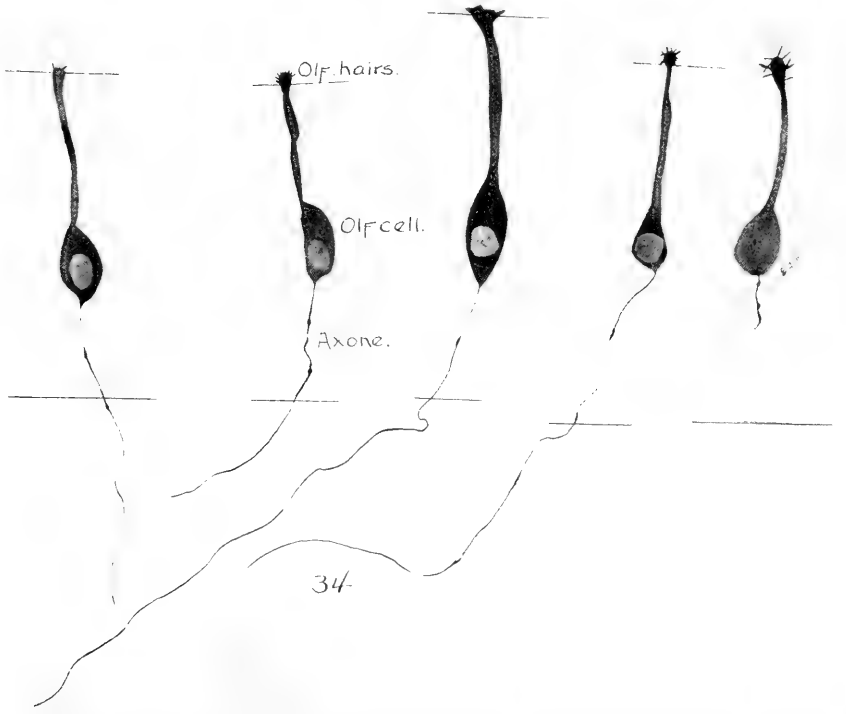
Cells stained with methylene blue.

FIG. 34 (× 625).

Cells stained by the Golgi method. Olfactory hairs are very distinct at the free end of several of the cells.



33



34

PLATE XIV.

FIG. 35-38 ($\times$ 760).

Olfactory cells. (Enclosing lines indicate the thickness of the epithelium.)

FIG. 35.

Olfactory cells from the dog, stained with gold chloride.

FIG. 36.

Olfactory cells from the dog, stained with gold chloride.

FIG. 37.

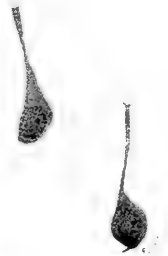
Olfactory cells from the cat; isolated by formaldehyde dissociater.

FIG. 38.

Olfactory cells from the nasal mucosa of man, stained with gold chloride and dissociated by formaldehyde. Note the short axones in two of the cells.

35

36



37

38.

PLATE XV.

FIGS. 39-45.

FIG. 39 (× 450).

Olfactory epithelium of the cat; formaldehyde dissociation.

FIG. 40 (× 450).

Isolated sustentacular cells of the cat.

FIG. 41 (× 300).

Duct of Bowman's gland of the cat. Golgi stain.

FIG. 42 (× 450).

Olfactory epithelium of an embryo dog; gold chloride stain.

FIG. 43 (× 450).

Ciliated cells from the respiratory epithelium of the nose of the cat.

FIGS. 44, 45 (× 450).

Free nerve terminations of the 5th nerve in the nasal mucosa of the cat.

FIG. 44.

In the respiratory region.

FIG. 45.

In olfactory region.

EFFIE A. READ

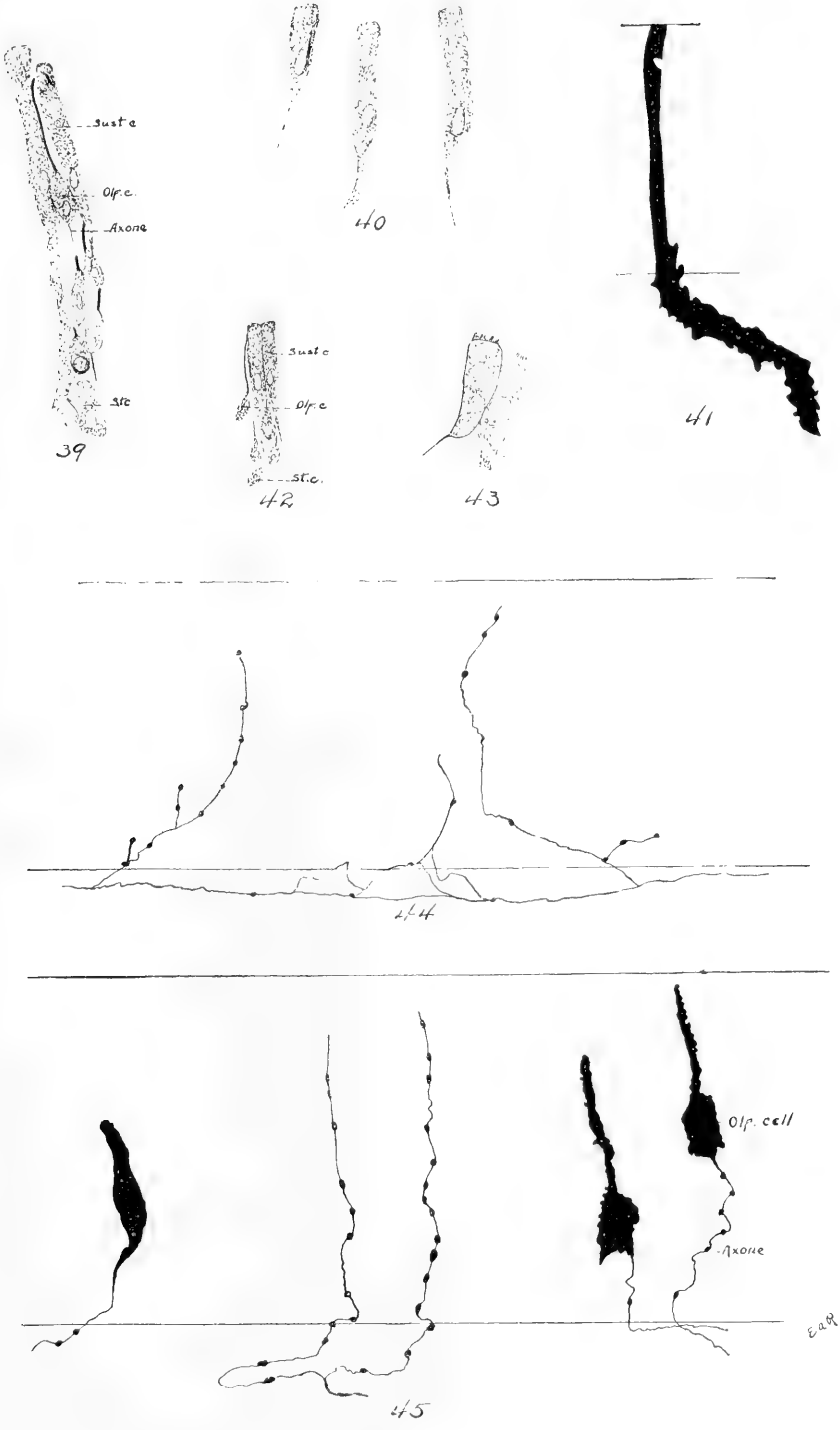

Sust c
Olf c
Axone
Ste
39
40
41
Sust c
Olf c
Ste
42
43
44
Olf. cell
Axone
45

PLATE XVI.

FIGS. 46, 47.

Glomeruli of the olfactory bulb in the dog (Golgi stain), showing the end brushes of the olfactory axones.

FIGS. 48-50.

Glomeruli of the olfactory bulb in the dog (Golgi stain), showing the end brushes of the mitral cell dendrites.

FIG. 48 ($\times$ 310).

Three glomeruli formed by the branching of one dendrite.

FIG. 49 ($\times$ 310).

Glomerulus formed of dendrites from two different mitral cells.

FIG. 50.

Glomerulus formed by the branching of one dendrite.

FIGS. 51-53.

Glomeruli of the olfactory bulb of the cat. Golgi stain. Mitral cells and dendrites.

FIGS. 51, 52.

Glomeruli formed of three dendrites from at least two mitral cells. Fig. 51 ($\times$ 310), Fig. 52 ($\times$ 475).

FIG. 53 ($\times$ 310).

Glomerulus formed by two dendrites from the same mitral cell.

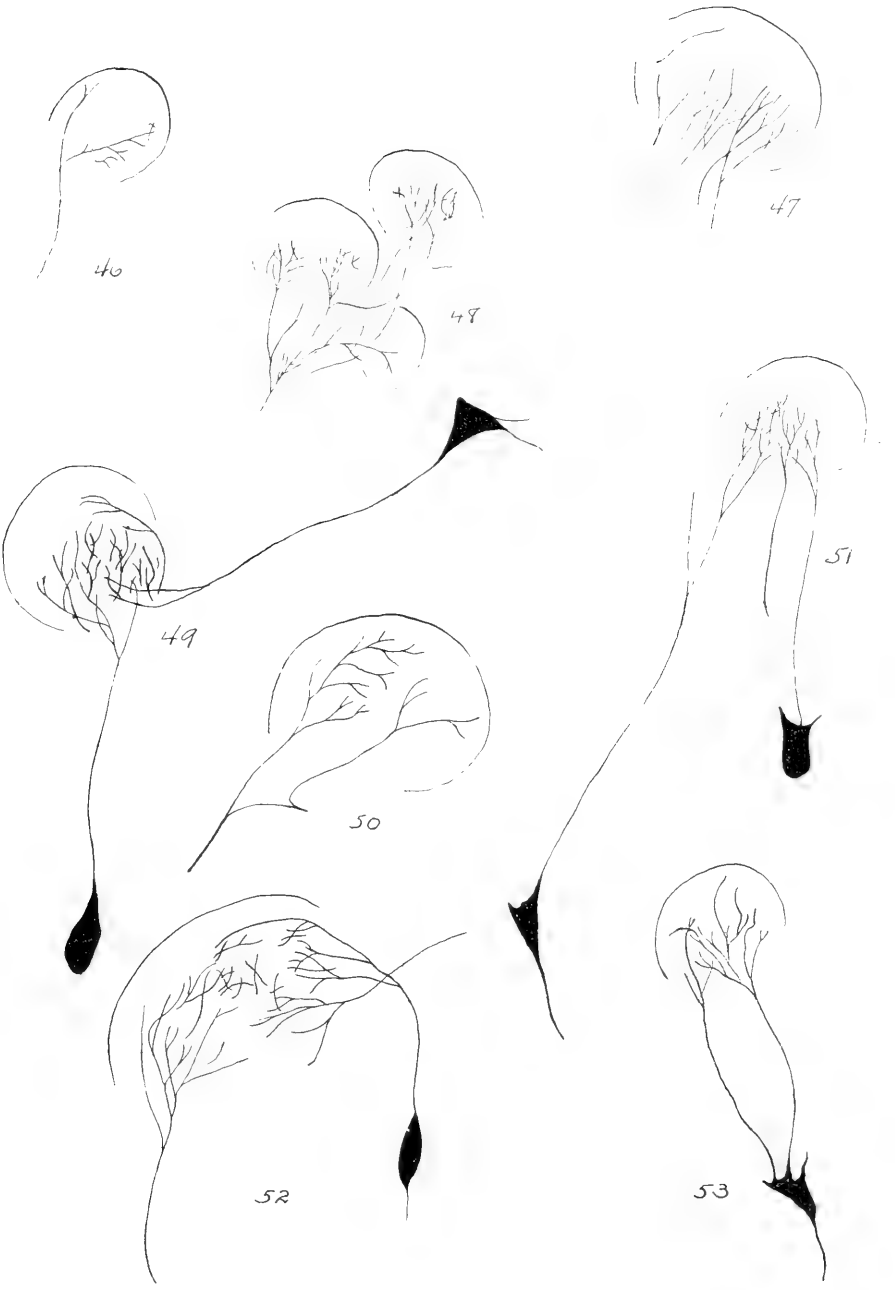

40
47
48
49
50
51
52
53

PLATE XVII.

FIGS. 54-55A.

FIG. 54 ($\times$ 50).

Vomeronasal organ in an embryo kitten.

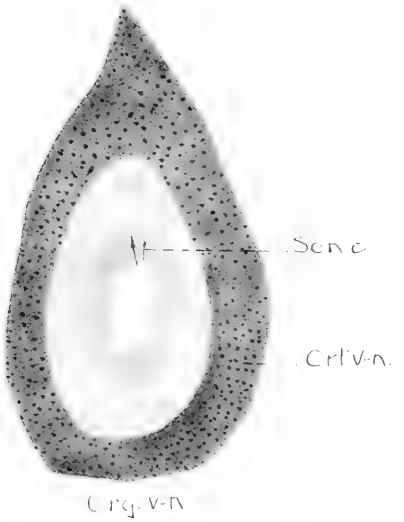
Section through the cephalic region of the organ, the cartilaginous capsule entirely enclosing it. Two olfactory cells are shown in the upper part of the lining of the epithelium.

FIGS. 54A, 55A ($\times$ 488).

Olfactory cells of the vomeronasal organ, with varicose axones. The cell with the longest axone was drawn from a different region of the same organ (enclosing lines indicate the thickness of the epithelium).

FIG. 55 ($\times$ 30).

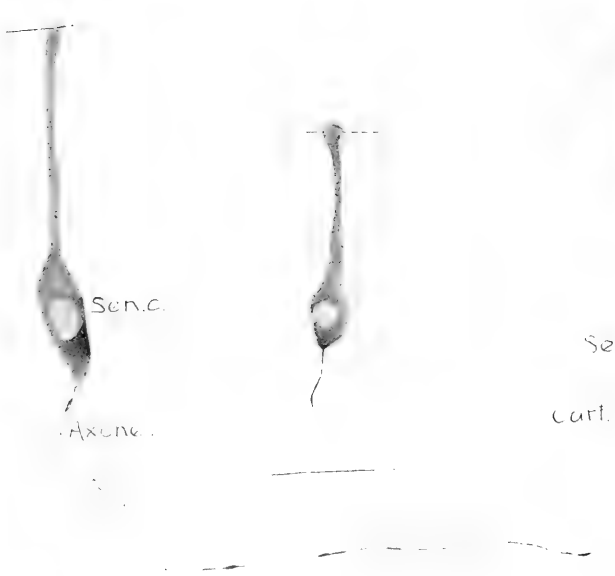
Section through the middle of the vomeronasal organ; cartilagenous capsule not entire. Note the difference in thickness of the median and lateral epithelium; an olfactory cell is shown in the epithelium of the median wall.


Sen.c.
Cart.V-n.
Org.V-n.

54


Cil.hair
Axone.

54A


Sen.c.
Axone.

55A


Sen.c.
Cart.V-n.
Org.V-n

55

DISTRIBUTION OF THE SUBCUTANEOUS VESSELS IN THE TAIL REGION OF LEPISOSTEUS.

BY

WILLIAM F. ALLEN.

From the Herzstein Marine Laboratory, Pacific Grove, Cal.

WITH 25 FIGURES.

INTRODUCTION.

The following is merely a continuation of a recent article[1] on the distribution of the subcutaneous vessels in the head region of the Ganoids *Polyodon* and *Lepisosteus;* which was an attempt to see what light a study of these vessels in this group would throw on the general problem as to whether these vessels in fishes are veins or lymphatics; or a common system that may function for both; or if perchance they might not function as veins in the lower or more generalized forms and lymphatics in the higher or more specialized forms. In other words, to ascertain, if possible, what bearing, if any, they might have on the origin and phylogeny of the lymphatic system.

Material and Method of Procedure.—Two species of *Lepisosteus* were studied, namely, *L. tristœchus* and *L. osseus.* They were obtained from the Ohio and Mississippi Rivers about Cairo, Illinois. The tails of these specimens were transversely severed immediately in front of the dorsal and anal fins; and the caudal vein and one of the lateral subcutaneous trunks were injected caudad from the cut ends with a Prussian blue gelatin mass. Ordinarily when injecting one of the lateral trunks, the opposite trunk and the dorsal and ventral subcutaneous trunks were plugged with cotton. With a few specimens the caudal artery was injected with Hoyer's lead chromate gelatin mass. In making the injections the cut end of the specimen was raised consid-

[1] "Distribution of the Subcutaneous Vessels in the Head Region of the Ganoids, *Polyodon* and *Lepisosteus*," *Proc. Wash. Acad. Sci.*, Vol. IX, pp. 79-158, 1907.

erably higher than the tail end. After a specimen had been satisfactorily injected it was placed in a pail of cold water till the gelatin mass was hardened, and then preserved in a 4 per cent solution of formalin until needed for dissection. All of the dissections were made at the University of California Marine Laboratory, Pacific Grove, California.

The observations made from these dissections were checked up from several transverse series of larva or small adult *Lepisosteus,* but mostly from a 90 mm. *L. osseus* tail, which had been killed and fixed in Tellyesniczky's potassium bichromate-acetic mixture, imbedded in paraffin, cut 10 microns, and stained in Heidenhain's iron hæmatoxylin and counterstained in a concentrated alcoholic solution of orange G plus a little acid fuchsin.

Blood-Vascular Supply for the Caudal Fin Region.

Before taking up this most interesting system of subcutaneous vessels it might be well, in order to avoid confusion, to first describe briefly the distribution of the blood vessels for this region.

The arterial trunk which supplies the caudal fin is the posterior continuation of the dorsal aorta or the *caudal artery* (Figs. 1-3, 9-19, C. A.). This trunk follows along in the hæmal canal of the vertebral column immediately above the caudal vein. Under the ninth from the last vertebra it sends off a left caudal branch, which in company with the corresponding vein passes between the superficial and deep muscles of the fin to supply each. Then for a short distance the main artery travels along the right side of the ninth or tenth hæmal spines of the tail (counting ventro-dorsad), between the vertebral column and the caudal subcutaneous or lymphatic trunk to send off a branch which pursues a dorso-caudal direction in company with the vertebral column; while the main stem continues caudad with the caudal trunk. Before the caudal fin is reached it crosses the right side of the subcutaneous trunk, arriving at a position between the trunk and the ninth or tenth hæmal spine of the tail, and finally when the distal end of the spine is reached it makes a sharp curve at right angles to travel ventrad through the basal canal of the fin. Its position in this canal is at first laterad of the caudal vein and in front of the caudal trunk, but further on in its ventral course it comes to lie in front of the vein. Throughout this canal it sends off two *caudal fin ray branches* (Figs. 1, 2, 18 and 19, C. R. A.), which run along the dorsal and ventral surfaces of each ray to give off a network for the fin membrane.

Running parallel with the caudal artery, but below in the hæmal canal, is the *caudal vein* (Figs. 1-7 and 9-19, C. V.). Although its walls are much thinner, yet, when expanded, its diameter is much greater than the arterial trunk, and below the tenth from the last vertebra it resembles a sinus. At this point it receives a large neural vein from above and the two caudal sinuses from above and the rear. The entrances of the latter are guarded by a pair of semi-lunar valves. Tracing the caudal vein posteriorly, it was found to leave the hæmal canal at the seventh or eighth hæmal spine of the tail (counting ventro-dorsad), in company with, but ventral to, the left caudal sinus. Occasionally, however, the vein accompanies the right caudal sinus; in which case the left caudal vein is the main stem, and drains the fin. At first, the caudal vein is a more superficial vessel than either the caudal artery or the so-called caudal subcutaneous trunk, for it passes caudad between the superficial and the deep muscles of the fin. Upon reaching the basal canal of the tail, between the third or fourth and the fourth or fifth rays (counting dorso-ventrad), it immediately makes a curve at right angles to pass ventrad through this canal in front of the caudal subcutaneous trunk and either lateral to the caudal artery or between it and the caudal trunk. From each ray it receives two branches that traverse the upper and lower surfaces of the ray and collect a capillary network from the fin membrane. This vein usually lies between the caudal ray artery and the caudal ray subcutaneous canal, but frequently, toward the base of the ray, it runs laterad with the artery, immediately proxamad of the caudal ray canal.

Fig. 22 is from a posterior view of a transverse microscopic section taken through the hæmal canal of a 90 mm. *L. osseus*. The *caudal artery* (C. A.) presents no special peculiarities. It is composed of a muscular layer, which is lined internally with an endothelial layer, and is filled with corpuscles, mostly red. The *caudal vein* (C. V.), on the contrary, is devoid of all muscular elements, and in specimens of this size is composed solely of a layer of endothelium, containing very few corpuscles. Both the artery and vein are supported in the hæmal canal by a spongy connective tissue, and are accompanied by two additional longitudinal trunks, which will be described later on.

In Fig. 11 Hopkins[2] figures the caudal vein of *Amia* (=*Amiatus*) as ending under the eighth from the last vertebra and here receiving

[2]Hopkins, G. S. "The Lymphatics and Enteric Epithelium of *Amia calva*," *The Wilder Quarter-Century Book*, Ithaca, N. Y., pp. 367-385, 1893.

the caudal sinuses. Likewise Hyrtl,[3] in Figs. 1, 2 and 4, V., represents the caudal vein in *Esox* (= *Lucius*) and *Leuciscus* as terminating under the last vertebra, and receiving a papilla from each of the caudal sinuses. With the bony fishes Sappey[4] (p. 46) states that the caudal vein takes its origin in two branches from the base of the caudal find and is so figured in the pike (Pl. XII, Fig. 2, 7). With the Selachians and *Polyodon* the structure of the caudal fin is so different that a comparison is hardly permissible. Mayer[5] (p. 325) finds that the caudal vein extends much further caudad with the dogfish than with the roaches. With the latter it may become paired, then reuniting, finally terminates, and its place farther caudad is taken by branches that form a vasa vasorum with similar branches from the caudal artery.

The distribution of the caudal artery and vein doubtless conforms to the same general plan in all fishes, but in a great many excellent papers on the circulation of blood in fishes there has been a marked tendency to overlook the final ending of the caudal artery in the caudal fin and the origin of the caudal vein from the same. It may be that the caudal vein in some fishes is not continued into the caudal fin, but I mistrust in those instances that the injection mass has failed to reach the posterior end of this trunk. If such were not the case, it would materially strengthen the hypothesis that the subcutaneous vessels which came from the tail and emptied into the caudal sinuses and then into the caudal vein were veins rather than lymphatics.

Intercostal Arteries and Veins.—These are among the most important branches of the caudal artery and vein. Ordinarily, as with the Teleosts, a neural and hæmal artery arise from under each alternate vertebra, and a neural and hæmal vein empty into the caudal vein beneath the intermediate alternate vertebræ. The hæmal vessels follow the hæmal spines, and the neural vessels after crossing their respective vertebræ run along the neural spines. From some of the neural arteries and veins, but not from all, a *lateral artery* or *vein* (Fig. 8, L. A. and L. V.) is given off or received. Tracing these vessels, laterad, they are found

[3]Hyrtl, Jos. "Ueber die Caudal und Kopf-Sinuse der Fische, und das damit zusammenhängende Seitengefäss-System," *Archiv für Anatomie und Physiologie*, pp. 224-240, 1843.

[4]Sappey, P. C. "Etudes sur l'appareil mucipare et sur le système lymphatique des poissons," pp. 1-64, Paris, 1880.

[5]Mayer, P. "Ueber Eigenthümlichkeiten in den Kreislaufsorganen der Selachier," *Mittheilungen aus der zoologischen Station zu Neapel*, VIII Bd., 1888.

to run along the septum between two myotomes to the great lateral subcutaneous trunk. Mesad of this canal they break up into numerous branches, which for the most part follow, superficially, dorsad, or ventrad, along the septa between the myotomes, to form a network in the connective tissue that binds the skin to the body muscles.

One of the largest of the neural veins is the last one (Figs. 1, 3 and 14, Neu. V. (1)). It takes its origin in the posterior dorsal corner of the caudal peduncle. After passing obliquely cephalad for a short distance, it curves ventrad to cross the left surface of the eighth vertebra from the last. It then crosses the left sinus (x) and finally empties dorsally into the caudal vein a little anterior to the openings of the caudal sinuses. In Fig. 5 the abbreviation Neu V. (1) O. marks the opening of this vein into the caudal. In the first dissections this vein was taken to be a part of the subcutaneous system opening into sinus (x).

Vascular Supply for the Dorsal Fin.—In the region of the posterior part of the dorsal fin two of the neural vessels are greatly enlarged to supply the dorsal fin. In the specimen from which Fig. 9 was drawn the *dorsal fin artery* (D. F. A.) took its origin from the caudal artery at about the level of the third vertebra from the posterior end of the dorsal fin. After crossing the right side of this vertebra it crossed the two preceding interneural spines obliquely to enter the basal canal of the dorsal near the middle part of the fin. Here it separated into three branches; two of which supplied the anterior part of the fin and the third the posterior part. From these branches one or two *dorsal ray arteries* (Fig. 9, D. R. A.) were given off to pass along either the anterior or posterior surfaces of the ray or both. In this specimen a second neural or a minor dorsal fin artery supplied the posterior part of the fin (see Fig. 9). With another specimen of *L. tristœchus,* where the dorsal fin artery was dissected out, it had its source about nine vertebræ cephalad of its position in Fig. 9, and approached the dorsal fin from in front. The *dorsal fin vein* (Fig. 9, D. F. V.) emptied into the caudal vein two vertebræ behind the origin of the dorsal fin artery. Tracing this vein peripherally, it was seen to cross the left side of the second vertebra, behind the dorsal fin artery. Continuing dorsally behind its neural and interneural spines it entered the basal canal of the dorsal spine from the rear, and traveling clear through this canal it was supplied from numerous *dorsal fin ray veins* (Fig. 9, D. R. V.), which may traverse either the anterior or posterior

or both surfaces of the rays, parallel with, but usually distal to, the corresponding arteries.

With the Selachians in addition to the subcutaneous vessels described by Sappey (*op cit.*, p. 39) for the dorsal fin, Parker[6] (p. 720) and Mayer (*op. cit.*, pp. 333-5) find a deeper vein, which is in connection with this system and helps drain this region. By Mayer it has been styled as the *vena profunda* (Pl. XVI, Figs. 21, 23 and 24, v. prof.), and, in brief, Mayer sets forth the union of the so-called subcutaneous veins with the profundus as follows: The dorsal subcutaneous vein, at the insertion of the dorsal fin separates into two *venæ circulares,* which encircle the fin and collect subcutaneous branches from it. Posteriorly they reunite at the base of the fin in a reservoir. This reservoir also receives one or two *vena postica* (V. P.), which travel along the distal edge of the fin cartilage and collect the blood from the inner parts of the fin. The *vena profunda,* in addition to collecting numerous branches from the fin muscles, which run parallel to the corresponding subcutaneous branches, communicates directly with the above mentioned subcutaneous reservoir at the posterior insertion of the fin, and eventually passes along the sheath that separates the great lateral muscles, to terminate in the caudal vein, or, acording to Parker, with *Mustelus* empties into the left renal portal vein.

If in *Lepisosteus* we had the dorsal fin vein fusing with the dorsal subcutaneous trunk at the posterior end of the dorsal fin, or, better still, if the dorsal subcutaneous trunk (Figs. 1 and 2, D. T.), instead of passing through the basal canal of the fin, had formed two circular canals around the base of it, and had joined the dorsal fin vein in a sinus at the posterior base of the fin, we would have a condition of affairs almost identical with that found in the Selachians. Can it not therefore be possible that farther back in the phylogeny, or possibly in the embryo of *Lepisosteus,* the dorsal fin vein had such a comunication, and that as specialization advanced the subcutaneous vessels became more and more separated from the deep, and with this differentiation a change in function occurred? In such a case the *vena profunda* and the *vena postica* of the Selachians would be homologous to the dorsal fin vein and its branches of *Lepisosteus.*

[6]Parker, T. J. "On the Blood-Vessels of Mustelus antarcticus: a Contribution to the Morphology of the Vascular System in the Vertebrata," *Phil. Trans.*, pp. 685-732, 1886.

The distribution of the blood vessels to and from the anal fin was not studied. One, however, would naturally expect to find it supplied by an enlarged hæmal artery and vein, somewhat after the general plan of the dorsal fin.

Subcutaneous Vessels of the Caudal Fin.

As with most fishes four longitudinal subcutaneous trunks, respectively, dorsal, lateral and ventral, are to be found immediately below the skin in *Lepisosteus*. In one way or another they discharge themselves posteriorly into two caudal sinuses, which empty into the caudal vein.

Ventral Subcutaneous Trunk (Figs. 1, 2, 3, 5 and 10-16, V. T.).—This important canal travels along the ventral median line, directly under the skin, in a mass of connective tissue that binds the two great lateral muscles. As stated in a previous paper (*op. cit.*, p. 114), this canal usually bifurcates anteriorly, each fork terminating in its respective pericardial sinus. Upon tracing this canal caudad it was found to enter the basal canal of the anal fin, and to receive an *anal fin ray canal* (Figs. 1 and 2, A. R. C.) from the anterior and posterior surfaces of each ray, which drains a network of canals from the membrane connecting each two rays. After leaving the anal fin, this trunk continues along the ventral surface of the caudal peduncle, to penetrate the basal canal of the caudal fin, and to become the *caudal subcutaneous trunk* (Figs. 1-5, 7, 17-19, C. T.). It receives here, as within the anal canal, two *caudal fin ray canals* (Figs. 1, 2, 18 and 19, C. R. C.), which run along the dorsal and ventral surfaces of each ray, and receive a network of canals from the membrane joining two rays Upon reaching the third or fourth ray (counting dorso-ventrad) the caudal trunk makes a sharp curve at right angles to pass cephalad along the upper margin of the ninth or tenth of the last hæmal spines (counting ventro-dorsad), in company with, but below, the caudal artery, to empty into either the right or the left caudal sinus; oftener into the right.

Fig. 18 shows the caudal trunk of a 90 mm. *Lepisosteus osseus,* twice, in cross section. Toward the lower part of the figure it is seen traveling along through the basal canal of the caudal fin, and below the vertebral column it is seen again not far from its entrance into the right caudal sinus. In Fig. 23 we have a view of the posterior part of the caudal trunk highly magnified. It consists solely of a layer of endothelium

imbedded in a mass of fibrous connective tissue. A few red corpuscles were found in this trunk throughout this series. In Figs. 18 and 19 several of the caudal rays, together with their blood vessels and subcutaneous canals, are seen in section. These subcutaneous canals or lymphatics are readily distinguishable from the blood vessels on account of their larger size, and by the additional fact that they frequently surround the blood vessels to a considerable extent.

With the Selachians, Mayer (*op. cit.*, pp. 316-7) is the only writer to throw much light on the caudal termination of the *vena ventralis*, as he styles it. Like the dorsal vein, he finds it paired at the origin of the tail, each fork ending in its corresponding lateral vein, and these latter being in communication with the caudal vein. Parker (*op. cit.*, p. 721) notes with *Mustelus* that the posterior ventral vein forms a loop around the anal fin, and after bifurcating at the cloaca, each fork anastomoses with its corresponding cloacal vein. As with the Selachians, there has been a notable silence concerning the caudal termination of the ventral subcutaneous trunk in the Teleosts. With *Pleuronectes*, Sappey (*op. cit.*, p. 49) finds that the ventral lymphatic trunk (Pl. XII, Fig. VI, 4) is continuous with the caudal and dorsal trunks and forms an ellipse around the body, which ends ventro-cephalad in the ductus of Cuvier and dorso-cephalad in the jugular vein. With *Amiatus*, Hopkins (*op. cit.*, pp. 372-3) represents the ventral trunk (Pl. II, Fig. 11, O. and V.) as arising from the base of the caudal fin, and extending cephalad along the ventral side of the body to the heart, where it ends in the pericardial sinuses. In one instance an anastomosing trunk (Fig. 11, t) connects the tail part of the trunk with the lateral trunk, as the latter bends mesad to join the caudal sinus. This communication recalls a somewhat similar arrangement in *Lepisosteus*, where the caudal trunk or the posterior continuation of the ventral trunk was just described (p. 55) as terminating in the right caudal sinus after traveling through the basal canal of the tail.

Dorsal Subcutaneous Trunk (Figs. 1-3, 5, 10, 12-13, D. T.).—In many respects this trunk in *Lepisosteus* is similar to the ventral canal. It follows the dorsal median line in a layer of tough connective tissue that binds the great lateral muscles together. As stated in an earlier paper (*op. cit.*, pp. 113-4), when not far from the posterior end of the skull it empties into the left branchial sinus, which is in direct connection with the cephalic sinus, and through the latter it reaches the jugular. When the dorsal fin is reached, instead of forming two

circular trunks about its base as in most fishes, it passes entirely through its basal canal, and receives two *dorsal fin ray canals* (Figs. 1 and 2, D. R. C.), which traverse the anterior and posterior surfaces of each ray to receive a network of vessels from the fin membrane. In position the fin ray canals are more distal from the rays than the corresponding arteries and veins. Unlike the ventral trunk, the dorsal does not extend to the tail, but about midway between the posterior end of the dorsal fin and the beginning of the caudal it makes a sharp bend at right angles to continue ventrad across either the right or the left side of about the eleventh vertebra from the last, and here culminates in a longitudinal sinus, designated as *sinus* (x). With both *L. tristœchus* and *L. osseus* the dorsal trunk may empty into either the right or the left sinus (x), but in no specimen did the dorsal trunk bifurcate and each fork terminate in a sinus (x). In the specimens from which Figs. 2 and 5 were drawn the dorsal trunk crossed the right side of the vertebral column and ended in the right sinus (x); while in the specimen from which Fig. 3 was drawn it crossed the opposite or left side of the vertebral column and emptied into the left sinus (x). Fig. 12 shows the dorsal trunk of a 90 mm. *L. osseus,* in section, passing across the left side of the vertebral column, and Fig. 13 its termination in the left sinus (x).

Sinus (x) (Figs 1-6 and 11-16, x).—The two sinuses so designated are situated deeply along the lower and outer surface of the vertebral column, somewhere between the sixth and the thirteenth from the last vertebra. They are variable in length, position and in their mode of connections; both in different specimens and on the opposite sides of the same individual. Both of these sinuses receive a lateral subcutaneous trunk and a hæmal longitudinal trunk, communicate ventrad with a caudal sinus that empties into the cardinal vein, and one or the other of them receives the dorsal subcutaneous trunk. In Figs. 1, 3, 4, 5 and 6 the anterior end of sinus (x) received the lateral trunk from the side and the hæmal trunk from below and within; while in Fig. 2, which is the opposite side of the same individual as Fig. 1, the lateral trunk joined this sinus considerably caudad of the union of the dorsal trunk; in fact, the opening was about opposite the connection of sinus (x) with the caudal sinus. In the dissection of *L. tristœchus* from which Figs. 1 and 2, and the dissection of *L. osseus* from which Figs. 5 and 6 were drawn, the dorsal trunk terminated in the right sinus (x), about midway between the anterior and posterior extremities; while

with the *L. tristœchus* from which Figs 3 and 4 were drawn the dorsal trunk culminated in the left sinus (x), nearer its anterior extremity than its posterior. In Figs. 1 and 2, especially the former, sinus (x) extends some little distance caudad of its ventral communication with the caudal sinus; while in Figs. 3-6, sinus (x) might be described as discharging itself caudad and ventrad into the caudal sinus. As a matter of fact, sinus (x) in Figs. 3-6 appeared to be merely a deep continuation of the lateral trunk, which empties into the caudal sinus. No valves were observed at the entrance of any of the subcutaneous trunks into sinus (x), or guarding the exit of the latter into the caudal sinus.

Some interesting observations should be recorded in connection with the dorsal trunk and sinus (x) from a series of transverse sections taken through the tail of a 90 mm. *L. osseus:* The right sinus (x) (Figs. 11-16, x) in this larva or small adult had a length of 1.42 mm. It began anteriorly as a blind sac, and upon following this series toward the tail the right sinus (x) was found to receive the hæmal longitudinal trunk .43 mm. and the lateral trunk .82 mm. caudad of its origin. The left sinus (x) has about the same length as the right, but is unlike it in that it is merely a continuation of the left hæmal trunk. It receives the left lateral trunk .6 mm. and the dorsal trunk .28 mm. cauded. The two sinuses (x) terminate in their respective caudal sinuses, and in section (see Fig. 16, x) their walls are continued some little distance into the caudal sinuses. Both sinus (x) and the dorsal trunk are surrounded by a mass of connective tissue. They are composed of a single layer of endothelium, and contain only a very few red corpuscles. No leucocytes were observed.

With the Selachians, Parker (*op. cit.*, p. 720), Sappey (*op. cit.*, p. 38), and Mayer (*op. cit.*, pp. 316-8, find a dorsal cutaneous vein or lymphatic trunk extending from the head to the tail. Sappey states with *Squalus* that it bifurcates anteriorly, each fork terminating behind the eye in the jugular vein. Parker describes the lateral cutaneous vein in *Mustelus* (p. 721) as anastomosing caudad with both the caudal and the dorsal cutaneous vein; while Mayer portrays the *vena dorsalis* as anastomosing caudad with the *vena lateralis.* Of these three writers, Mayer gives us the most comprehensive description of the distribution of the subcutaneous vessels in the dorsal fin. He sets forth the *vena dorsalis* (pp. 333-4 and Pl. XVII, Fig. 17, *v. d.*) as separating into two *venæ circulares* (Fig. 17, *v, circ.*), which encircle the fin, collect

subcutaneous vessels from the fin, and reunite in an unimpaired trunk at the posterior insertion of the fin. At the junction a reservoir of considerable size is formed, which is also in communication with the *vena postica* and the *vena profunda,* as has already been noted under the head of the dorsal vein (p. 54).

Concerning the caudal distribution of the dorsal trunk in Teleosts, Trois tells us with *Lophius*[7] (pp. 6-7) and *Uranoscopus*[8] (p. 23) that the dorsal lymphatic trunk divides into three in the region of the dorsal fin; one branch passes through the median basal canal, and the other two encircle the base of the fin. With *Lophius,* Fig. 3, shows this trunk as having superficial connections with the lateral trunk, and Fig. 4 represents the dorsal, ventral, neural and hæmal longitudinal trunks as anastomosing at the base of the tail; while the neural vessels connect the dorsal with the neural trunks, and the hæmal vessels the ventral and the hæmal trunks. A somewhat similar arrangement was found by Sappey for the carp and the pike (*op. cit.,* p. 47, and Pls. XI and XII, Figs. V, I and II, 4, 8 and 15), except that the dorsal trunk was not prolonged to the tail. In *Pleuronectes,* Sappey notes (p. 50) that the dorsal lymphatic trunk (Pl. XII, Fig. IV, 1) is continuous with the caudal and the ventral, forming an elliptical trunk about the body, which ends dorso-cephalad in the jugular vein, and ventro-cephalad in ductus of Cuvier. Throughout its course it was said to be a single trunk, passing through the basal canal of the fins. In a previous paper[9] it was stated (pp. 54-5) that the distribution of the dorsal lymphatic trunk of *Scorpænichthys* (Figs. 1 and 4, *d. l. v.*) was not dissimilar to Trois' description of it for *Lophius.* It was connected with the lateral trunk, the intermuscular or transverse vessels, and with the neural trunk through the neural vessels. Its caudal distribution has also been studied, but has been reserved for a separate paper.

As for the Ganoids, Hopkins contends (*op. cit.,* p. 373) that the dorsal lymphatic trunk (Fig. 10, n.) of *Amiatus* is a single trunk, which extends along the dorso-meson from the caudal end of the body to the base of the cranium. At the cranium the dorsal trunk is said to

[7]Trois, E. F. "Ricerche sul sistema linfatico del Lophius piscatorius," *Atti del R. Instituto Veneto di scienze, lettere ed arti,* pp. 3-20, 1878.

[8]Trois, E. F. "Richerche sul sistema linfatico dell' Uranoscopus scaber," *Atti del R. Instituto Veneto di scienze, lettere ed arti,* pp. 19-36, 1880.

[9]Allen, W. F. "Distribution of the Lymphatics in the Head, and in the Dorsal, Pectoral, and Ventral Fins of Scorpænichthys marmoratus," *Proc. Wash. Acad. of Sci.,* Vol. VIII, pp. 41-90, 1906.

bifurcate, each branch extending laterad to join its respective cephalic sinus. At the caudal end Hopkins states that "it anastomoses with the lateral lymph vessel, joining it just after the latter turns at right angles to enter the caudal sinus." Hopkins further believes that the dorsal trunk bifurcates, each fork terminating in a lateral trunk immediately after it bends to join the caudal sinus. This is so represented in Fig. 10, r.

From the above paragraphs it is evident that the distribution of the dorsal subcutaneous trunk of *Lepisosteus* most closely resembles Hopkins' description of a similar trunk for *Amiatus*. On the contrary, the dorsal trunk never forks caudad or terminates in the lateral trunk, but rather in one of the sinuses (x), each of which is a deep reservoir formed by the union of lateral and hæmal trunks which culminates in its respective caudal sinus. As with *Amiatus* and *Pleuronectes,* it is a single median trunk in the dorsal fin region. Since there is no longitudinal neural trunk in *Lepisosteus,* there are no neural vessels to communicate with the dorsal trunk, as is the case with some Teleosts. Later on the lateral trunk will be described as collecting numerous intermuscular or transverse vessels, which doubtless communicate above with the dorsal trunk as in *Scorpænichthys,* but this point was not determined for a certainty. In the basal canal of the dorsal fin the dorsal trunk received a canal from the anterior and posterior surfaces of each ray, which collected a network of canals from the fin membrane. These dorsal ray canals were accompanied more proximad by dorsal ray veins, which gathered a venous network from the fin membrane, and ultimately discharged into a dorsal fin vein that emptied into the caudal vein. As previously stated (pp. 7 and 8), this system of veins may be homologous to the deep dorsal fin veins of the Selachians, which were described by Mayer as anastomosing with the dorsal subcutaneous vein in a reservoir at the posterior end of the fin, but with *Lepisosteus* there was no anastomosis between the venous system and the subcutaneous system. The two systems were distinctly separate. We have, therefore, in *Lepisosteus* a more specialized condition than is to be found in the Selachians. It might also be mentioned that these two systems are clearly unconnected in the dorsal fin region among the Teleosts. With *Scorpænichthys,* however, there is no one vein that collects the entire venous blood from the dorsal fin, but several of the neural veins are extended to the fin and send off branches that traverse the fin rays and receive the capillary network from the fin.

Lateral Subcutaneous Trunks.—Unquestionably these subcutaneous trunks have received far more attention than any of the others.

With the Selachians, Parker (*op. cit.,* p. 721) observed that the lateral cutaneous vein in *Mustelus* anastomoses posteriorly with both the dorsal cutaneous and the caudal veins. Sappey (*op. cit.,* p. 38) found two lateral lymphatic trunks in *Squalus. Le tronc latéral supérieur* (Pl. X, Fig. III, 2) is represented as running along parallel with the mucous canal; caudad it expands into a fibrous caudal sinus, which opens into the caudal vein. *Le tronc latéral inferieur* (Pl. X, Fig. III, 11) is portrayed as traveling along the median lateral line, parallel to the lateral line, but more superficially. Posteriorly this trunk is indicated as gradually rising higher and higher until it eventually anastomoses with the superior lateral trunk. Sometimes (evidently meaning in some species) Sappey notes that the inferior lateral trunk is absent. Certain cross vessels (Fig. III, 14, 12 and 3) connect the ventral trunk with the inferior lateral, the inferior lateral with the superior lateral, and the superior lateral with the dorsal, and the cross vessels drain a subcutaneous network (13). Mayer (*op. cit.,* pp. 316-7, and Pl. 16, Figs. 2-4, *v. l.*) describes the *vena lateralis* as receiving the *vena dorsalis* and anastomosing with the *vena ventralis,* which has already been cited as emptying into the *vena caudalis.* In a footnote on p. 317, Mayer states that in a section through an injected specimen of *S. canicula* he saw a minute connection between the lateral and the caudal veins. This communication is recorded as being caudad of the anastomosis of the laterals with the ventral.

Hyrtl (*op. cit.,* p. 233 and Fig. 7) represents the lateral lymphatic in various Teleosts as collecting numerous paired cross vessels, which receive a superficial network. On pp. 234-5, he states that each lateral trunk terminates in a caudal sinus (Pl. X, Figs. 1, 2 and 4, a) immediately behind the last vertebra. A longitudinal neural and a hæmal trunk culminate in one of these sinuses, and both of these sinuses empty into the caudal vein. Besides terminating in a caudal sinus, each lateral trunk in *Salmo* is described by Vogt[10] (pp. 135-6 and Pl. K, Figs. 3-5, 66) as continuing to the base of the tail, where it separates into a dorsal and a ventral sinus, each of which communicates on the opposite side with a similar sinus. Both of the caudal sinuses open into the caudal vein and the orifice is said to be guarded by a valve.

[10]Vogt, C. "Anatomie des Salomes," *Mémoires de la société des sciences naturelles de Neuchatel,* 1846.

Vogt found no transverse branches uniting with the lateral trunk, and he was of the opinion that such vessels were only extravasations of the injecting mass. Trois' description of the caudal ending of the lateral trunk in *Lophius* (*op. cit.*, p. 5) and that of Sappey for the pike and carp (*op. cit.*, pp. 46-7) are very similar to what Hyrtl found for the perch.

Concerning the Ganoids, Hopkins (*op. cit.*, p. 372) notes that the lateral lymphatic trunk in *Amiatus* (Fig. 11, l.) extends caudad as far as the posterior end of the dorsal fin, where it suddenly bends at right angles toward the meson, to terminate in a caudal sinus, which lies beneath the vertebral column and empties into the caudal vein. Just as the lateral lymphatic trunk bends to empty into the caudal sinus it receives a connecting branch (Fig. 11, t) from the tail portion of the ventral trunk (o), and immediately before uniting with the caudal sinus it is joined by the dorsal trunk, or, as represented in Fig. 11, a fork of the dorsal (r).

In *Lepisosteus* there is but one *lateral subcutaneous trunk* (Figs. 1-5, 8, 10-12 and 25, L. T.) on each side of the body. It occupies a like position to a homologous canal of other fishes, which is in a median lateral line, in a sheath of connective tissue, just within the skin. The anterior connections of the lateral trunk in *Lepisosteus* have been given in a previous paper (*op. cit.*, p. 113). As with other fishes, it collects numerous paired *intermuscular* or *transverse branches* (Figs. 1 and 2, Intm. C.), which travel along superficially in the connective tissue, joining two myotomes, and gather a network of vessels from the connective tissue that binds the skin to the trunk muscle. Doubtless these vessels are continued dorsad and ventrad to anastomose with the dorsal and ventral trunks as in *Scorpænichthys* and other bony fishes, but this point remains undetermined. When about half way between the posterior end of the dorsal fin and the base of the tail, the lateral trunk bends mesad, at right angles, to culminate in, and help form, what has been designated and described as sinus (x). Ordinarily, as shown in Figs. 1, 3, 4, 5 and 6, the lateral trunk joins the hæmal in forming sinus (x), but in Fig. 2, which is the opposite side of the same specimen as Fig. 1, the lateral trunk did not join sinus (x) until after it collected the dorsal trunk. In fact, the point of union was considerably behind that of the dorsal trunk, being almost opposite the opening of sinus (x) into the caudal sinus. A description of the union of the hæmal and the dorsal trunks with sinus (x) and the culmination of the latter in the caudal sinus has already been given under a separate paragraph.

The following observations have been made from a series of transverse sections through the tail region of a 90 mm. *L. osseus:* As shown by Fig. 10, c, there is a conspicuous connecting vessel uniting the right lateral with the right hæmal trunk. This communication, which is cephalad of the origin of sinus (x), was not noticed on the opposite side of this series or in any of the gross dissections. In Fig. 12, the left lateral trunk is seen in section uniting with the left sinus (x). Fig. 21 is drawn from a portion of the same section as Fig. 10, showing the right lateral trunk and its communication (c) with the right hæmal trunk, greatly magnified. From this diagram it will be seen that the lateral trunk of a 90 mm. *L. osseus* lies imbedded in a mass of connective tissue directly mesad of the *ramus lateralis vagi.* Both the lateral trunk and its communicating vessel (c) are composed of a single layer of endothelium, and at the point of anastomosis is a mass of plasma and corpuscles; of these corpuscles the red greatly outnumber the white. The communicating vessel (c) is joined to the body myotomes by a very dense layer of fibrous connective tissue (F. Con. T.).

Fig. 25 is from part of a section taken through the lateral trunk of an adult *L. osseus* as seen with a high-power objective. When compared with Fig 21, it will be found to be almost identical in structure. Internally it consists of a layer of endothelium (End.), which is attached externally to a layer of fibrous connective tissue (F. Con. T.), and, as was the case with the 90 mm. specimen, the red corpuscles greatly predominate.

In *Lepisosteus* the lateral trunk has a most remarkable size. Its diameter exceeds that of the caudal vein plus the caudal artery, and it maintains this caliber throughout its entire length. Since it is in connection with veins at either end, the flow of lymph or blood, whichever it may be, can pass in either direction. The resistance should be about the same, unless the movement of the tail favored the forward movement.

Except for its caudal termination, the distribution of the lateral trunk in *Lepisosteus* is not notably different from other fishes, especially *Amiatus,* but instead of emptying into the caudal sinus after making its posterior-mesal bend as in *Amiatus,* it first empties into what has been designated as sinus (x), which has already been described as also receiving the hæmal trunk, and sometimes the dorsal trunk, before culminating in the caudal sinus. In *Lepisosteus* there is never any connection between the lateral trunk and the posterior part of the

ventral or the caudal trunk as Hopkins describes for *Amiatus;* on the other hand, the caudal trunk empties directly into one of the caudal sinuses.

Hæmal Trunks (Figs. 2-4, 10-12 and 20, Hæ. T. or R. and L. Hæ. T.).—In *Lepisosteus* two such longitudinal trunks traverse the hæmal canal. Their position is perhaps best portrayed in a transverse section, as, for example, in Fig. 10; here, on either side of the caudal artery, a little above the level of the caudal vein, are the right and left hæmal trunks (R. and L. Hæ. T.). A comparison of Figs. 20 with 22, shows us that in a 90 mm. *L. osseus* the size and structure of the caudal vein and the hæmal trunks are almost identical. Both consist of a single layer of endothelium (End.), and contain but few corpuscles, while the caudal artery (C. A.) had an additional muscular layer, and was filled with corpuscles. As previously stated, in the specimen from which Fig. 10 was taken, there was a connecting trunk (c) between the right lateral and the right hæmal trunks. This communication was not observed on the opposite side or in any of the gross dissections. Its position in this specimen is some little distance cephalad of the point where the hæmal trunk leaves the hæmal canal to empty into sinus (x). Ordinarily, as shown in Figs. 2 and 3, the hæmal trunks leave the hæmal canal opposite the point where the lateral trunks bend mesad, and the two unite on the ventro-lateral surface of the vertebral column in what has been described as sinus (x); but in some instances, as in Fig. 1, which is the opposite side of the same specimen as Fig. 2, and on both sides of the 90 mm. *L. osseus* series, they leave the hæmal canal first, and form or empty into sinus (x), before the lateral trunk bends inward to join sinus (x). In *Lepisosteus* no *hæmal* or *intercostal vessels* were found connecting the hæmal with the ventral trunks, as is the case in the Teleosts. Since the lymphatics of the viscera have not been studied, the anterior termination of the hæmal trunks has not been traced out, but the natural supposition is that they would end in an abdominal sinus, situated either below the kidney or between the kidney and the vertebral column.

With the Teleosts, Trois (*op. cit.,* p. 11 and Fig. 4, A.) finds in *Lophius,* that what he terms as the *tronchi linfatici spinali inferiori* travels along in the hæmal canal and collects the intercostal vessels. In Fig. 4 Trois portrays this trunk as anastomosing at the base of the tail with the superior spinal, the dorsal and the ventral lymphatic trunks. *Le tronc sous-vertébral* of the pike is briefly set forth by Sappey (*op.*

cit., p. 49) as following along in the same canal with the caudal artery and vein. A similar vessel is also noted by Sappey (p. 50) for *Pleuronectes*. In Pl. XII, Sappey represents this trunk in the pike (Fig. II, 10) and in *Pleuronectes* (Fig. IV, 17) as receiving numerous hæmal or intercostal vessels, but its posterior ending is not given; from his figures, however, it appears to end blindly before the base of the tail is reached.

In addition to the caudal artery and vein, Mayer (*op cit.*, p. 320) finds a longitudinal trunk in the hæmal canal of *Scyllium, Mustelus* and *Squatina,* which he takes to be a vein that collects a vasa vasorum, originating from little paired arteries that leave the caudal artery between the intercostal arteries (Pl. 17, Fig. 11, avas.). Again, further on (pp. 325-6), Mayer states that the caudal vein is very irregular, changing from side to side, becoming paired, then unpaired, to finally disappear altogether, and its place is taken by a vasa vasorum (hæmal trunks). After which there is nothing in the hæmal canal but the caudal artery in the center, surrounded by connective tissue and small blood spaces. Mayer conjectures that possibly in the past these blood cavities had a different function, that they may have been derived from a degeneration of the body cavity. Hopkins does not record any such trunk for *Amiatus*.

Caudal Sinuses.—These sinuses have received considerable attention from all workers on the subcutaneous system of fishes. Naturally they fall into two classes: pulsating hearts resembling the lymphatic hearts of the Batrachians, and non-pulsating sinuses. In some fishes or fish-like vertebrates that swim by a snake-like movement, we find a pulsating heart in the tail; while in other fishes which swim by a lateral movement of the tail, the caudal sinuses are simply reservoirs, and strange to say with the Selachians no such receptacle has been found; in this group the subcutaneous trunks empty directly into the caudal vein.

Greene[11] and Klinckowström[12] found two pulsating caudal hearts in the tails of *Polistotrema* (= *Bdellostoma*) and *Myxine*. Each of these hearts, which are separated from one another by the median caudal

[11]Greene, C. W. "Contributions to the Physiology of the California Hagfish, Polistotrema stouti: 1. The Anatomy and Physiology of the Caudal Heart," *American Journal of Physiology*, Vol. III, 1900.

[12]Klinckowström, A. Title not known, *Verhandlungen des biologischen Vereins in Stockholm*, 1890 and 1891.

cartilage, open dorso-cephalad into the caudal vein, the orifice being guarded by a valve. In the ventro-cephalic corner there is a second opening, also guarded by a valve, through which the subcutaneous lymphatic or blood canals empty. According to Greene, the caudal hearts in the hagfish are not of themselves muscular or contractile, but are filled and emptied by a contraction of the *musculi cordis caudalis,* which lies laterad of the heart and presses it against the median cartilage. These muscles are said to be entirely separated from the heart, and are not to be regarded as part of it. In the hagfish, then, the caudal hearts or sacs receive the blood or lymph from the subcutaneous spaces and drive it into the caudal vein.

By far the best description of the caudal heart of the eel is given by Jones.[13] From pp. 676-9 and Figs. 1 and 2, the caudal heart is represented as separating, caudad, into a small dorsal branch (D) and a larger ventral branch (C). Between these two forks, or, to be more exact, between the ventral branch below and the caudal artery and dorsal branch above, there is a pulsating heart (E), which communicates anteriorly with the dorsal fork of the caudal vein, a short distance from its union with the ventral fork. A valve is said to guard the entrance of the heart into the vein. These observations of Jones', which were microscopic, were made upon the tail of a small eel that had been placed upon a thin plate of glass. Upon contracting, as is graphically shown in Fig. 2, a colorless stream of lymph was seen to enter the vein. Strange to say, Jones found no definite afferent lymphatic trunks emptying into the caudal heart, and contends that such lymphatic canals as were described by Müller could not have escaped his attention. Furthermore, Jones points out that since the lymphatic vessels of Müller are identical in position with the caudal blood vessels, that they must be such. On p. 679, Jones gives the credit of the discovery of the caudal heart in the eel to Hall in 1831, but it seems that Hall regarded it as a blood heart. Continuing, Jones insists that the relation of the blood vessels to the heart as set forth by Hall is incorrect, as will be seen by comparing Hall's figure (see p. 679) to Fig. 1. Likewise Jossifoo[14] overlooked the connection of the lymphatic system with the

[13]Jones, T. W. "The Caudal Heart of the Eel a Lymphatic Heart," *Phil. Trans.,* 1868.

[14]Jossifoo, S. M. "Sur les voies principales et les organes de propulsion de la lymphe chez certains Poissons," *Archives d'anatomie microscopique,* 1906.

caudal heart in *Anguilla*. He failed to inject the caudal heart from the caudal vein, but states that when a pulsating caudal heart is seen through a microscope, it is colorless, except a little rose red, due to the adjacent blood capillaries, and that it is in great contrast to the connecting and surrounding blood vessels. Some year ago I injected some tails of the Mississippi River *Anguilla* from the dorsal and the ventral subcutaneous trunks, and hope in a later study to be able to demonstrate their connections with the caudal heart.

In many Teleosts Hyrtl (*op. cit.*, pp. 226-231 and 238, and Figs. 1, 2 and 4 a) finds two caudal sinuses situated immediately behind the last vertebra. These sinuses (see Fig. 4) are connected and both communicate anteriorly with the caudal vein, the orifice being guarded by a valve. The shapes of these sinuses are at variance in different species. According to Hyrtl, the caudal sinus is composed internally of a layer of endothelium, bounded by a layer of longitudinal fibers, outside of which there is an additional layer of transverse fibers. It is described as being contractile and comparable to the lymphatic hearts of the Batrachians. Furthermore, Hyrtl claims that the caudal sinus is no blood reservoir, for its serum is clear, and contains small, round, granular corpuscles. Vogt's description of the caudal sinus of *Salmo* (*op. cit.*, pp. 135-6, and Pl. K, Figs. 3-5, 54) is almost identical to Hyrtl's for the perch. He finds a valve in the opening between the two sinuses, and each sinus is said to contain a few muscle fibers, is contractile, and contains a clear fluid in which there are a few granular corpuscles. Sappey (*op. cit.*, p. 47, and Pl. XI, Fig. VI, 6, and Pl. XII, Fig. II, 5) speaks of the caudal lymphatic sinuses of Teleosts as being non-contractile papillæ, which are non-pulsating in the sense of the caudal hearts of the eel and Batrachians, and he was unable to find valves at the entrances of these sinuses into the caudal vein.

As for the Ganoids, Hopkins (*op. cit.*, p. 372, and Fig. 11, s.) represents each caudal sinus in a 53 cm. *Amiatus* as being a reservoir about 1 cm. long by 3 to 5 mm. at its greatest width, situated ventrad of the last vertebræ. It is said to empty cephalad into the caudal vein, the entrance being guarded by a valve, and to communicate mesad with its fellow sinus. As has already been quoted, the lateral lymphatic trunk, after receiving the caudal trunk and a fork of the dorsal, joins the caudal sinus from the side, near its anterior end.

The caudal sinuses of *Lepisosteus* (Figs. 1-6, 16 and 17, L. and R. Cau. S.) have almost exactly the same position as in *Amiatus*, and

about the same as in the Teleosts.[15] Like *Amiatus,* the caudal sinuses of *Lepisosteus* are situated ventrad and to the side of the last vertebræ. They do not lie in a longitudinal plane, but are tilted a little obliquely ventrad, following the general contour of the vertebral column in that region. Usually they cross the vertebral bases of the eighth and ninth or the ninth and tenth caudal hæmal spines (counting ventro-dorsad). These reservoirs are somewhat elongated, ordinarily deeper anteriorly than posteriorly, but in some instances, as shown in Figs. 1 and 4, they have little the appearance of sinuses, but rather maintain the same diameter throughout, which is slightly, if any, greater than the adjacent subcutaneous trunks. The contents of these sinuses was not examined, nor were they sectioned, save in a 90 mm. *L. osseus* and a few smaller specimens, where they were found to be composed of a single layer of endothelium, not unlike the longitudinal subcutaneous trunks or the caudal vein, and contained, especially, at their posterior ends and their junction with the caudal vein, a mucous or plasma-like substance, in which there were a few red and white corpuscles.

Considerable has already been said concerning the various openings of the caudal sinus. There is always a communication between the two sinuses (Figs. 1-7, o), which passes between the eighth and ninth or the ninth and tenth caudal hæmal spines (counting ventro-dorsad). The aperture of this connection is through the mesal wall of the sinus, at about its center near the floor, but in the specimen from which Figs. 1 and 2 were drawn it was nearer the roof. No valves were found guarding this orifice, and in Fig. 17 (o) this communication is shown in cross section. One or the other of the caudal sinuses, more often the right, receives the posterior continuation of the ventral trunk or what has been described as the posterior trunk (Figs. 1-5 and 7, C. T.) from the rear. As has already been stated, each of the sinuses (x) (Figs. 1-6) joins its respective caudal sinus at the dorso-cephalic corner; while the opening through the ventro-cephalic corner leads into the caudal vein (see Figs. 1-7 and 15). The venous opening of the caudal sinus that receives the caudal trunk is always much larger than the other, as is shown in Fig. 7. Unlike the other orifices of the caudal sinus, the

[15]In both *Lepisosteus* and *Amiatus* we have a masked heterocercal tail, which is more primitive than the tails of bony fish in that the caudal hæmal and interhæmal spines, although fused to each other, have not fused together in forming two hypural bones, as is the case in the Teleosts.

venous opening is guarded by a pair of *semi-lunar valves* (Figs. 4, 5 and 7, R. and L. Cau. S. V.), which open into the vein.

That part of the caudal vein which receives the caudal sinuses is enlarged almost into a reservoir, which in addition receives the last neural vein and the posterior part of the caudal vein from the tail.

With *Lepisosteus* the term caudal sinus is nothing more than an arbitrary term applied to two non-contractile reservoirs situated ventrad of the last vertebræ, near the base of the tail, which collect four longitudinal subcutaneous trunks, together with two longitudinal hæmal trunks, and empty into the caudal vein.

Summary and General Considerations.

In the tail region of *Lepisosteus* there are four longitudinal subcutaneous vessels and two profundus trunks in the hæmal canal, which collect a subcutaneous network that so far as could be determined is entirely separated from the arteries or their capillaries, and which in one way or another terminate in two caudal sinuses that discharge themselves in the caudal vein.

The two caudal sinuses are elongated reservoirs situated ventrad of the posterior end of the vertebral column. They communicate mesad with each other, dorso-cephalad with what has been designated as sinus (x), and ventro-cephalad with the caudal vein, the latter orifice being guarded by a pair of semi-lunar valves.

Posteriorly one of the caudal sinuses, more often the right, receives what has been described as the caudal trunk, which is merely a prolongation of the ventral trunk passing through the basal canal of the caudal fin, where it runs parallel to a corresponding caudal artery and vein. From each ray it receives two branches which traverse the dorsal and ventral surfaces of the ray and collect a rather coarse network of vessels from the fin membrane. This network is not continuous with arterials from the fin ray arteries. The caudal trunk in its course from the tail to the caudal sinus follows the caudal artery, and is in fact a deeper lying trunk than the caudal vein, which passes cephalad between the superficial and profundus muscles of the caudal fin.

The ventral trunk, of which the caudal is a posterior continuation, travels along the ventro-median line, just within the skin. In passing through the basal canal of the anal fin it collects paired branches from each ray, which receive a network from the fin membrane similar to that found in the caudal fin.

Each caudal sinus receives a most important communication through its dorso-cephalic wall, which has been described as sinus (x). These sinuses, which follow along the ventro-lateral surfaces of the preceding vertebræ, collect a lateral and a longitudinal hæmal trunk, and one or the other of them, the dorsal trunk.

The dorsal subcutaneous trunk travels along the dorso-median line just below the skin, but when the dorsal fin is reached, instead of dividing into two circular canals at the insertion of the dorsal fin, as in the Selachiàns and most Teleosts, it passes completely through the basal canal of the fin, and, like the caudal trunk, receives a pair of canals from each ray. These canals drain a network of vessels which is decidedly lymphatic in the character of its meshes, and which, so far as I am aware, has no connection with the arteries. When about equidistant from the posterior insertion of the dorsal and the base of the caudal fin it makes a ventral bend to cross the vertebral column, usually the right side, and culminates in the corresponding sinus (x), differing considerably in its termination from Hopkin's description for *Amiatus,* where it bifurcated, each fork uniting with the lateral trunk, immediately before the latter joined the caudal sinus.

As has been pointed out, the venous supply from the dorsal fin is collected by a pair of dorsal fin ray veins from each ray. In position these veins and the corresponding arteries are nearer the surfaces of the rays than the dorsal fin ray subcutaneous canal. In the basal canal of the fin they unite to form a dorsal fin vein, which passes through the basal canal in company with the dorsal subcutaneous trunk and the dorsal fin artery. Upon leaving this canal the dorsal fin vein in the two specimens in which it was traced out crossed the left side of the vertebral column to terminate in the caudal vein. The distribution of this vein recalls the *vena postica* of Mayer and Parker for the Selachians, and had it anastomosed with the dorsal subcutaneous trunk at the posterior border of the dorsal fin we would have had a condition of affairs almost identical with that found in the Selachians.

With *Lepisosteus* the lateral subcutaneous trunk offers few peculiarities not found in *Amiatus* or the Teleosts. In the Selachians and in *Polyodon* they are less sinus-like than in the bony Ganoids and in the Teleosts. In *Lepisosteus,* as in other fishes, they collect numerous paired transverse or intermuscular branches, which receive a rather coarse network of branches from the connective tissue binding the skin to the myotomes. These transverse branches are undoubtedly prolonged dorsad

and ventrad to anastomose with the dorsal and ventral trunks as in *Scorpænichthys* and in other fishes, but this point was not determined for a certainty in *Lepisosteus.* Instead of emptying directly into the caudal sinus as in *Amiatus* the lateral trunk in *Lepisosteus* unites with a hæmal trunk in forming sinus (x), which terminates in the caudal sinus. In a 90 mm. *L. osseus* series a connecting canal was found joining the right lateral trunk with the right hæmal trunk. This communication was in advance of the union of the lateral with the hæmal in forming sinus (x). It was not observed on the opposite side of this series or in any of the dissections.

Two longitudinal hæmal trunks were found above the caudal vein on either side of the caudal artery in the hæmal canal of *Lepisosteus.* They are undoubtedly homologous to what Mayer has described in the Selachians as vasa vasorum and to a similar trunk in the hæmal canal of the Teleosts. The cephalic distribution of this trunk was not traced out. No hæmal vessels were found connecting it with the ventral trunk as in the Teleosts, and, as stated above, it emptied into sinus (x).

In *Lepisosteus* no longitudinal neural trunk was found in the neural canal, as is the case with many Teleosts, and consequently there are no neural vessels to communicate above with the dorsal trunk.

Microscopic sections of a 90 mm. *L. osseus* showed the subcutaneous trunks, the caudal sinus and the caudal vein to be composed of a single layer of endothelium, surrounded by a mass of connective tissue. They contained but few corpuscles, the red predominating over the white.

No valves were found in the subcutaneous system of the tail region of *Lepisosteus,* save two semi-lunar valves guarding the entrance of each caudal sinus into the caudal vein.

Resumé.—From the above summary the subcutaneous system of *Lepisosteus* should fall under the head of a lymphatic system, or a separate subcutaneous venous system that has no counterpart in the arterial system and which may function both for veins and lymphatics.

In favor of the hypothesis that this system in the tail region of *Lepisosteus* are veins, we find from microscopic sections of a 90 mm. *L. osseus* that the structure of the subcutaneous vessels and the caudal vein are almost identical, and while they contain but few corpuscles, yet the red predominate.

As opposed to this supposition and in favor of the hypothesis that they are lymphatics, this study has revealed the subcutaneous system of the tail region of *Lepisosteus* to be entirely separate from the blood-

vascular system, save at the points where the caudal sinuses empty into the caudal vein. This system of vessels collects a network which is decidedly lymphatic in the character of its meshes, is coarser than the blood capillaries, and so far as observed had no connection with the arteries. Furthermore, the peripheral regions are sufficiently supplied with veins. For most of the smaller subcutaneous vessels are accompanied by corresponding arterial and venous branches; the lateral arteries and veins supply the peripheral region of the trunk, the dorsal fin artery and vein nourish the dorsal fin, and the caudal artery and vein do the same for the caudal fin. If the subcutaneous vessels are classed as veins it would be necessary to consider them as a distinct venous system that had no counterpart in the arterial system.

We are compelled to admit that the evidence is insufficient to warrant any sweeping statement as to the exact nature of this system of vessels in fishes. The little data we have, when considered in the light of certain recent studies on the embryology of the lymphatics in mammals, supports the supposition that, in the more primitive Selachians, certain subcutaneous vessels, probably veins, have become separated to some extent from the main venous system. According to Sappey, in the skates the communications of this system with the veins are quite numerous. In *Mustelus* and *Squalus,* Parker and Mayer found these points of union less abundant, but in addition to the connections of the subcutaneous vessels with the caudal vein in the tail region of the Ganoids and Teleosts, they note that the so-called dorsal cutaneous vein anastomoses behind the dorsal fin with a deep dorsal fin vein. Such a vein was found in *Lepisosteus,* but no anatomosis with the dorsal subcutaneous trunk occurred, indicating, of course, that in *Lepisosteus* the separation of this subcutaneous system had become more complete.

In the head region we find that the same differentiation of the subcutaneous system has gone on as we pass from the Selachians to the Ganoids, and from the Ganoids to the Teleosts and Batrachians, but in this region it is more obscure. In an earlier paper it was pointed out that each of the branchial lymphatic trunks (nutrient branchial veins?) of *Polyodon* anastomosed above with the subcutaneous system and below with the inferior jugular vein; that they received a coarse network from the branchial arches and from their filaments, which, so far as could be ascertained, had no capillary connections with the arterial system. In *Lepisosteus* these branchial trunks were separated into dorsal and ventral branchial lymphatic trunks (nutrient branchial veins?), which

were not connected, and which drained their respective halves of the arches. Those from the ventral portion of the arch emptied into the inferior jugular, while those from the dorsal portion terminated in dorsal branchial sinuses, which were in communication with the subcutaneous system and with the jugular through the cephalic sinus. Similar dorsal branchial lymphatic sinuses were described in *Scorpænichthys* as being in communication with the subcutaneous system and with the jugular through the cephalic sinus. No branchial lymphatic trunks were seen emptying into them, but both dorsal and ventral nutrient branchial veins were shown uniting directly with the jugular and the inferior jugular veins. It would seem that the only explanation of the above complicated condition of affairs is that a part of the subcutaneous system found in the region of the gills has become entirely separated and has reverted back to veins in the higher orders of fishes.

In the Teleosts there is a further differentiation or rather addition. Here we find that the rudimentary hæmal trunk in the hæmal canal of the Selachians and Ganoids has developed into a conspicuous trunk with numerous hæmal branches that communicate ventrad with the ventral trunk. There is also in *Scorpænichthys* and in many Teleosts a large and important neural longitudinal trunk, which traverses the neural canal above the spinal cord and sends off numerous anastomosing branches to the dorsal trunk.

In conclusion it may be said that considerable anatomical data support the hypothesis that the subcutaneous vessels of the Teleosts and Batrachians, which are evidently lymphatics, have their homologue in the somewhat similar system of the Selachians, which has much the appearance of veins. The subcutaneous system of the Ganoids is apparently a sort of intermediary; that of *Polyodon,* one of the cartilaginous Ganoids, resembling the arrangement of the Selachians, and that of *Lepisosteus,* one of the bony Ganoids, approaching the system of the Teleosts and Batrachians.

LIST OF ABBREVIATIONS USED IN THE FIGURES.

A. or P. prefixed to an abbreviation signifies anterior or posterior; R. or L., right or left; a series is numbered from cephalad to caudad.

A. R., anal fin rays.

A. R. C., anal ray subcutaneous canals.

A. R. M., anal ray levator and depressor muscles.

C., in Fig. 10, communication between the lateral and hæmal trunks.

C. A., caudal artery.
Cau. S., caudal sinus.
C. F., caudal fin.
Con. T., connective tissue.
C. P. M., caudal fin profundus muscles.
C. R., caudal rays.
C. R. A., caudal ray arteries.
C. R. C., caudal ray subcutaneous canals.
C. R. V., caudal ray veins.
C. T., caudal subcutaneous trunk or posterior continuation of the ventral subcutaneous trunk.
C. V., caudal vein.
Der., dermis.
D. F. A., dorsal fin artery.
D. F. V., dorsal fin vein.
D. R., dorsal fin rays.
D. R. A., dorsal ray arteries.
D. R. C., dorsal ray subcutaneous canals.
D. R. M., dorsal ray levator and depressor muscles.
D. R. V., dorsal ray veins.
D. T., dorsal subcutaneous trunk.
End., endothelium.
F. Con. T., fibrous connective tissue.
Hæ. C., hæmal canals.
Hæ. S. (1) to (9), caudal hæmal spines. Hypural bones of Teleosts.
Hæ. T., hæmal longitudinal trunk.
I. Neu. S., interneural spines.
Intm. C., intermuscular or transverse subcutaneous canals.
L. A., lateral arteries.
L. C. A., left caudal artery.
L. Cau. S., left caudal sinus.
L. Cau. S. O., left caudal sinus opening into the caudal vein.
L. Cau. S. V., semi-lunar valves guarding entrance of the left caudal sinus into the caudal vein.
L. Hæ. T., left longitudinal hæmal trunk.
L. T., lateral subcutaneous trunks.
L. V., lateral veins.
My., myelon or spinal cord.
Myo., myotomes of the great lateral muscles.
Neu. S., neural spines.
Neu. V., neural veins.
Neu. V. (1), last neural vein.
Neu. V. (1) O., opening of the last neural vein into the caudal vein.
o., connection or communication between the two caudal sinuses.
Pig., pigment.
Pl., blood plasma.

R. C., red corpuscles.
R. C. A., right caudal artery.
R. C. S., right caudal sinus.
R. Cau. S. O., right caudal sinus opening into the caudal vein.
R. Cau. S. V., semi-lunar valves guarding the entrance of the right caudal sinus into the caudal vein.
R. Hæ. T., right longitudinal hæmal trunk.
R. Lat. X., ramus lateralis vagi.
Uro., urostyle.
Ver., vertebral column or centrum.
V. T., ventral subcutaneous trunk.
W. C., white corpuscles or leucocytes.
x., a sinus in *Lepisosteus* formed by the union of a lateral, hæmal and often the dorsal trunk, which terminates in one of the caudal sinuses.

DESCRIPTION OF THE FIGURES.

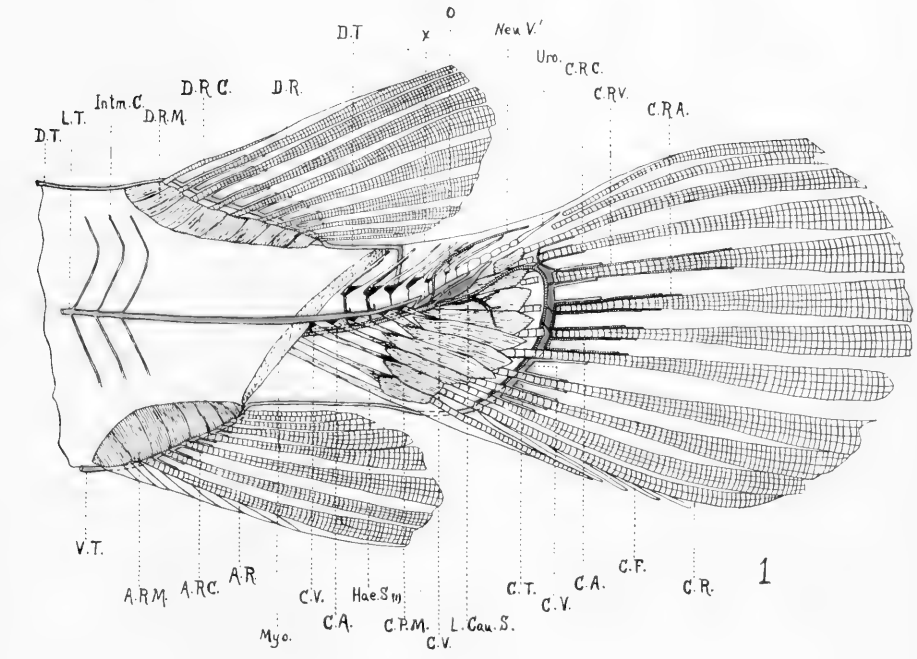
Figs. 1 to 9 were drawn to a scale from dissections of injected specimens; 10-24 are from a transverse series through the tail region of a 90 mm. *Lepisosteus osseus;* and Fig. 25 is taken from a cross section of the lateral trunk from an adult *L. osseus.* In general, the subcutaneous or so-called lymphatic canals are colored yellow or drawn in outline, the arteries are stippled, and the veins cross-barred. A vessel drawn in dotted outline signifies that it passes within or behind a muscle, bone or other vessel. All outlines for the microscopic drawings were made with the aid of a camera lucida and the details were filled in afterward.

Fig. 1. Represents a lateral dissection of the tail region of a small *Lepisosteus tristœchus* as seen from the left side. The myotomes bordering the tail are removed in order to best portray the lateral trunk emptying into the left caudal sinus, the connection of the latter with the corresponding right sinus, and the termination of the left caudal sinus in the caudal vein, together with the origin and course of the vein. The outline for this drawing was traced from a photograph and the details were filled in afterward. × ½.

Fig. 2. Is a similar dissection from the opposite or right side of the same specimen as Fig. 1. On this side the dorsal, hæmal and lateral trunks fuse to form sinus (x), which with the caudal trunk terminates in the right caudal sinus, and the latter empties into the caudal vein. The distribution of the caudal artery is also shown, and, like Fig. 1, the dissection was first photographed and the details were filled in afterward. × ½.

SUBCUTANEOUS VESSELS IN TAIL OF LEPISOSTEUS

WILLIAM F. ALLEN



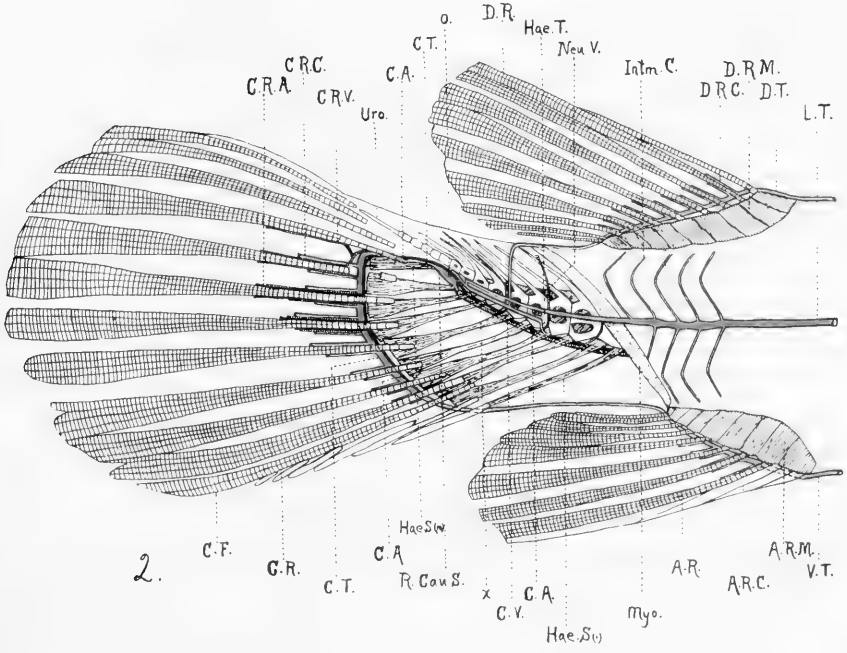


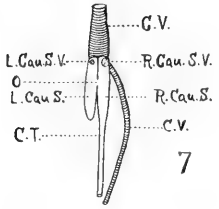
Fig. 7. Dorsal view of the caudal sinuses of a small *L. osseus;* the dorsal walls of each being removed to show their median communication and the semi-lunar valves guarding their exit into the caudal vein. Natural size.

Fig. 8. Shows distribution of a lateral artery and vein as seen from the left side of a small *L. tristœchus.* In this dissection the great lateral trunk was removed, but its position is indicated by dotted lines. × ½.

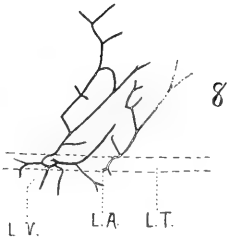
Fig. 9. The distribution of the dorsal fin vein and artery as seen from the right side of a small *L. tristœchus.* All of the musculature in this region is completely removed. In another specimen where these vessels were traced out the artery took its origin seven or eight vertebræ cephalad of its position here, and approached the basal canal of the dorsal from in front. × ½.

Fig. 10. From a transverse section through the caudal peduncle region of a 90 mm. *L. osseus* about midway between the dorsal and the caudal fins as seen from the rear (caudad) ; showing the caudal artery and vein, together with the dorsal, ventral, lateral and hæmal trunks in section. Note the connection between the right lateral and the right hæmal trunks. × 9.

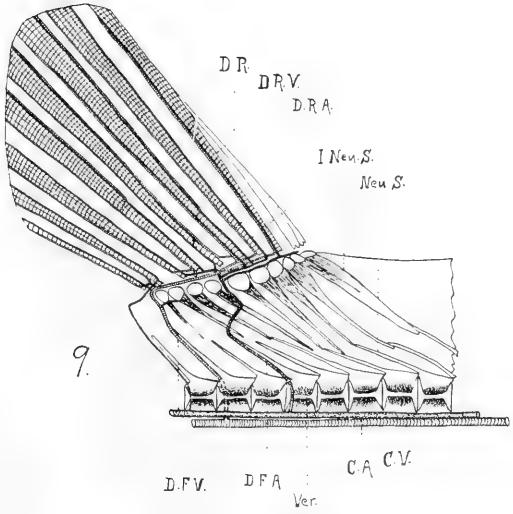
Fig. 11. A portion of a transverse section .07 mm. caudad of Fig. 10. Here the caudal artery and vein, together with the right hæmal and the two sinuses (x), are seen in section. In a section .04 mm. cephalad the right sinus (x) takes its origin blindly, and the left hæmal trunk is leaving the hæmal canal to become the left sinus (x). × 9.


C.V.
L.Cau.S.V.
R.Cau.S.V.
L.Cau.S.
R.Cau.S.
C.V.
C.T.

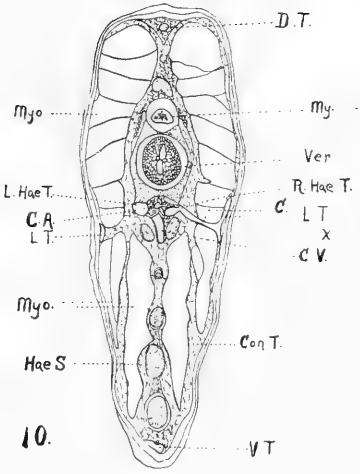
7


L.V.
L.A.
L.T.

8


D.R.
D.R.V.
D.R.A.
I Neu.S.
Neu.S.
D.F.V.
D.F.A.
C.A.
C.V.
Ver.

9.


D.T.
Myo.
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C
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Hae S.
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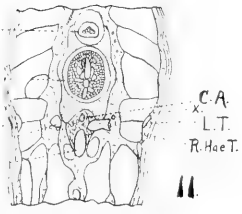
V.T.

10.


C.A.
x
L.T.
R.Hae.T.

11.

Fig. 12. Transverse section taken .35 mm. caudad of Fig. 11 as seen from the rear (caudad). Left lateral trunk emptying into the left sinus (x), and the dorsal trunk crossing the left side of the vertebral column preparatory to emptying into the left sinus (x). The right hæmal trunk terminates in the right sinus (x) .06 mm. caudad of this section, while the right lateral trunk does not join the right sinus (x) until a point .45 mm. caudad of this section is reached. × 9.

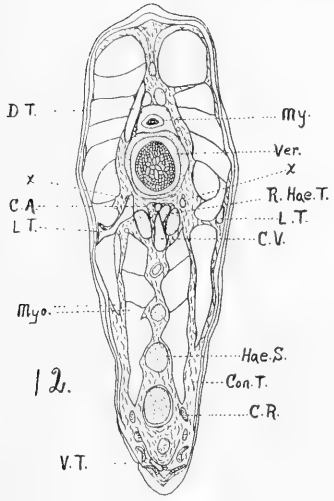
Fig. 13. Is from a section .22 mm. caudad of Fig. 12 viewed from the rear (caudad); dorsal trunk terminating in the left sinus (x); caudal artery and vein, ventral trunk and sinuses (x) seen in cross section. × 9.

Fig. 14. A transverse section .05 mm. caudad of Fig. 13 as seen from the rear (caudad); last neural vein crossing the left sinus (x) and emptying into the caudal vein. The caudal artery has bifurcated, and its two forks, together with the caudal vein, the ventral trunk and the two sinuses (x) are seen in section. × 9.

Fig. 15. Taken from a transverse section 23 mm. caudad of Fig. 14 examined from the rear (caudad). The two caudal sinuses are seen in section emptying into the caudal vein. Both caudal arteries, both sinuses (x), the last neural vein and the ventral trunk are also shown in section. × 9.

Fig. 16. From a transverse section .43 mm. caudad of Fig. 15 viewed from the rear (caudad). The left sinus (x) is seen in section terminating in the left caudal sinus, but the right sinus (x) does not empty into the right caudal sinus till a section .09 mm. caudad is reached. The caudal vein is bearing off to the left. Both caudal arteries, the right sinus (x) and the ventral trunk are seen in section. × 9.

Fig. 17. A transverse section .67 mm. caudad of Fig. 16 as seen from the rear (caudad). The right caudal sinus communicates mesad with the left through the canal (o). The two arteries and caudal vein are seen in section, and the ventral trunk is traveling dorsad in the basal canal of the caudal fin to become the caudal trunk (C. T.). × 9.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Myo.
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Con.T.
C.R.
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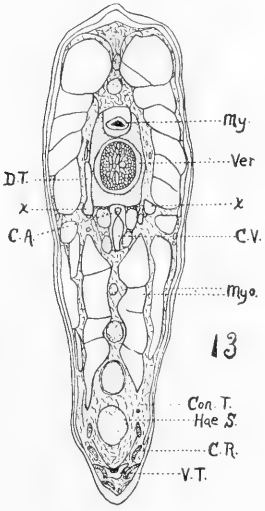
My.
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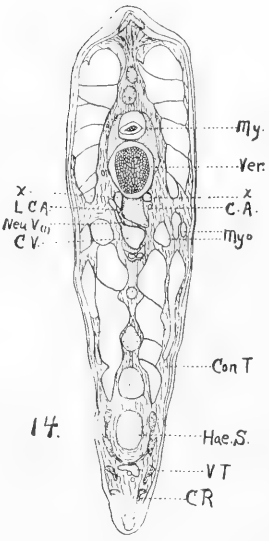
My.
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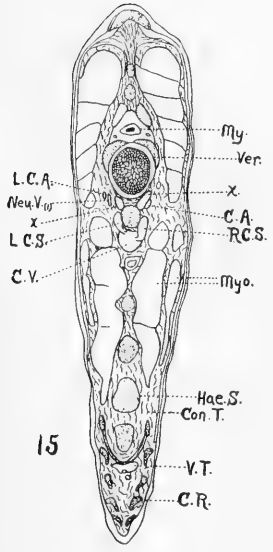
My.
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x
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Con.T.
15
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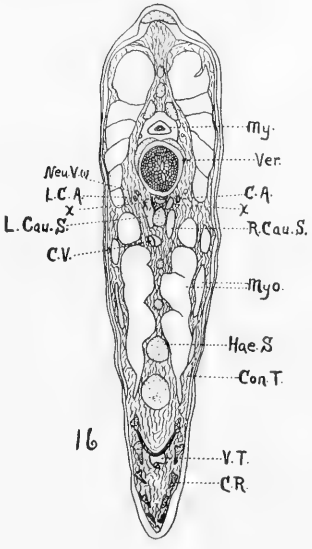
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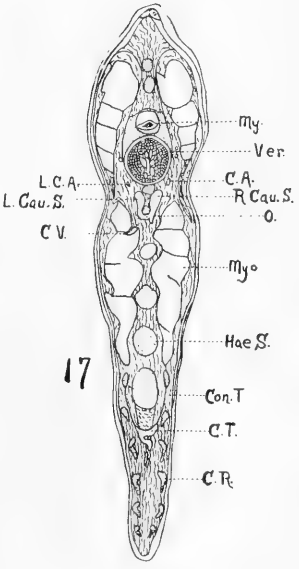
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Fig. 18. Taken from a transverse section .47 mm. caudad of Fig. 16 as seen from the rear (caudad). Continuation of the right caudal sinus is observed in section a little below the vertebral column as the caudal trunk (C. T.). The fin portion of the caudal trunk (C. T.), or the continuation of the ventral trunk, is becoming more and more dorsal in the basal canal of the caudal fin, and branches to it from the fin (C. R. C.) are seen in section, as are also the corresponding arteries and veins. Both caudal arteries and the caudal vein retain their former positions. × 9.

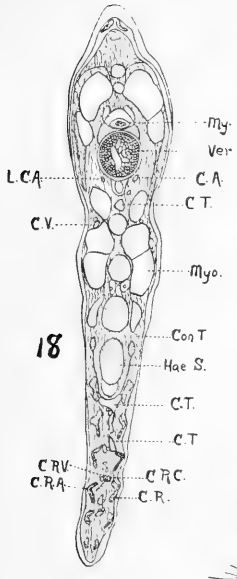
Fig. 19. Transverse section taken through the caudal fin 1.18 mm. caudad of Fig. 18 as viewed from the rear (caudad). Caudal vein and caudal trunk will be found passing through the basal canal of the fin; the caudal ray vessels are seen in section; while the caudal artery has not yet left for the basal canal of the fin. × 9.

Fig. 20. One of the hæmal trunks from a cross section through the caudal peduncle of a 90 mm. *L. osseus*. Like the caudal vein, it is composed of a single layer of endothelium, and no corpuscles of any kind were found for a distance of several millimeters. × 225.

Fig. 21. From a transverse section through one of the lateral trunks of a 90 mm. *L. osseus* as it sends inward a connecting vessel (C) to join the hæmal trunk. Note that the walls of both the lateral and the connecting vessels, which are composed solely of endothelium, are bounded by a fibrous connective tissue. Also that the red corpuscles greatly outnumber the white. × 225.

Fig. 22. A portion of a transverse section through a 90 mm. *L. osseus*, showing the caudal artery and upper part of the caudal vein imbedded in a mass of loose connective tissue within the hæmal canal. Corpuscles are very abundant in the artery, while in the vein they are very scarce. Note that the caudal veins consist of but a single layer of endothelium, which is almost identical with the hæmal trunks. × 225.

WILLIAM F. ALLEN



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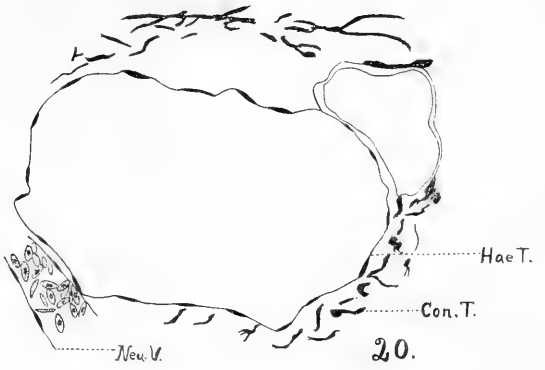

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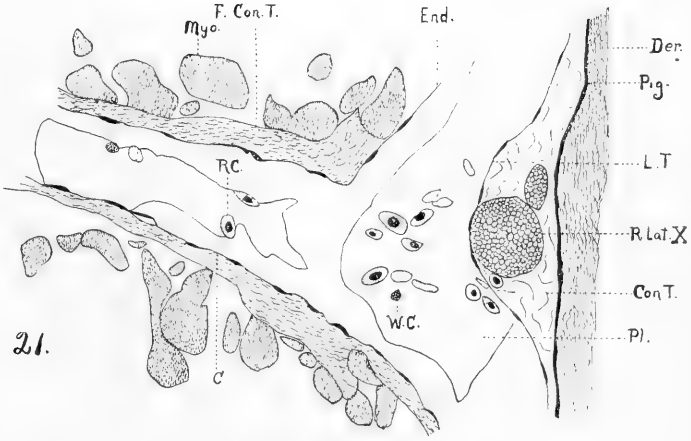

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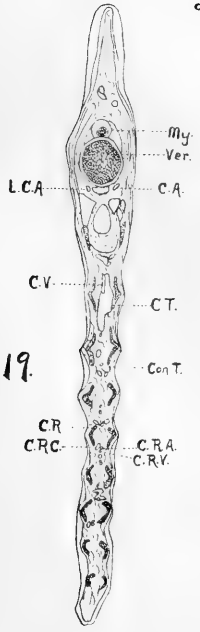

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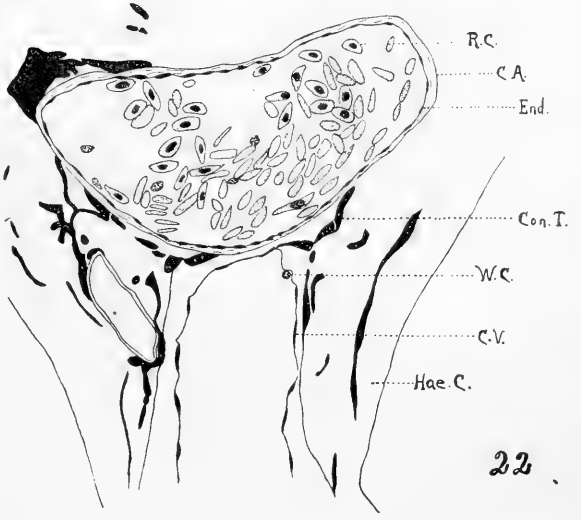

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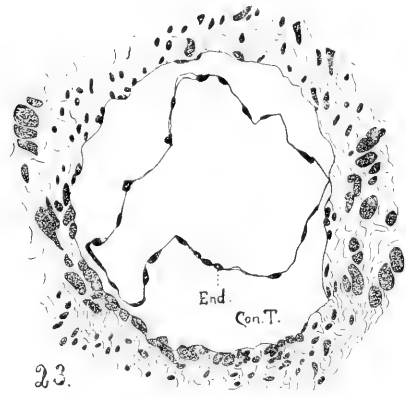
Fig. 23. From a transverse section through the caudal trunk of a 90 mm. *L. osseus*. No corpuscles of any kind were found within this trunk throughout this series of sections. × 225.

Fig. 24. Transverse section through the caudal ray vessels of a 90 mm. *L. osseus*. × 225.

Fig. 25. Is from a transverse section through the lateral trunk of an adult *L. osseus*. Note that the endothelial canal is bounded by a fibrous connective tissue and that the red corpuscles greatly predominate over the white. × 225.



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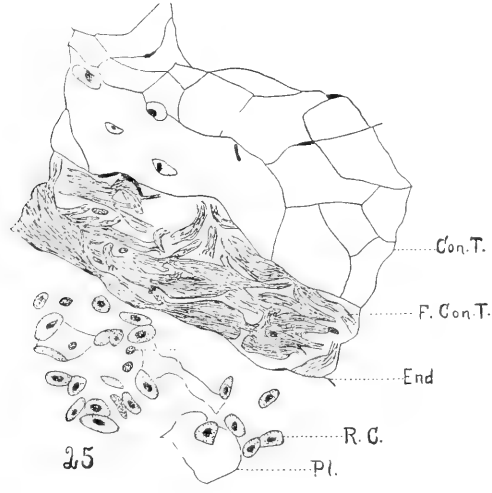

25

THE DEVELOPMENT OF THE HYMEN.

BY

FRED. J. TAUSSIG, M.D.

From the Anatomical Laboratory of Washington University, St. Louis.

WITH 14 FIGURES.

Observations thus far collected concerning the origin and development of the hymen may broadly be divided into clinical and embryological. The clinical evidence is based on the study in adult life of the congenital anomalies such as hymen duplex with double vagina, hymen with absent vagina, etc. The interpretation of these anomalies is very difficult, and their value in an embryological study is really only of a confirmatory nature. Consideration of them alone can never result in a solution of the problem of hymeneal development. The embryological evidence on the development of the hymen is based on gross anatomical dissections, single microscopic sections, and on serial sections of the hymen and its surrounding structures. Accurate conclusions must be based on a correct valuation of these three sorts of evidence. For the proper study of so minute a structure as the fetal hymen, the last named method—serial sections—is of paramount value.

An extensive review of the various opinions on hymeneal development has recently been made by Gellhorn ('04). From the standpoint of time, we may distinguish a convaginal theory, according to which the hymen is formed at the same time as the vagina, and a postvaginal theory, according to which the hymen is formed after the development of the vagina. It is, however, better to classify the various views from the standpoint of origin. They may be grouped under four heads:

(1) Vulvar Theory, Pozzi ('84).

(2) Bilamellate Vulvo-vaginal Theory, Schaeffer ('90).

(3) Uni-lamellate Vulvo-vaginal Theory, Nagel ('97), Budin ('79), Webster ('98), Klein ('94).

(4) Vaginal Theory, Dohrn ('75), Veit ('99), Gellhorn ('04).

(1) Vulvar Theory. Pozzi ('84) bases his theory wholly on the clinical findings in cases of malformation of the genital tract, above all on the presence of a hymen in the absence of the vagina, the occasional occurrence of a urethral hymen, and the presence of a single hymen in double vagina. Such anomalies he believes could only occur if the hymen developed from the vulva or sinus urogenitalis.

(2) Bilamellate Vulvo-vaginal Theory. In 53 out of 190 specimens of fetal hymens (28.8 per cent) Schaeffer ('90) was able to find a more or less distinct double hymen. The two folds were connected by bands of tissue, and according to his theory later coalesce to form the hymen. The one fold springs from the vulva, the other from the vagina. Thus we would have a four-layered hymen, two layers from each fold.

(3) Uni-lamellate Vulvo-vaginal Theory. Budin ('79) explains this theory in the following way: The hymeneal ring is the outer end of the vagina. The latter opens into the sinus urogenitalis, at the same time pushing the walls of its canal outwards, just as the portio vaginalis uteri protrudes into the vagina. Thereupon an opening forms in the centre, but the peripheral ring-like protrusion remains, covered externally by the mucosa of the urogenital sinus, internally by the vaginal mucosa. Nagel's ('97) description (Fig. 9) differs only slightly from this. He says: "In embryos of the third month there is an increase and accumulation of the upper layers of the epithelium occurring at first just above the vaginal orifice, whereby the vagina becomes dilated at this point (in embryos of 7-10 cms. length). Through this dilatation arises the hymen. For since the edge of the original opening is not affected by the dilatation, the orifice, on the contrary, retaining its original narrowness, a ring must thereby be formed by which the vagina is shut off from the urogenital sinus. The opening of this ring, up to embryos of 20-22 cms. length, remains filled with epithelium."

According to this view, therefore, the hymen is made up of a single fold, one side of which is formed by the vagina, the other by the vulva.

(4) Vaginal Theory. Dohrn's ('75) work supporting this theory is based on median sagittal sections through the pelvis of twenty-five fetuses from the ninth to the twenty-eighth week of development. No microscopic study was made. From the ninth to the fifteenth week he finds a stronger growth of the posterior wall of the vagina so that its canal becomes wider and bends more sharply forward. From the seventeenth to the nineteenth week there is a marked proliferation of the inner wall of the vagina, so that it seems made up of tooth-like projec-

tions. By the beginning of the nineteenth week the hymen is visible as a fold rising from the posterior wall of the vagina directly above the point of entrance of the vagina into the sinus urogenitalis. To meet this a shorter fold from the anterior wall grows downward. The two folds unite, leaving a semi-lunar opening. The growth of the hymen is very rapid. He continues:

"Der Umstand dass die Hymenalmembran in der Nähe der Stelle entsteht an welcher sich die Allantois und Mueller'schen Gänge in der Cloake begegnen, und der Sinus Urogenitalis abscheidet, hat wiederholt zu der Vermuthung geführt, dass der Hymen mit einem Entwickelungsgebilde der früheren Zeit in Zusammenhang stünde. Je genauer man aber die früheren Entwickelungsstufen in ihrer Weiterbildung verfolgt, desto mehr wird man überzeugt, dass ein solcher Zusammenhang nicht vorliegt. Wir haben beim menschlichen Embryo einen langen Zeitraum, den Abschnitt von der 9-17ten Woche, in welchem wir den Mittelstufen zwischen Hymen und den an seiner Entwickelungsstelle früher zusammengetroffenen Gebilden nachspüren können. Das Resultat ist negativ. Der Hymen ist lediglich eine spätere Bildung, welche sich nicht in continuirlicher Fortenwickelung an frühere Formen anschliesst."

Gellhorn ('04) also holds to the vaginal theory, although I believe he does not sufficiently emphasize in his article the difference between his conception and the above-mentioned vulvo-vaginal theory. Budin describes the vaginal bulbus as projecting into the urogenital sinus. Into this protruding conus, according to Gellhorn, the vaginal connective tissue grows, so that, with the possible exception of a thin layer of epithelium of the urogenital sinus on the outside, the entire hymen is of vaginal origin.

While it is thus seen that there is no lack of theories, their foundation is for the greater part the most meagre and inconclusive evidence. Only one man so far as I know studied serial sections of the hymen microscopically, and that one—Klein ('94)—studied but a single case in this way.[1] No one has thus far made use of serial sections in a number of embryos of various stages of development for an investigation of the

[1]I do not include in this consideration the two embryos that Klein cut in transverse serial section, but only the one sectioned sagittally. Transverse sections, unless some sort of reconstruction is made (and this was not done), are not favorable for a study of the hymen in its relations to neighboring structures, a point which Klein himself concedes.

hymen. It was this fact that induced me to study the five embryos at my disposal by this method. They were the following:

Embryo 1. 18 cms. long, well preserved. No abnormalities of development as far as examined.

Embryo 2. 18 cms. long, slightly macerated, no abnormalities.

Embryo 3. 18 cms. long, well preserved, normal.

Embryo 4. 21 cms. long, removed by laparotomy, excellent preservation. No abnormalities in development.

Embryo 5. Six months gestation. Legs have been removed for another purpose, hence exact length could not be determined. Preserved in Mueller's fluid. No abnormalities of development.

The measurements of these embryos were taken from the vertex to the heel.

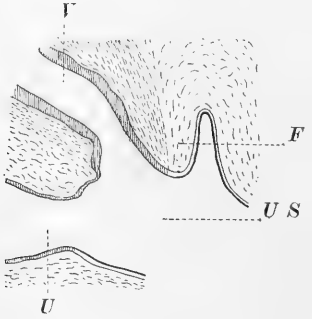

Fig. 1. Median sagittal section at entrance of vagina into urogenital sinus (Embryo 1). It is seen that the fold at the entrance is in connection partly with the vagina, partly with the sinus. F., fold; U., urethra; U. S., urogenital sinus; V., vagina. Magnified 20 X.

Paraffin was used in Embryo 1, celloidin in Embryos 2, 3, 4 and 5, as an imbedding medium. All sections were cut sagittally, in series, 25 microns in thickness and were stained, some with van Gieson, some with hematoxylin and eosin.

Before proceeding with the description of the microscopic findings, it will be well to point out the difference between the epithelium of the vagina and that of the urogenital sinus. Sinus epithelium as usually seen in section is a narrow, deeply staining band of small, round or spindle cells, with a nucleus almost filling the cell, whereas vaginal epithelium is a wide mass of large polygonal, faintly staining cells. Only the basal cells of the vagina are small and these take a deeper stain (see Fig. 8a). Klein gives the following measurements:

Sinus epithelium: thickness of entire layer, 0.073 mm.; cells, 13 microns high, 6 microns broad; protoplasmic mantle about one-third the diameter of the nucleus. Vaginal epithelium: thickness of entire layer, 1.75 mm.; cells, 17-44 microns in diameter; nucleus one-fifth the size of the cell. The great variation in size of the vaginal cells is worthy of special attention.

Embryo 1 (*Fig. 1*). The vaginal canal in this 18 cm. fetus can be seen extending a distance of about one centimeter from the cervical indentation to the point where it breaks into the vulva. In its upper four-fifths there is no lumen, the central portion being occupied by an irregularly branching trunk of epithelium, four or five cells in diameter. In the lowest one-fifth the canal suddenly widens, the mass of epithelial cells becomes much thicker and a lumen is to be seen that is partly filled with desquamated epithelium. Beneath this epithelial layer lies an area of loose connective tissue cells possessing an embryonal character, with only here and there a connective tissue fibre stained pink by the fuchsin. This layer of embryonal cells is several times thicker than the rod of epithelium in the centre. The outer covering of the vaginal cylinder consists of a thin mantle of connective tissue fibres whose red color, when stained with van Gieson, serves to outline it sharply from the surrounding structures.

The point where the vaginal cylinder enters into the urogenital sinus can be followed in nineteen sections. The vaginal conus bends ventrally at its point of entrance into the sinus and thereby a fold is formed between its dorsal wall and the sinus. Microscopically this fold can be seen to consist of the following structures from within outwards: (1) vaginal epithelium, (2) vaginal embryonal connective tissue, (3) fully formed connective tissue fibres from the vagina, (4) fully formed connective tissue fibres from the vulva, (5) vulvar or sinus epithelium. This fold is, therefore, of vulvo-vaginal origin. It corresponds in shape and position to the hymen.

Embryo 2 (*Fig. 2*). Fetus 18 cms. long. Owing to the poor state of preservation the epithelium is partly cast off and the hematoxylin stain rather diffuse. In general the state of development approximates that described in Embryo 1. A vaginal lumen can be seen, but it seems to be an artifact due to the desquamation of epithelium. There is no proliferative tendency in the vaginal connective tissue. The bulk of the vaginal conus is composed of embryonal connective tissue cells. The growth along the posterior vaginal wall is less marked, so that the fold

left at the point of entrance into the sinus is less pronounced. However, such a fold can be distinctly followed through a considerable number of sections. From the direction of the connective tissue fibres it can be seen that both vulva and vagina enter into its composition.

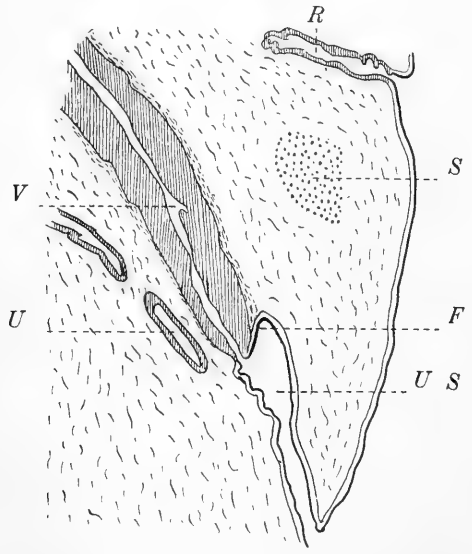

Fig. 2. Median sagittal section through lower portion of genital tract (Embryo 2). F., fold; R., rectum; S., sphincter ani muscle; U., urethra; U. S., urogenital sinus; V., vagina. Magnified 20 X.

Embryo 3 (*Fig. 3*). Fetus 18 cms. in length, good state of preservation. The three layers of the vagina previously described are here also to be seen in about the same stage of development. No vaginal lumen can be distinguished. The convex bulb of the vaginal cylinder projects but slightly into the cavity of the sinus urogenitalis. There is no special growth of the posterior wall, and nowhere is there to be seen any fold[2] such as was found in Embryos 1 and 2. There is no proliferation of the vaginal connective tissue.

[2]Since the completion of this article, I was able to obtain a sixth embryo and made serial sections of the genital tract. The embryo was 18 cms. in length and in an excellent state of preservation. The conditions were similar to those of Embryo 3. The vagina consisted mostly of embryonal connective tissue, with a central, somewhat branching core of epithelium, a few cells in thickness. At the point of its entrance into the sinus urogenitalis, there was no sign of a connective tissue fold such as Nagel describes (Fig. 9).

Embryo 4 (*Figs. 11-13*). Fetus 21 cms. in length. The vagina is seen to possess a lumen in its lower half, this lumen being filled almost entirely with desquamated epithelial cells, whose nuclei and protoplasm, though greatly shrunken, can still be differentiated. The three layers of the vagina differ greatly in character from those described in Embryos 1-3. The inner epithelial layer is here the thickest of the three. The cells lie 12-15 rows deep and differ in size and staining character in a way similar to that of the adult vagina; *i. e.,* the superficial cells are large, somewhat spindle-shaped, their protoplasm and

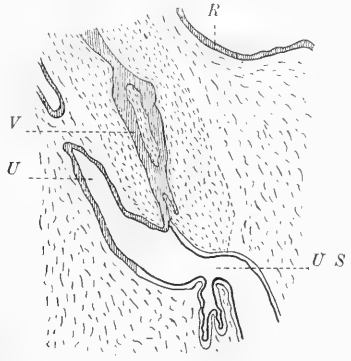

Fig. 3. Median sagittal section through entrance of vagina into urogenital sinus (Embryo 3). No fold is here visible. R., ventral wall of rectum; U., urethra; V., vagina; U. S., urogenital sinus. Magnified 20 X.

nucleus staining faintly; the deeper cells, especially the basal layer, are small, cubical, with deeply staining nucleus and scanty protoplasm. Into the layer of loose connective tissue cells outside this epithelial layer the latter sends finger-like processes, so that at times apparent islands of connective tissue cells are seen to lie in the midst of the epithelium. In serial sections these can be seen to be continuous with the connective tissue layer. Judged by the pictures in the previous cases, it would seem more rational to interpret this intertwining of connective tissue and epithelial process as due to an outward growth of the epithelium rather than an inward growth of the connective tissue.

The inner connective tissue layer is not as wide but more dense than in the embryos just described. The nuclei are smaller and stain more deeply, and here and there beginning connective tissue fibrillæ are to be noted. The outer layer of connective tissue is not clearly differentiated

from surrounding structures. We find the connective tissue fibres more developed and an admixture of unstriped muscular fibres.

Following the vagina down to its point of entrance into the sinus urogenitalis, we are struck by the difference in size and staining property of the vaginal and sinus epithelium. The sinus epithelium at this point consists of three or four layers of small cubical cells with deeply staining nucleus. This difference in the epithelium, already emphasized by Klein, together with the direction of the connective tissue fibres, makes it easy to determine how much is vagina, how much is sinus.

It is seen in studying the series that a crescentic fold of tissue attached to the dorsal and lateral aspect is left at the point of entrance of vagina into sinus. This fold is lined on the inner side by vaginal, on the outer side by sinus epithelium (Fig. 12). It is not by any means a well-formed membrane.

Just anterior to this fold the connective tissue of the vagina both ventrally and dorsally (but principally dorsally) sends a proliferating branch in through the epithelium. The two join to form a membrane that, with the exception of one small opening, completely closes the vaginal canal. It is clear that this membrane must be the hymen, and it is also indisputable that, in this case at any rate, it is of vaginal origin, since it lies internal to the point of junction between vagina and sinus urogenitalis, is lined on both sides by vaginal epithelium, and has its connective tissue directly continuous with the connective tissue of the vagina.

That this membrane is not one of the secondary folds occasionally to be seen internal to the hymen, where there is a marked proliferative tendency on the part of the vaginal connective tissue, is evident by the fact that (with this one exception) there are to be seen no high papillary projections. The sections in this case seem to represent about the same stage of development as do those of Klein, but his interpretation of the findings is different, as will be subsequently shown.

Embryo 5 (*Figs. 4-8*). Development that of about 5-6 months. The vagina is 3 cms. in length and from 2-6 mms. in diameter. The narrowest portion is the upper fifth, in which there is no lumen and the epithelium is only a few layers of cells in thickness. Here there is also little connective tissue proliferation. Further down the canal, and particularly near the vulvar end, this proliferation is very extensive, so that there appear bands, papillæ and islands, depending on the way the sections happen to be cut through the projections. Here we should

be at a loss to interpret the various structures were it not that we are able to follow them in series and thus to determine their relationship to their surroundings. Only two layers can be differentiated in this specimen, the middle layer of embryonal connective tissue being absent. The epithelial layer is similar to that in Embryo 4, except that larger

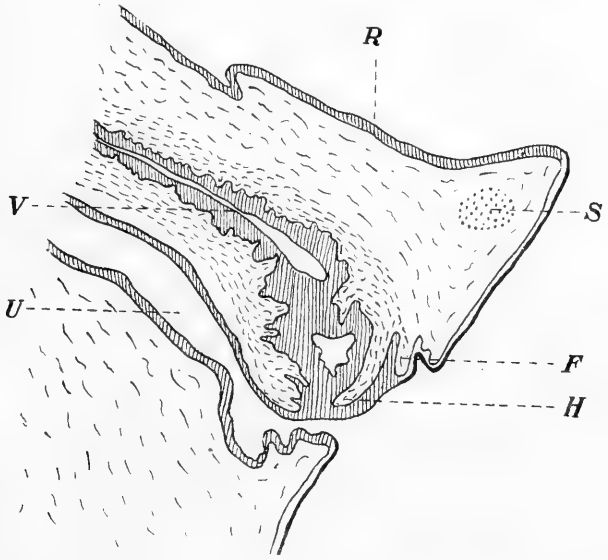

Fig. 4. Sagittal section a little to right of median line through lower genital tract (Embryo 5). Section No. 179. F., fold; H., hymen; R., ventral wall of rectum; S., sphincter ani muscle; U., urethra; V., vagina. Magnified 5 X.

quantities of desquamated cells are found lying in the vaginal lumen. The connective tissue fibres take the fuchsin stain deeply and are more densely compacted than in Embryo 4.

We can again distinguish two folds or membranes. The outer fold is lined externally by vulvar epithelium, internally by vaginal epithelium (Fig. 8a). Its connective tissue fibres (Fig. 8) are partly continuous with the connective tissue of the vagina. In part they intermingle with the connective tissue of the vulva and perineum. Reconstructed, this fold has somewhat the shape of a thin crescent, whose concave margin faces the urethra. It springs almost wholly from the dorsal wall. A short projection can be seen opposite on the ventral

wall. Directly anterior to this fold is the true hymen, a membrane two to three millimeters in height and about one-half to one millimeter in thickness, likewise springing mainly from the dorsal wall (Figs. 4 and 5), with a smal oval opening high up near the urethra corresponding to the hymeneal orifice. Its epithelium and connective tissue are vaginal. Papillary proliferations are found on its inner and outer surfaces.

The evidence of these five embryos can be briefly summarized as follows:

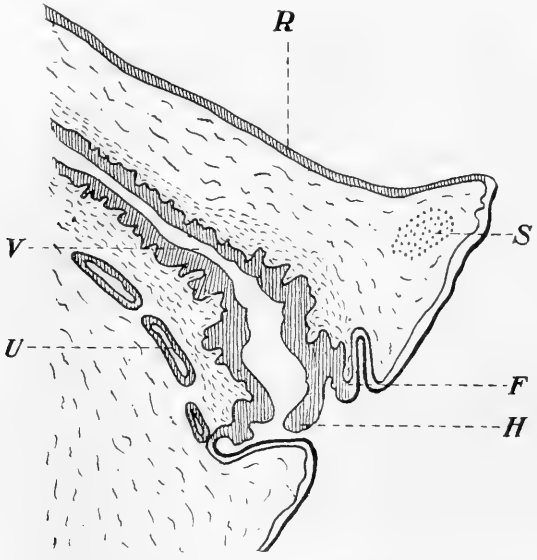

Fig. 5. Median sagittal section (Embryo 5). Section No. 187. F., fold; H., hymen; R., ventral wall of rectum; S., sphincter ani muscle; U., urethra; V., vagina. Magnified 5 X.

In the fetus 18 cms. long (Embryos 1 and 2) there may be seen at the point of junction of vagina and sinus urogenitalis, rising mostly from the dorsal wall, a crescentic fold composed of elements coming both from the vagina and the vulva or sinus urogenitalis. Occasionally, as in Embryo 3, this fold is absent. In the fetus 21 cms. long this crescentic fold is again to be seen, but not so well marked. Anterior to it and lying wholly within the vagina is a thick membrane, the hymen, almost completely closing the vaginal canal, composed only of vaginal elements. No other similar folds or membranes are present.

In the fetus 25-30 cms. long the crescentic vulvo-vaginal fold is still recognizable, but the true hymeneal membrane is evidently anterior to

it. It is here very well developed and is composed entirely of vaginal elements.

The explanation that suggests itself from the study of my sections is similar to Dohrn's ('75). It points to the hymen as of vaginal origin, independent of the place at which the vagina breaks into the urogenital sinus.[3] This spot is already clearly to be seen in the 14 cm. fetus as shown in Nagel's illustration (Fig. 9). Within arises a fold of vaginal tissue, the true hymen, stretching almost completely across the vaginal canal. At the point where the vaginal bulbus breaks through,

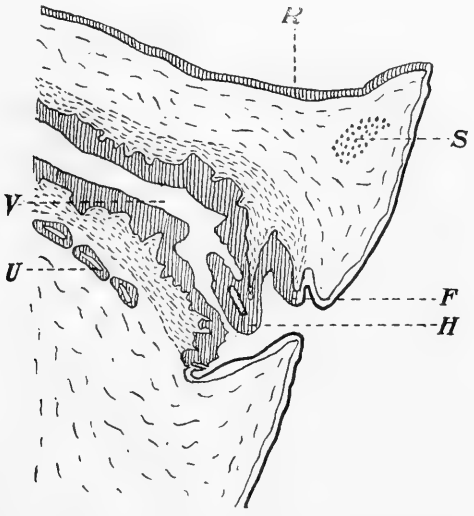

Fig. 6. Sagittal section a little to left of median line (Embryo 5). Section No. 191. F., fold; H., hymen; R., ventral wall of rectum; S., sphincter ani muscle; U., urethra; V., vagina. Magnified 5 X.

the so-called Muellerian eminence, a more or less well marked fold of tissue is left. As the fetus develops this fold becomes obliterated. In cases of arrested development we may have the fold persisting almost to birth, thus giving the picture of a bilamellate or double hymen.

[3]In this and subsequent arguments I have assumed that the vagina is entirely formed by the coalesced Muellerian ducts and not to any extent by the sinus urogenitalis. Practically the only testimony that would speak against this view is the occasional presence of epithelial areas that appear to come from the urogenital sinus. The interpretation of such epithelial areas is, however, a matter of great uncertainty, as has recently been pointed out by Meyer ('07) in a discussion on the remnants of the Wolffian ducts.

Let us now see how this explanation agrees with the findings, clinical and microscopic, that have been brought forward by other observers.

Considering in the first place the clinical evidence, we would emphasize the variations in the shape of the hymeneal orifice. This has, I believe, not been given due importance. We have on the one hand authors as Nagel ('97) and Klein ('94), who hold that the formation of the hymen is passive, *i. e.*, merely due to a bulging forward of the vaginal bulb, particularly of the dorsal wall, into the urogenital sinus, and a consequent thinning out of the intervening septum. On the other

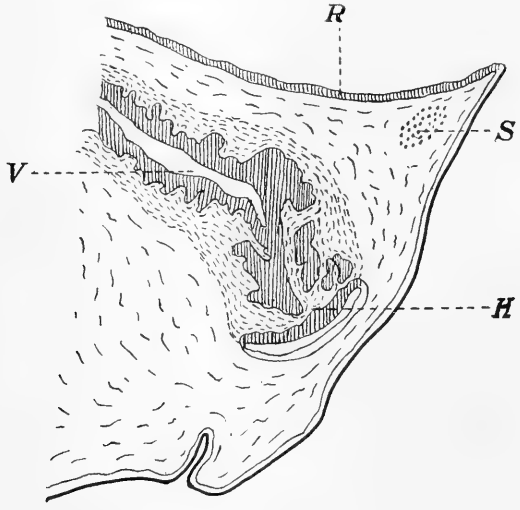

Fig. 7. Sagittal section about 1 mm. to the left of plane of Fig. 6. Urethra and vulvo-vaginal fold are not to be seen in this section, No. 207. H., hymen; R., ventral wall of rectum; S., sphincter ani muscle; V., vagina. Magnified 5 X.

hand, some investigators, as Dohrn ('75) and Schaefer ('95), consider its formation as active, *i. e.*, a proliferation of connective tissue with the production of a membrane more or less completely shutting off the vagina from without. It seems to me the variations in position, shape and size of the hymeneal orifice point distinctly to a proliferative process. If we conceive the evolution as passive, we should expect a round or oval orifice near the upper portion of the hymen. Such a view cannot explain the cases of denticulate, cribriform and fimbriate hymens. Even Klein takes for granted, in the last named form, a papillary growth along the edge of the hymen. In other words, he claims the process is

passive except when it is active. This seems irrational. Apparently the hymen does not represent a thinned out membrane, but a proliferation of connective tissue. That such a proliferating tendency of the vaginal connective tissue exists, all writers, including Klein ('94), agree.

The next clinical fact to be considered is that occasionally a hymen is to be found in the absence of a vagina. This point is emphasized by

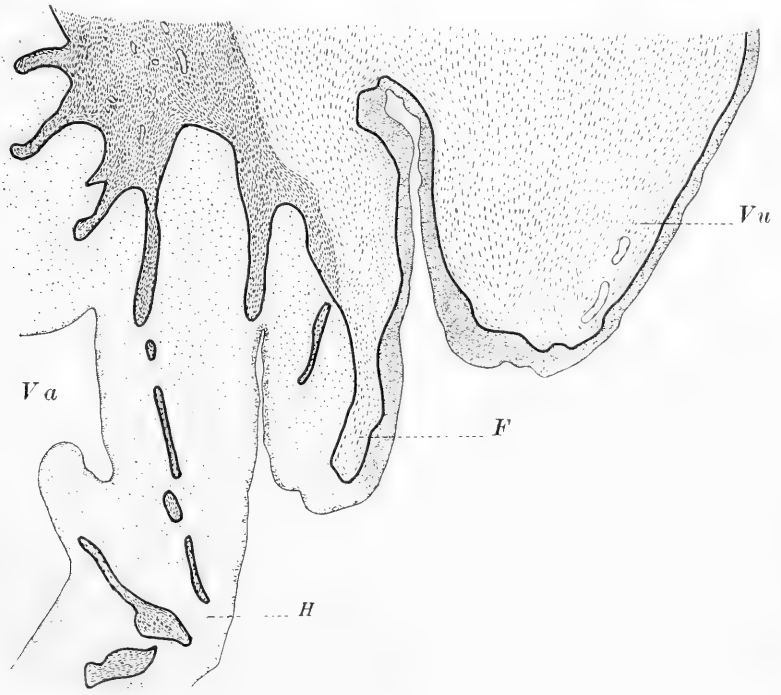

Fig. 8. Drawing of dorsal portion of hymen, vulva and vagina in median sagittal section (Embryo 1). Section No. 183. This shows clearly how the vulvo-vaginal fold is distinct from, and posterior to, the hymen. By their density and direction, the connective tissue fibres of the vagina are set off from the vulvar connective tissue. The difference in epithelium is also indicated in a general way. F., fold; H., hymen; Va., vagina; Vu., vulva. Magnified 40 X.

Pozzi ('84), as favoring his conception of the vulvar origin of the hymen. It is, however, here as elsewhere that the exception proves the rule. In the large majority of cases where the vagina is absent, a hymen is also not to be found. Thus the weight of the evidence favors the vaginal theory. Furthermore, as Veit points out, the occurrence of

a hymen in atresia vaginæ can be readily explained. We know that, at some places, portions of the vagina may remain obliterated while at other points a lumen is formed. If the extreme lower end of the vagina be the only portion that so develops it might readily present the picture of a hymen in absence of the vagina.

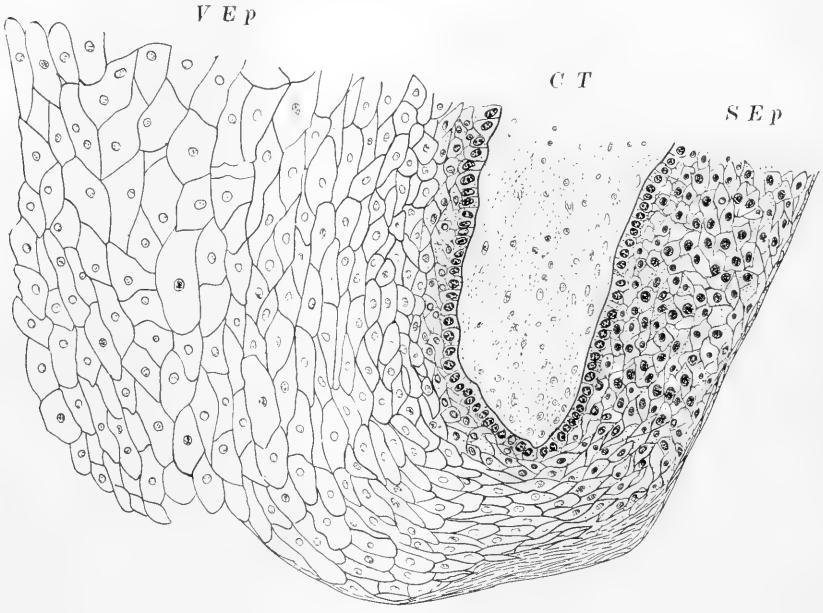

Fig. 8a. Detail drawing of the tip of the vulvo-vaginal fold seen in Fig. 8 to show the difference in character between vaginal epithelium and sinus epithelium. C. T., connective tissue; V. Ep., vaginal epithelium; S. Ep., sinus epithelium. Magnified 100 X.

A few cases have been reported in which a single hymen was found with double vagina. This fact is brought forward by the upholders of the vulvar theory as proof of their contentions, in spite of the fact that here, too, the rule is that the hymen is double, one for each vagina. The burden of proof is here likewise against them. The unusual cases of single hymen can, moreover, be readily explained on the basis of an incomplete vaginal septum, that is, one in which the septum dividing the two vaginas does not fully reach to the hymeneal ring.

From the anatomical dissection of 190 specimens of fetal hymens Schaeffer ('90) concluded, as already stated, that this structure was composed of two folds. Gellhorn ('04) has raised the objection to these

investigations that they were based upon pathological material. According to Schaeffer's own statement 42 per cent of his cases showed some maldevelopment of the genital tract. When we consider what we mean by maldevelopment, Schaeffer's cases acquire a distinctive value of their own. We mean not a different method of development, but an arrest of development.[4] If in 42 per cent of his specimens there was arrest of development in other portions of the genital tract, we have a right to

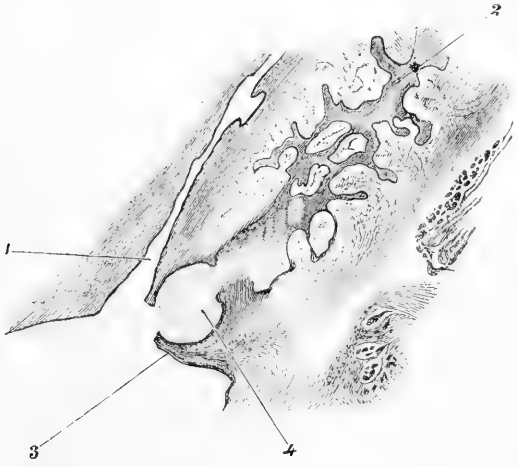

FIG. 9. Sagittal section through the posterior end of the vagina of a human embryo of 14 cm. body length (Nagel). 1, urethra; 2, vagina; 3, posterior surface of the hymen; 4, widened portion of the vagina immediately back of the hymen.

expect a rather large percentage to show an arrest of hymeneal development. Now Schaeffer found in 28.8 per cent of all cases a bilamellate hymen, whereas other investigators—Klein ('94), Hart ('02), Gellhorn ('04)—found bilamellation but rarely or not at all. Is the inference not justifiable that the additional lamella represents a membrane left by some previous step of development that persisted instead of becoming obliterated? But what membrane could that be? Only the membrane

[4]It is of interest in this connection that the hymen, according to Nagel, appears as a membrane only in the human race. In elephants, hyenas and other quadrupeds there is usually a constriction at the point of entrance of vagina into sinus urogenitalis, but no true hymeneal membrane. Corresponding to this constriction, we have at this point in man the vulvo-vaginal fold.

left at the point where the vaginal bulbus breaks into the sinus urogenitalis. It is this vulvo-vaginal fold, I believe, so clearly to be seen in my specimens, that in Schaeffer's cases persisted to a later date in a number of instances and gave the appearance of an additional fold of the hymen. This assumption is further supported by the following table in Schaeffer's work:

Length of Fetus.	Number of Specimens.	Bilamellate Hymen.	Percentage.
16-25 cms.	9	5	55.5
26-30 cms.	8	4	50.
31-35 cms.	26	10	38.5
36-40 cms.	41	15	36.6
41-45 cms.	58	15	24.1
Over 45 cms.	28	4	14.3

The steady decrease in the percentage of bilamellate hymen as the state of development increases is very striking and certainly would incline one to the belief that the bilamellate hymen represents a more primitive stage of development.

So much for the clinical and gross anatomical evidence on this subject. Coming now to the microscopic investigations, we must put aside as of secondary value all those based on fetuses previous to the fifth month of development, at which time the hymen, according to the consensus of opinion, first makes its appearance.[5] This would include Nagel's ('97) sections of a 14 cm. fetus (Fig. 9) which gives pictures of a vulvo-vaginal septum similar to that found in my Embryos 1 and 2. In the series of sagittal sections of a 26 cm. fetus studied by Klein ('94) (Fig. 10) we have valuable evidence. A comparison of his illustrations with mine are very interesting. He finds a vulvo-vaginal fold that he interprets as the hymen at the point of junction of vagina and urogenital sinus. Just anterior to this fold and extending from both ventral and dorsal walls is a fold considerably thicker than the so-called hymen. Klein's explanation of this fold is that it is a column of vaginal tissue such as we occasionally find in hymen columnatus. Neither in his pictures nor in his description has Klein proven this, and *a priori* it is

[5]This excludes the work of Berry Hart ('02), who argues from the serial sections of two embryos of three months development that the hymen is formed from the Wolffian ducts. Webster ('98) has clearly pointed out the fallacy of his conclusions.

difficult to see how such an explanation is possible. In a sagittal median section through a hymen columnatus we should expect to find the column as a broad surface continuous with the hymen. In Klein's sections it is comparatively narrow and there is a considerable hiatus between the column and hymen. A more plausible explanation would be that the so-

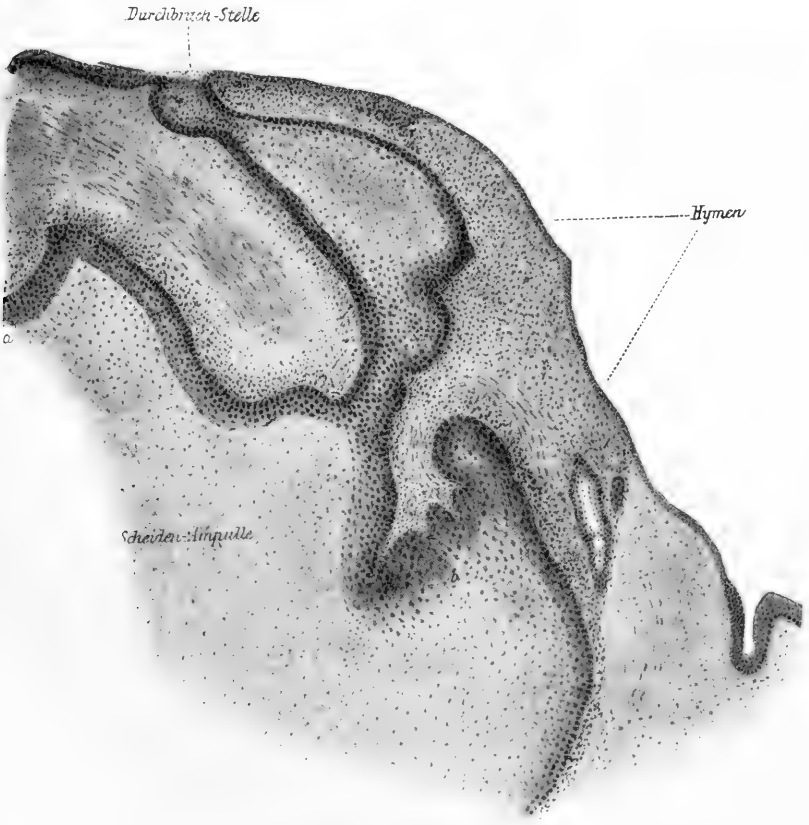

Fig. 10. Sagittal section of the posterior end of the vagina and the hymen (after Klein). Of the two folds Klein interprets the left hand one as a columnar branch of the right hand one, the hymen. Magnified 60 X.

called column is one of the secondary folds or papillæ occasionally found in the vagina back of the hymen. These secondary proliferations are, however, found primarily in later stages of fetal development when there is a general proliferative tendency in the entire lower vagina. In Klein's embryo there is no such general reduplication of vaginal connective tis-

sue. There are really only the two folds, just as in my sections, the one vulvo-vaginal, the other vaginal; the former a thin septum, the latter a thick membrane. In the absence of contradictory evidence, I feel justified in considering Klein's case as rather supporting than opposing my views.

The character of the epithelial covering also gives support to the vaginal theory. Klein lays stress on the marked differences between the vaginal and the vulvar epithelium. Gellhorn's ('04) microscopic sections of seven hymens at various stages of fetal development show that vaginal epithelium lines both sides of the hymen.

The direction of the hymeneal connective tissue fibres has been emphasized by Gellhorn ('04) as being of considerable importance. Even in fetuses at full term they could be seen running parallel and continuous with the vaginal connective tissue fibres. From the vulva no fibres enter into its composition.

I am well aware that the evidence of the serial sections in these five embryos is insufficient to firmly establish my contentions. Further investigations are necessary. Unfortunately, the material in a fresh state is not easily collected. Progress in this question can, however, only be made by the study of serial microscopic sections of the lower genital tract in fetuses of 18-30 cms. length.

Evidence of the sort that has heretofore been employed to support theories of hymeneal development, even if absolutely contradictory, cannot invalidate the views expressed in this paper. It would require evidence of the same character, serial sections of a number of embryos, to do this. Until such evidence is at hand, therefore, we must consider the hymen as a vaginal structure formed in the fifth month of fetal life by connective tissue proliferation directly anterior to the point where the vagina enters into the urogenital sinus.

In conclusion, I wish to thank Dr. R. J. Terry, Professor of Anatomy at Washington University, for assistance in getting material for this work and many helpful suggestions; also Dr. H. P. Wells for his excellent micro-photographs.

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Figs. 11-13. Sagittal sections through the hymen (Embryo 4). The dotted line is drawn at the level of the entrance of the vagina into the urogenital sinus. It is to the left of this that the hymen is formed. Fig. 11 (Section No. 61) strikes about the centre of the hymen, so that it appears as folds from above and below that do not meet (hymeneal orifice). To the right of it lies a high, narrow fold, rising from below, lined on the left (anterior) side by vaginal, on the right (posterior) side by sinus epithelium. In Fig. 12 (Section No. 63) the exact position of this fold and its relations can be better seen. The hymen can be clearly recognized to the left of it as a connective tissue membrane lined on both sides by vaginal epithelium. This is the most convincing picture in the series. Fig. 13 is taken lateral to this (Section No. 67). Only a teat-like remnant of the vulvo-vaginal fold can be seen below and to the right. The hymen is seen as a thick band. Papillæ appear on the posterior side. Magnified 45 X.

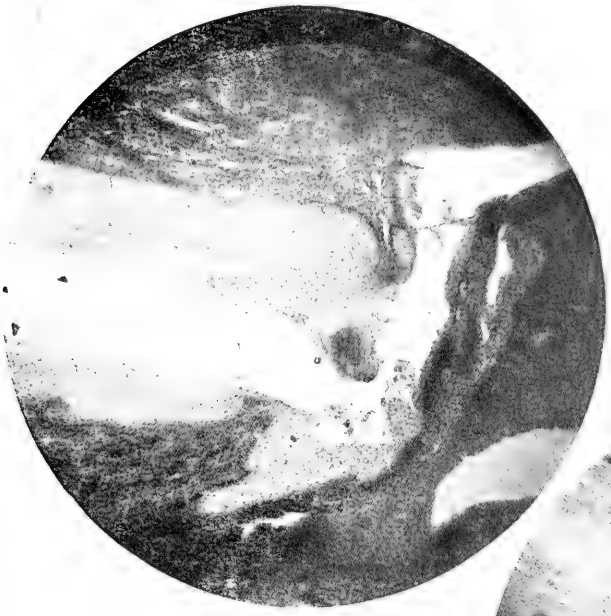

FIG. 11.

FIG. 12.

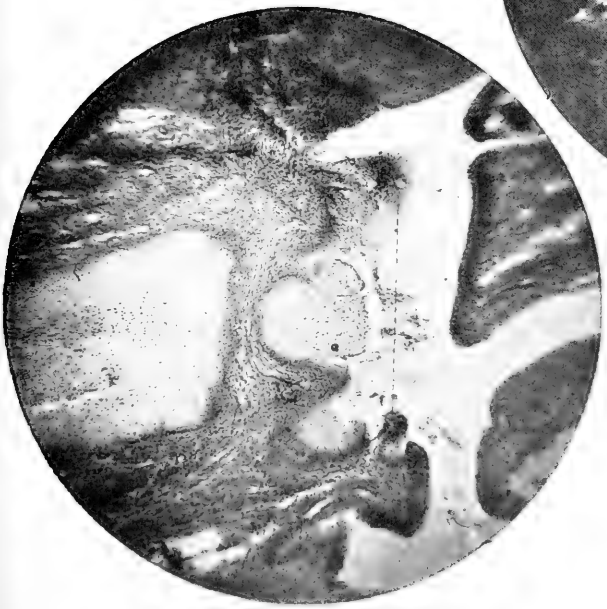

FIG. 13.

ON THE NATURE OF THE TECTORIAL MEMBRANE AND ITS PROBABLE ROLE IN THE ANATOMY OF HEARING.

BY

IRVING HARDESTY.

From the Anatomical Laboratory of the University of California.

WITH TWELVE FIGURES.

This investigation has been undertaken with the hope of contributing something to the knowledge of the shape, character and intimate structure of the mammalian tectorial membrane. Of all the organs of special sense, the ear seems to be the most complex and its functional action least understood. As voluminous as is the literature upon it, investigators, as yet, by no means wholly agree even as to the detailed anatomy of the inner division of the auditory apparatus. In running over the papers published, one is struck by the fact that they may be quite definitely separated into two classes: anatomical investigations, and physico-physiological treatises, the latter being, in most cases, purely theoretical. Quite often does it appear that the investigator in the latter class maintains that his conclusions are correct on the basis of his correct application of physics and mathematics to structures of unproven existence.

Of the four mechanisms deemed essential in the auditory apparatus, all the recent papers practically agree as to the identity and action of the transforming and regulation mechanism and the conducting mechanism, and all agree that the hair cells of the organ of Corti comprise the stimulative mechanism; but they disagree as to what comprises the vibratory or resonance mechanism. Most of the older papers attribute the faculty of selective or sympathetic vibration, in accord with the waves imparted to the endolymph in the cochlea, to the basilar membrane. Of the four more important papers of recent date, two still assume that the basilar membrane is adapted for and serves as the vibratory structure, while the other two advance the idea, but occa-

sionally held previously, that the tectorial membrane is the structure acted upon by the transferred sound waves. Either view admits that the hair cells are stimulated by impact or contact with the under surface of the tectorial membrane. The very evident disagreement of these papers in their descriptions and assumptions as to the character, form and intimate structure of the tectorial membrane, and the fact that none of the descriptions of the membrane seemed to apply correctly to some preparations of the cochlea in the possession of the author, suggested the undertaking of the study of the nature of that membrane.

Materials and Methods.

The material used for this study has been almost wholly obtained from the pig, and all the illustrations given are made from the preparations of cochleæ of this animal. Preparations from other mammals, including man, being obtainable with less ease and abundance, have only been used for occasional comparison with the preparations from the pig.

Pig fœtuses of about term, that is, from 26 to 30 centimeters, and a litter of four pigs of about two weeks after birth were used. In all cases, the heads were severed, the vault of the cranium and the encephalon removed and the cochleæ then broken out from the inside and made use of as soon as possible after obtaining the material. The entire inner ear or bony labyrinth of the pig may be shelled out from its lodgment in the temporal bone from the fact that osseous fusion with this bone is of late occurrence. Kolmer, '07, mentions that even in the adult hog the cochlea is not so firmly fused in the petrous part of the temporal bone as it is in other mammals.

All the published illustrations and all the ordinary laboratory preparations of cochleæ agree in indicating one fact, namely, that the tectorial membrane is invariably and badly shrunken and distorted by the action of the usual reagents used in fixing, dehydrating, etc. Since the chief deficiency of the papers describing the membrane appears to be failure to determine and study its normal characters, it was deemed especially necessary for the present study to obtain at least portions of it in the fresh and natural condition. Attempts toward this end were first made with frozen sections. The fresh cochleæ were oriented and frozen on the Bardeen Freezing Microtome and sections clipped into petri-dishes, some containing normal salt solution alone, others 0.1 per cent methylene

blue in normal salt. Though a few fairly satisfactory bits of the membrane were obtained from the methylene blue solution, the method had to be early discarded as being too coarse. The action of the section chisel in crashing through the bony labyrinth lacerated sorely the delicate structures within, the very action of the freezing appeared to result in distortion and dissociation, and positive orientation of the bits of membrane obtained was impossible.

Lightly crushing of the cochlea followed by gently teasing away the parts under fluid was next resorted to. A cochlea was held upon a solid surface and gently tapped around with a light hammer till the bony wall was sufficiently cracked without rupturing the wall of the membranous labyrinth and the whole placed in a petri-dish of amniotic liquor obtained from the sacs of younger fœtuses. Under the dissecting microscope the bits of the crushed bone were then carefully removed with fine pointed forceps, and, with the same forceps and with teasing needles, the outer wall of the scala vestibuli gently torn away from as nearly as possible the entire length of the cochlea. Even with the greatest care, this tearing usually ruptures the vestibular (Reissner's) membrane and thus seriously disturbs the structures below it. With practice, portions of the vestibular membrane could be removed separately and the tectorial membrane identified.

The tectorial membrane floats free from its attachment upon the labium vestibulare of the spiral limbus during the disturbance necessary for the removal of the structures and the consequent agitation of the fluid in which it is immersed, but, because of the fact of its being so very delicate and flexible and so extremely subject to surface tension, only short pieces could be obtained (3 to 5 millimeters in length) undistorted and free from adhering particles of bone and other debris. It was found that these pieces had to be isolated and handled by producing currents in the fluid to waft them to desired positions, for upon touching them they would adhere to the point of the teasing needle so closely that freeing them meant distortion or destruction. These pieces were stranded upon the end of a clean slide, to which they were found to adhere less than to the ordinary section lifter, and some were mounted directly in glycerine and in glycerine jelly. Others were washed from the slide into a 0.1 per cent solution of methylene blue in normal salt and let it remain in this from 30 minutes to 2 hours. With the dish of stain over a white surface, these were again stranded upon the slide, rinsed as quickly as possible in salt solution to remove the surplus stain, and

transferred for 5 to 10 minutes to a saturated aqueous solution of ammonium picrate. From this they were mounted in equal parts of pure glycerine and ammonium picrate solution. While the methylene blue brought out the structure of the membrane quite successfully at times, it was found, by comparing with those pieces mounted direct in glycerine, that the ammonium picrate produced in places a certain amount of shrinkage and distortion. Dehydration of these pieces, however gradually and carefully undertaken, was found impossible from the fact that in the higher grades of alcohol they invariably shrunk and crumpled almost beyond recognition. In this way, especially from the unstained pieces, a fair idea was obtained of the normal contour and appearance under the compound microscope, and measurements of breadth could be made.

Owing to lack of sufficient amniotic liquor at times when material was obtained, it was found that teasing under normal salt solution gave apparently as good results, and most of the best bits of fresh tectorial membrane were obtained with its use.

In no case, however careful the procedure, could a whole or even a half of the entire length of a tectorial membrane be obtained from a fresh cochlea. This was due to some extent to the violent disturbance necessary with the crushing and removal of the bone, but largely was because of the extreme flexibility and delicacy and the remarkable adhesiveness of the fresh membrane. Of the pieces obtained with portions undistorted, many would be covered with particles of debris by the time they could be mounted. Furthermore, extreme difficulty was met in orienting these pieces with certainty as to their upper and under surfaces. Others who have attempted examination of the membrane in the fresh condition seem to have encountered similar difficulties. The descriptions of Retzius, '84, who worked in aqueous humor, of Kishi, '07, who used salt solution, and of others to be referred to, show that they obtained but small pieces of the membrane, and that these were unfortunately distorted.

Therefore, the hope of obtaining an entire membrane in the fresh and normal condition had to be abandoned, and experiments were begun for a fixing fluid whose action would result in the least possible distortion of this evidently peculiar structure. This fluid should preferably be a decalcifying fluid as well. It was already apparent that the fluid could not contain alcohol unless accompanied by some ingredient which would counteract its shrinkage effect. Van Gehuchten's (Carnoy's)

fluid was found unsuitable, though, in addition to its alcohol and chloroform, it contains acetic acid. Perenyi's fluid was found impossible, for, while it fixes with little or no shrinkage, and decalcifies well, it has a softening and macerating effect unless followed by washing in alcohol, which latter produces violent shrinkage. Depuis, '94, teased after fixing with Müller's fluid and with chromic acid, both of which decalcify and neither of which causes shrinkage, but he does not seem to have obtained whole or even long pieces of the tectorial membrane. Both of these reagents were found to act so slowly that they were deemed undesirable. Gilson's fluid fixes and decalcifies more rapidly and was found to give much better results than any of the above.

The best results were obtained with Zenker's fluid, which contains the bichromate of potassium, the bichloride of mercury and acetic acid, all of which have a decalcifying action and none of which, combined, seemed to cause shrinkage or distortion of the tectorial membrane. Furthermore, as is well known, a prolonged application of this fluid is less injurious to tissues than are most of the fixing fluids, and cochleæ immersed in it very seldom show the bubbles of gas within the membranous labyrinth, always produced by the more rapid decalcifying agents, and which disturb the arrangement of the structures within. It was found that 48 hours in this fluid resulted in good fixation and sufficient decalcification for the purpose in mind. The entire apex and the outer, thin bony wall of the entire coil were softened, while the thicker base and basal portion of the modiolus were still hard. This undecalcified base and core were found of considerable advantage in holding the specimen firmly during the careful process of teasing.

Removed from the fluid, the cochleæ were washed an hour or more in water and teased under the dissecting microscope in a petri-dish containing enough water to well cover the specimen. Holding the specimen down firmly by the semi-circular canals and vestibular portion, it was found that, with practice and the exercise of care, the outer portion of the decalcified bony wall of the coil could be stripped off in pieces, leaving the membranous labyrinth intact and not even crumpled. The next task was to remove the outer membranous wall of the scala vestibuli without injury to the structures below it. The vestibular (Reissner's) membrane was found to be fixed stiff in itself, and, being very loosely attached along its edges, it could be removed, board-like, and taken out of the way; but in doing this the tectorial membrane, easily identified below it, was necessarily disturbed and sometimes injured. Only after the

vestibular wall and membrane had been carefuly removed was it found advisable to touch the tectorial membrane. This, in the meantime, could be seen, parts waving upward and downward with the agitations in the water about it, parts floating entirely free, and, at times, parts more firmly held in place. These more stationary portions were afterward found to be small areas adhering to the organ of Corti due to the coagulative action of the fixing fluid, probably upon the albumens and mucoids in the intervening endolymph.

The action of the fixing fluid results in a decrease to some extent of that remarkable adhesiveness displayed by the fresh tectorial membrane and also renders it somewhat less flexible, but, even after fixation it is so very sensitive to touch with the needles and to currents in the fluid about it that Reissner's and the basilar membrane appear as boards compared with a strip of thin silk. Fortunately, in the fixed condition, it comes away quite freely from its attachment upon the labium vestibulare ("Huschke's teeth") of the limbus spiralis. When ready to remove the membrane the water in the dish was drawn off and replaced with clean to avoid the debris resulting from the teasing. Agitations of the water and occasionally lifting it lightly with the needle where it appeared most firmly attached were found sufficient to detach it. It was best removed from the cochlea to the floor of the dish by the gentle use of a small pipette, washing it from around the coil and over the torn edges of the cochlear wall, occasionally guiding it with a needle. This removal proved the most trying part of the whole process in attempts to obtain the membrane in its entirety. It must not be allowed to adhere to structures over which it passes, it must not be straightened too much from its natural coil, and, above all, it must not be allowed to double upon itself lest it cohere and the entire region so doing be spoiled.

Orientation of the entire membrane, or of large pieces, was not found difficult, from the fact that one becomes familiar with its differences of width while working with it, and, it being in the form of a coil, it does not turn over readily or may be easily seen when doing so.

When washed out into the dish, the tectorial membrane remains for a time suspended in the water, and one has to watch it and quietly wait for it to settle to the bottom. In settling, it will return, to a certain extent, to its original coiled form.

Membranes thus obtained were stranded upon clean slides and some were mounted, unstained, in glycerine and in glycerine jelly, while

others were gently washed from the slide with and into the stain chosen. After trying several stains, including hæmatoxylin and methylene blue upon the fixed specimens, the best results were obtained with 0.1 per cent aqueous fuchsin, applied from 30 to 60 minutes. While this stains the interfibrillar matrix of the membrane, it stains the fibers more deeply, and it is both permanent and desirably transparent. From the stain solution, the specimens were carefully rinsed in water and mounted in glycerine or glycerine jelly, usually with the under surface upward. Some of the membranes removed entire were broken in handling during the staining; others were broken by the cover glass in mounting, but at these stages the pieces could be oriented with ease, and studies and measurements of them could be made with practical certainty as to locality. In all the author was able to obtain nine tectorial membranes deemed sufficiently intact and oriented for such measurements as are here given.

The study of the teased specimens was supplemented by the use of sections, some in celloidin and some in paraffin. Some cut vertical to the apex of the cochlea, some tangential and some horizontal. Certain of them were stained with the usual hæmatoxylin-Van Gieson stain; others, for microchemical studies, after being appropriately fixed and embedded, were stained, some with Meyer's muchæmatin, others with Mallory's stain for white fibrous tissue.

To study a point which arose concerning the development and later attachment of the tectorial membrane, sections were made of the cochleæ of pigs varying gradually from 3 centimeters to 18 centimeters in length. These were fixed, some in Zenker's and some in Gilson's fluid, and all were stained by the hæmatoxylin-Van Gieson method.

The Physical Characters of the Tectorial Membrane.

The investigation of the mammalian cochlea may be said to have begun in 1847 with the researches of Todd and Bowman, but Corti's *"Recherches sur l'organe de l'ouï des mammifères,"* appearing in 1851, really formed the starting point of the long series of observations which have appeared about equally distributed through the years since that time. It was in this monograph that Corti not only described for the first time the organ which now bears his name, but also the structure which spans the spiral sulcus and extends above his organ. This superstructure was shortly afterwards again described by Claudius and

Henle, the former of whom discovered it independently and gave it the name, *membrana tectoria*. Embryological investigations of the structures found in the cochlea began almost simultaneously with the purely anatomical. As early as 1854 Reissner described in embryos the separate existence of the *ductus cochlearis*, discovering its limiting spiral lamella, afterwards called Reissner's membrane by Kölliker and *membrana vestibularis* by Henle. However, it was Kölliker who, in 1861, first described the formation of the ductus cochlearis from the ectodermal tube and suggested the process by which Corti's organ is elaborated and also the normal position and morphological significance of the tectorial membrane.

None of these earlier papers and but few of those following indicate satisfactory or complete observations as to either the consistency, bulk, extent, shape or actual structure of the tectorial membrane. Most of them saw in their preparations little more than an amorphous mass of very varying shape and very varying relation to the cells of the organ of Corti. Henle, in volume 2 of his Handbuch (1866), believed the membrane to be very delicate, yet firm and resistant, and of an especial elasticity; Böttcher, '69, also concluded that it possesses a high degree of elasticity; Nuel, '75, cited by Retzius, denied elasticity, but claimed for it a soft gelatinous nature; Gottstein, '72, considered it strongly elastic, and Lavdowsky, '77, considered it a soft, elastic mass, fragile and distensible and in large part homogeneous. Retzius, '84, examined it in aqueous humor and pronounced it transparent, soft, gelatinous, tolerably elastic, capable of some stretching, but that it would split under increased stress in the direction of evident fine fibers present in it, and found it more firm after the action of fixing fluids; Dupuis, '94, considered it not of a mucous consistency, but decidedly elastic; Van Ebner, '02, describes it as a fragile, easily distorted, fibrous structure. Kishi, '07, who examined it in salt solution as well as in the fixed condition, found it to possess a marked elastic character and to shrink when subjected to the ordinary procedures; while Shambaugh, '07, in a theoretical paper, considered it a lamellar structure of the same specific gravity as the endolymph in which it lies.

It will be noted that a majority of the authors cited above agree on one point, namely, that the tectorial membrane possesses elasticity. In my trials to obtain intact specimens of the membrane in the fresh condition, several physical characters seemed manifest. In the first place, even in proportion to its size, it is, in the fresh, most incon-

ceivably delicate and flexible. It is by far more sensitively flexible in the transverse than in the longitudinal direction and the readiness with which it bends when touched or even agitated is beyond description. Mounted bits, carefully removed, in the fresh seldom showed longitudinal folds or crumples, but it was very difficult to avoid their being bent upon themselves or sometimes tied into impossible knots and gnarls. For the greater part, the tectorial membrane is much wider and thicker than a medullated nerve fiber, for example, but the manipulation of a fresh nerve fiber, especially under fluid, is quite an easy task when compared with attempts to manipulate this membrane. Again, its quality of adhesiveness is phenomenal. It is so subject to surface tension that, it matters not how clean the needle point may be, to touch the membrane is to have it stick, and to remove it from the needle usually means totally spoiling the specimen throughout the region of contact. Scraps of debris and shreds of tissue will adhere to it, and, when bent upon itself, it will often cohere. The membrane had to be moved chiefly by carefully inducing currents in the fluid in which the work was done.

Its specific gravity is manifestly slightly greater than that of the fluid in which it normally lies. The amniotic liquor of the pig is supposedly about isotonic with the blood serum and lymph of the animal. When freed in this fluid, the membrane, or parts of it, will remain suspended and be wafted about for several seconds, moved by the slightest agitations, but gradually it comes to rest upon the bottom of the dish. Bunge's Physiological and Pathological Chemistry gives 0.81 per cent sodium chloride solution as isotonic or physiologically normal for the pig. In this solution the membrane finally sinks just as in the amniotic fluid. After fixation in Zenker's fluid, it sank similarly in the tap water of this laboratory.

As delicate and flexible as the membrane obviously is, the behavior of my preparations indicated that it does possess elasticity. Judging from their descriptions, and especially from their illustrations, most of the observers cited above did no more than to assume an elasticity for the membrane from its apparent consistency and the various positions and shapes it presented in their hardened preparations. Retzius and Kishi and the very few others who, in addition, observed the fresh membrane in indifferent fluids, pronounced it elastic from its behavior in these fluids, and the behavior of my preparations confirm their observations. Because of its extreme sensitiveness and flexibility, one

has to observe its behavior closely to perceive its elasticity. The elasticity apparent may be compared with that of a very thin strip of set gelatin immersed in cold water. If not injured by stretching or badly tangled, a piece of the tectorial membrane, as it floats around in a dish of unagitated salt solution, will gradually approach the coiled form similar to its natural shape when in the cochlea and thus come to rest upon the bottom of the dish. In case of whole membranes, or of longer pieces, the portion representing the upper or apical coils of the cochlea will assume the natural form more quickly than the other end or the portion from the basal coil, because of the fact that the membrane is thickest and broadest at the summit, gradually decreasing in size toward the base. Twists are far more common and more serious in the more slender region of the basal coil, and unless they disappear before the membrane reaches the bottom of the dish, the basal coil never assumes its natural form and thus pieces may come to rest with the apical coils well formed while the portion from the basal coils may be irregular or scarcely coiled at all. The more evident elasticity of the summit end of the membrane is explained as being due merely to the greater bulk of this end.

Whole membranes and pieces removed intact from the attachment upon the labium vestibulare, unless containing twists, always come to rest flat upon the bottom of the dish, the under surface either upward or downward, notwithstanding the fact that the inner zone of the membrane removed from the labium vestibulare is very thin and tapers to an edge. This behavior, coupled with the fact that the direction of its greatest flexibility is transverse to the long axis of the membrane, together with its shape in transverse section, indicates that its greatest elasticity must be in the direction opposed to longitudinal rather than transverse stress. Elasticity in this direction can be largely instrumental in inducing the membrane to resume its natural shape when in fluid, and the membrane, being laterally attached along the inner zone, elasticity in this direction must tend to maintain the outer zone in its position above the organ of Corti.

Experiments, intentional and accidental, in stretching the tectorial membrane longitudinally indicate a small amount of elasticity opposed to such force. Pieces of the fresh membrane in salt solution, if stretched very slightly indeed will return to apparently their original thickness; if stretches more strongly, they will suffer attenuation, part of which becomes permanent; if stretched further, they may be drawn

out into filaments of less than half the diameter of the original membrane and which seem to have lost all trace of elasticity. These filaments may be drawn asunder and the parts will remain with tapering and pointed ends. Pieces of membrane from cochleæ fixed in Zenker's fluid show a slight increase in rigidity and therefore greater elasticity when the slight strains are applied, but, if stretched further, they break with a transverse cleavage instead of suffering permanent attenuation. In the study of the structure of the membrane it was found that the lines of such cleavage follow the direction of the fibrous components of the membrane.

The tectorial membrane suffers severely in the presence of all reagents which are hypertonic to it. Most all the recent papers touching upon its structure admit that it undergoes shrinkage with treatment for embedding and sectioning. I made several careful attempts to prepare pieces of the membrane for mounting in balsam so as to get more permanent and probably more transparent preparations, but none were successful. However carefully the graded alcohols were applied, by the time dehydration was complete, the membrane would show shrinkage, constrictions and general distortion, and a bath in xylol would usually complete what the alcohols had begun. Results somewhat better were obtained by clearing with creosote after 95 per cent alcohol, but no preparations so made would bear comparison with the normal, mounted direct in glycerine, either as to shape, dimensions, evenness of contour or surface markings. The physical character of the membrane seems to be such that it is impenetrable to the alcohol molecule, or at least such that it cannot be dehydrated without shrinkage.

Under the dissecting microscope by reflected light it has a distinct glassy appearance and by transmitted light it is transparent. The compound microscope shows it to consist of fine colorless fibers embedded in a transparent matrix. This matrix has apparently the nature of a glutinous, collagenous semi-solid. It is hardened but slightly by fixing fluids containing no alcohol. It is about the first structure in the cochlea to be affected by maceration, for cochleæ taken from pigs not freshly obtained show evidences of liquefaction of the tectorial membrane when the organ of Corti may be practically intact. Sections of such cochleæ show above the organ merely a mass of tangled filaments resembling a coagulum. On the other hand, the membrane seems to be more readily fixed than the organ, for sections of cochlea pronounced

imperfectly fixed will often show the membrane with no sign of liquefaction when the cells of the organ are badly deranged.

It was thought that the matrix might probably have a mucous character from the fact that preparations are occasionally seen in which the membrane stains more or less deeply blue. To test this, specimens were appropriately fixed, prepared into sections and stained with Meyer's muchæmatin and mucicarmine according to the procedure followed by Bensley in his study of the glands of Brunner, but in no case did the matrix take the stain in the way considered differential for mucus. It was further found that the membrane never stains deeply blue with hæmatoxylin in preparations that have been carefully washed after fixing and decalcification. Orcein and Weigert's stain for elastic tissue likewise gave negative results. The matrix may be somewhat similar to that of certain cartilages only much softer, or, since studies of the development show the membrane to be a cuticular structure, and since it is derived from cells of octodermal origin, the matrix may be a variety of soft keratin.

The Shape and Dimensions of the Tectorial Membrane.

The cochlea of the pig is of the flat type. Gray, '07, has recently divided cochleæ into two general types, the sharp pointed and the flat. The flat type is most common, being possessed by several varieties of mammals, including the primates and ungulata, to which latter the pig belongs, while the sharp pointed type is possessed by the carnivora and rodents, the Edentata having an intermediate type and the Marsupials both types.

The pig has one turn more in the coil of its cochlea than in that of the human ear. While the human cochlea is usually described as having 2½ turns, Wiedersheim, '93, accredits it with nearly 3 turns, giving the pig 4 turns, the cat 3 turns, the rabbit 2½, the ox 3½, and the cetacea 1½ turns.

The tectorial membrane of the pig extends throughout the entire length of the ductus cochlearis (scala media), and thus it is about as long as the scala vestibuli, but not quite as long as the scala tympani. Therefore, it is not quite as long as the basal side of the membranous labyrinth. This relative extent is probably true for all the mammals. Dupuis, '94, who studied teased preparations after fixation with osmic acid, Müller's fluid, etc., and decalcification with hydrochloric acid,

reports that for the cat, guinea pig, dog and rabbit the membrane extends throughout the cochlea. Measurements of the lengths of nine tectorial membranes, seven from the cochlea of pig fœtuses at about term and two from pigs about two weeks old, gave an average length for the membrane of 25.5 millimeters.

In both breadth and thickness, the membrane gradually decreases from the apex of the cochlea toward the basal end (Fig. 1), and both the end at the apex and the basal end terminate bluntly, slightly tapering. The upper surface of the membrane is convex throughout its length (Figs. 2, 3, 4, 6 and 7), the height of the curvature being in the region which, in the natural condition, overlies the interclasped phalanges of the rods of Corti's organ. The under surface, or the surface next to the organ of Corti, is concave, but with a concavity of several curvatures. In the region of the apex of the cochlea, the outer edge of the membrane projects beyond the confines of the organ of Corti and here this edge bends downward slightly, resulting in an evident concavity of the under surface. The portion immediately imposed upon the surface of the organ of Corti is parallel with the surface of that organ and thus is usually plane; it may slant upward or downward from the horizontal plane of the cochlea or it may be slightly concave, depending upon the direction and the shape of the upper surface of the organ of Corti, which varies somewhat in the different regions. In the decrease in width of the tectorial membrane toward and in the basal coil, it gradually ceases to project beyond the organ of Corti, and thus finally there is no separate concavity of the outer edge to be considered (Figs. 4, 5 and 8). That zone of the under surface beginning with the inner border of the organ of Corti, spanning the spiral sulcus and including the inner, thin edge of the membrane, is, throughout, more deeply and regularly concave than any other portion. The greater concavity here is but an expression of the rapid decrease in thickness which is attained by the inner edge as it becomes attached upon the vestibular lip of the spiral limbus.

All the investigators mentioning it describe the inner edge as extending to the insertion of the vestibular (Reissner's) membrane. In the main, this has been found to be true in my preparations of the pig. Occasionally, observation and comparative measurements from the free membrane and of the width of the labium vestibulare have indicated that the inner edge does not necessarily in all regions extend quite to the vestibular membrane. Hensen, '63; Retzius, '84; Barth, '89;

Dupuis, '94, and others have described the inner edge as sometimes notched. Notches were frequently seen in my preparations, but they were always angular and could be explained as breaks suffered in freeing the membrane from its attachment.

The outer edge of the tectorial membrane in all my preparations is rounded and terminates bruskly. In discussing observations made by Kölliker in 1859 which denied an attachment of the outer edge of the membrane to the lamina reticularis and the cells of Hensen of the organ of Corti, Lowenburg, '64, described a delicate, almost invisible, seemingly frayed-out reticulum along the outer edge. Others have since mentioned this appearance, giving it the name, *Lowenberg's border plexus.* Dupuis, while admitting that it is very irregular, usually appearing in fragments, and not always present, referred to it as a third and outermost zone of the tectorial membrane, while Von Ebner, '02, among others, refers to it as a filamentous structure, adhering to and collapsed upon the outer zone of the membrane and representing its original connection with the lamina reticularis.

The existence of this border plexus as a normal appearance of the tectorial membrane is here denied.

Though the appearance observed may be seen at times in the preparations used here, there is evidence that it may be due to three causes, separately or in conjunction: First, it has always been observed in fixed preparations, and the fixing fluids and especially the alcohol produce coagulation of the albumens and globulins in the endolymph. Coagulum filaments, in forming, always appear most abundant on surfaces, and especially between surfaces which are close together. The places on the tectorial membrane where these filaments are most apt to be noticed are its outer edge and that portion of its under surface which is imposed upon the organ of Corti. Second, evidences of beginning liquefaction of the matrix of the membrane are, in the preparations used here, always most apparent along its outer edge and under surface. Portions of the fibers in the membrane, set free along the edge by the dissolution of the matrix, may produce a delicate, tangled, filamentous appearance which is no doubt augmented by coagulum filaments produced by the reagents. Third, in the study of the removed pieces of the tectorial membrane, I have now and then seen what appeared to be parts of Lowenberg's border plexus, but these appearances proved to be displaced portions of the accessory tectorial membrane described below (Figs. 3 and 5). In the region of the basal

coil, the outer edge of this accessory membrane nearly coincides with the outer edge of the main body of the tectorial membrane, and but slight displacements will result in its projecting far enough to be separately distinguished.

Corti, in first describing the tectorial membrane, expressed the belief that the outer edge was normally attached to the structures below it and located this attachment as far over as the epithelium upon the spiral ligament. Coyne and Cannieu, '85, agreed with Corti in so far as to place the attachment upon the cells of Claudius, and ever since Corti, investigators have looked for and claimed an attachment of the outer edge, though seldom agreeing as to the locality, and they have explained Lowenberg's border plexus as the outer edge of the membrane frayed by having been torn from its attachment. Quite recently, Kishi, '07, who seems to believe that the membrane is normally attached to the organ of Corti, states that the border plexus, or third zone, is only an artifact which results from the tearing of the membrane from the organ of Corti, and which consists either of the frayed edge of the membrane alone, or of this edge together with a portion of the lamina reticularis removed with it. On the other hand, beginning with Hensen, '63, and Böttcher, '72, the outer attachment has been frequently denied. Kölliker and Von Ebner admit, from the study of its development, that at one time the tectorial membrane is of necessity attached along its under surface, but that early, during the differentiation and elaboration of the organ of Corti, and the resultant displacement and adjustment, the attachment of the outer edge at least becomes obliterated. Ferré, '85, described the outer edge as bluntly rounded, and so it appears in the large majority of preparations, in both sections of fixed cochleæ, always allowing for shrinkage, and also in the fresh condition in teased preparations.

Measurements of the width of the tectorial membrane of the pig were carefully taken at the different turns of the coil of the nine teased preparations obtained. These measurements were transversely across each tip or extremity and across the intervening portions at intervals of each half turn of the coil. Now and then partial breaks or slight distortions appeared in short portions of a specimen, and if these appeared in the particular portion of the turn to be measured and seemed sufficiently serious to invalidate the measurement, the measurement for that interval had to be omitted. However, these injured places were not very numerous, and, from the nine specimens, enough trustworthy measure-

ments at the different turns were obtained from which to compute very fair averages. Fortunately, one of the membranes from the pigs two weeks old was more successfully manipulated, and, after mounting, was so nearly intact and uninjured that a complete set of measurements was obtained from it alone. The measurements of the membrane from the fœtuses at term averaged throughout so nearly identical with those from the pigs of two weeks that one could infer no essential dimensional differences between them. These transverse measurements were made with an ocular micrometer whose spaces were standardized in terms of microns. The measurements obtained from all the specimens gave the following averages for the total width of the tectorial membrane in the regions specified:

	tip of basal end	near basal tip	7th half-turn	6th half-turn	5th half-turn	4th half-turn	3d half-turn	2d half-turn	1st half-turn	width near tip at apex	tip of end at apex
microns	58.1	107.9	124.5	149.4	170.2	190.9	207.5	257.3	307.1	215.8	166.0

The measurements of the tip at the apex were taken transversely through the point at which the inner edge terminates, and those of the basal tip, transversely through the point at which the outer edge terminates (see Fig. 1).

What is very apparent in the actual specimen may be perceived from these figures, namely, that the tectorial membrane of the pig varies widely in breadth, but varies gradually and somewhat progressively from the basal end toward the apex. Each end terminates bluntly, the widths of the tips taken at similar levels being much less than the widths possessed by the half-turns to which they belong. The width of the tip at the apex of the cochlea is nearly three times that of the basal tip. At the apex the membrane rapidly increases to its greatest width, which is attained in the first half-turn. From the basal end, it increases in width gradually till the width in the first half-turn is 2.8 times greater than that of the last.

Almost the entire variation of the tectorial membrane occurs in its outer, free, portion, or that strip spreading from the outer edge of the labium vestibulare (Huschke's auditory teeth) over the spiral sulcus and the organ of Corti. That portion, or inner zone, which lies upon and adherent to the labium vestibulare varies relatively little in width.

However, like the total width of the membrane, this inner, attached, strip is narrowest in the basal turn and increases gradually, though slightly, toward the apex to attain its greatest width in the first turn. Owing to the extent and shape of the labium vestibulare at the ends of the coil, this attached strip terminates in a point, and is the first zone to terminate at the apex, while at the base it terminates bluntly rounded and is the zone which persists farthest, wholly constituting the basal tip of the membrane.

Dupuis and others to be mentioned below, who studied the markings on the under surface of the membrane, distinguished a boundary line representing the outer extent of the labium vestibulare, or the boundary of the zone of attachment upon it. Barth and Böttcher considered this line an artifact. In all my teased preparations, but especially those fixed in Zenker's fluid, this line was distinguishable and, from further study, it is evident that Barth and Böttcher were correct in considering it an artifact in so far that it only represents the impress of the edge of the labium vestibulare, and has nothing further to do with the structure of the membrane. Measurements of the attached zone taken transversely to the inner edge of the membrane showed it to vary gradually from 62.3 microns in the last half-turn to 87.2 microns in the first half-turn.

These measurements subtracted from the total width of the membrane at the same regions, give the free, outspanning portion of the membrane a width of only 45.6 microns near the basal end, while the free portion of the first half-turn attains a width of 219.9 microns. Kishi, '07, who studied the human tectorial membrane and that of a number of common mammals, states that this outer portion (second zones he calls it) is at least three times broader at the apex of the cochlea than it is in the basal coil. He does not give measurements. In Kölliker's Gewebelehre, Bd. 3, Second Half, Von Ebner states that the tectorial, like the basilar membrane, is widest toward the apex of the cochlea, and that, in man, the free portion has a width of 240 microns at the apex, and 120 microns in the basal region. These figures indicate that the free portion of the apical turn in man is only 2 times as wide as that of the basal region, while the above figures for the pig show the free portion in the first half turn to be 4.8 times as wide as it is in the last. However, Von Eben does not state at what particular portion of the coil the measurements were taken nor whether they were made from fresh or fixed specimens or from sections. Kishi, though he only

publishes some very misleading photographs of vertical sections of the cochlea, made some of his observations from isolated bits of the membrane teased free in fluid, and probably these bits suggested to him the greater difference in the width of the outer portion in the two regions. Obviously, measurements of the membrane from sections, necessarily treated with alcohol, etc., and therefore shrunken, would average less and be less regular than if taken from teased and unshrunken specimens, and, as may be seen from Fig. 1, such results depend materially upon the particular localities at which measurements of the free zone are taken. None of the literature I have consulted indicates the successful isolation of appreciable lengths of the tectorial membrane of any animal.

Fig. 1 illustrates the shape of the pig's tectorial membrane as seen from the under surface and with the coil slightly opened, and it is an attempt to indicate its appearance under low magnification. In its natural position in the cochlea, it is more closely coiled, and, especially in the apical turns, the outer edge of one turn appreciably overlaps the inner edge of the turn below it. Thus it was necessary to draw it less closely coiled in order to show it entire. When mounted in glycerine, the cover-glass presses the apical coils of the membrane together and radially outward from the center. The basal coils could not be induced to retain their coresponding curvature with the application of the cover glass, though carefully arranged in the glycerine beforehand. Therefore, it should be stated that none of the preparations obtained showed the membrane as evenly coiled as it is shown in Fig. 1. In making this drawing, the character and extent of the coil was taken from the labium vestibulare laid bare under the dissecting microscope, after the removal of the membrane, and from the appearance of the membrane resting upon the bottom of the dish in fluid. A coiled line was drawn representing the inner edge of the membrane and imitating the character of the coil of the cochlea, but opened sufficiently to avoid overlapping of the edges of the membrane. Then radially from this line, the width of the membrane at each half turn, obtained by measurement of the actual specimen, was indicated by dots. The character and dimensions of the ends and the lines of demarkation of the under surface were likewise sketched in from measurements and from the study of mounted specimens. The scale decided upon gave each space of the ocular micrometer the value of one millimeter. The outline being made, the width and variations of the different zones were determined and other

peculiarities of the difficult regions sketched in. The sketch was then transferred to a sheet of Ross-board, upon which it was thought advisable to make the attempt to represent the glassy, delicately fibrous character of the membrane as it appears over a black surface. Figs. 2, 3, 4 and 5 were outlined in the same way, but under higher magnification, and are intended to show greater structural detail.

Measurements of the thickness of the membrane could be obtained only from vertical sections of cochleæ made after the usual fixing, dehydrating and embedding. After getting some idea of the character of the membrane, a few specimens, carefully treated and embedded in celloidin, gave sections which showed considerably less shrinkage and distortion than is usually evident. Figs. 6, 7 and 8 were outlined from photographs of and drawn from a section of one of these specimens.

All the membranes showed some distortion and shrinkage. The latter especially is evident in a denser and more amorphous shell-like thickening about the entire periphery, which suggests a primary condensation due to the first attack of the shrinking agent, and which, once formed on the periphery may be less permeable and may result in the interior portion being subsequently more gradually and therefore less violently acted upon by the reagents. Fig. 8, from the seventh half-turn or basal coil, shows decided distortion and displacement due to shrinkage. This is from the more slender portion of the membrane, and, if the above suggestion is true, would necessarily be affected most by the reagents.

Measurements of the thickness taken from these specimens and corrected with the study of the isolated and supposedly unshrunken pieces indicate two relations:

(1) That, like the width, the thickness of the membrane begins with that of the outer zone in the rounded end at the apex (see Fig. 1), rapidly increases to its maximum in the apical region and thence gradually decreases toward the basal coil, in the end of which the minimum thickness occurs.

(2) That, throughout, the line of the greatest thickness, in the different transverse sections, runs approximately parallel to the edge of the labium vestibulare and approximately over or slightly to the inner side of the line of the enclasped phalanges of the rods of Corti.

The measurements of thickness were all taken from sections of the cochleæ of pigs at or very near term. They gave the following average thicknesses for the regions specified:

	tip at apex	1st half-turn	2d half-turn	3d half-turn	4th half-turn	5th half-turn	6th half turn	7th half-turn
microns	49.8	74.7	70 5	62.3	53.9	42.4	31.1	13.4

These averages are obtained from vertical, axial sections from each of four cochleæ. The thickness of the tip at the apex is computed from one measurement, for, unfortunately, the plane of only one of the sections was such as to pass transversely through the tip. Further, it is uncertain how far from the basal tip the measurements designated "seventh half-turn" were taken. Evidently they passed varying distances from it, for the measurements varied from 12.4 microns to 24.9 microns. The other regions did not vary so widely. All the measurements were made and recorded before the averages were computed and converted into the terms of microns.

It is seen from these figures that the greatest thickness of the membrane occurs in the first half-turn, and thence the thickness decreases gradually and somewhat progressively toward the basal end. A comparison of Figs. 6 and 7 indicates that in this cochlea the greatest thickness occurred in the third half-turn instead of in the first. The shrinkage here seems to have resulted in a lateral crumpling and probable increase of thickness in the third half-turn. The drawings of this specimen were made before the average thickness was ascertained; otherwise a more average specimen might have been used. This specimen was among those measured. The first and second turns all showed much smaller differences than any other adjacent half-turns. That the differences between adjacent basal half-turns are greater than those between the half-turns of the apex is due to the fact that the basal turns are longer, the basal coil of the cochlea being several times longer than the apical, and thus longer strips of membrane intervened between the measurements in the basal half-turns. The lack of greater uniformity in progressiveness of decrease is probably due both to irregularities in the shrinkage effects of the reagents and to lack of identical orientation of the plane of section of the different cochleæ, the plane passing nearer to the ends, especially the basal end, of some membranes than of others.

Von Ebner quotes Retzius for the statement that the thickest part of the human tectorial membrane measures from 24 to 25 microns. The particular turn from which this observation was made is not stated. The

figures seem rather low when compared with the 74 microns obtained here for the first half-turn of the membrane of the pig.

The Structure of the Tectorial Membrane.

Surface markings. Since the beginning of its study, the natural tendency has been to divide the membrane into zones. These zones vary in the different descriptions both as to their number and their boundaries, as is to be expected from the fact that some investigators have dealt wholly with appearances seen in vertical sections of the cochlea, others with the surfaces of isolated pieces of the membrane, and the majority with preparations more or less distorted by the action of reagents. Gottstein, '72; Coyne and Cannieu, '85; Barth, '89; Dupuis, '94, and others made three zones: (1) The inner zone, comprising the thin, attached strip spreading from the inner edge, at the insertion of the vestibular membrane, and terminating with Huschke's teeth or the edge of the labium vestibulare; (2) the middle or second zone, comprising the body of the membrane which spreads from Huschke's teeth to the outer, bruskly rounded border; and (3), believing Lowenberg's border plexus to be a part of the membrane, they called this the outer or third zone.

In 1863, Hensen, examining the surface of the membrane, observed a line running along the middle of the main body, approximately parallel with the edge of the labium vestibulare and apparently constant in occurrence. Later, this line was farther observed by Retzius and Schwalbe who described it as a transparent, glittering strand on the under surface of the membrane, having the appearance of a hyaline thickening along the middle zone. By both of these investigators it was given the name *"Hensen's stripe."* This stripe or streak, while it has been reported absent in some animals (the rabbit, for example), has been used as a boundary line by those who have chosen to divide the membrane into three zones, exclusive of Lowenberg's border plexus whether admitted or denied. Divided in this way, the first zone comprises the strip attached upon the labium vestibulare; the second or the middle is the strip between the labium vestibulare and Hensen's stripe, while the third or outer zone comprises the balance of the width from Hensen's stripe and including the outer edge of the membrane. Most of the more recent papers divide the membrane into zones in this way, though some, for example, Rickenbacher, '01, divide it into two zones: an inner, as

above; and an outer, comprising all of the outspanning portion and thus including Hensen's stripe.

Also, throughout the literature, occur descriptions of various lines and markings of the under surface in addition to Hensen's stripe and the line of impress of the labium vestibulare. Hensen's stripe has even been given various appearances, various widths and varied occurrence. Dupuis, '94, working with the tectorial membranes from the dog, cat, rabbit and guinea pig, found Hensen's stripe apparently absent in some cases, while in others it seemed to be represented by three lines, which, however, he thought might have been due to optical defects produced by the variations in the thickness of the membrane compressed under the cover glass. Various extra lines have been described upon the under surface of the membrane, some running longitudinally, others transversely or obliquely. Only recently, Kolmer, '07, working with various mammals, including the pig and man, describes a small piece of the membrane, giving it longitudinal lines upon its under surface which he interprets as bundles of longitudinally running fibers. In all of my preparations which proved to be shrunken, extra lines were always apparent. The prevailing direction of these was always longitudinal, and most of them appeared on the under surface. Especially, in all those pieces which I attempted to dehydrate and clear in oil, numerous lines were apparent, some of which ran obliquely and many of which anastomosed. Comparison with the fresh preparations and with those fixed with apparently little or no shrinkage made it very evident that these extra lines were due to the shrinkage effect of the reagents, and they were explained as crumplings and crimps of the shell-like peripheral condensation which is seen in all sections of embedded material and is probably produced in the first attack of the reagents upon the matrix of the membrane. Further shrinkage or extraction of water from the interior can but result in crimps of this outer, already condensed layer. As Kolmer says, such lines always seem to stain more deeply than the adjacent material, but this must be due to their greater condensation, and therefore greater capacity for holding stain. Though seeming more or less amorphous, as do all condensations of the membrane, a fibrous structure may be detected in them; but neither in these lines nor in any parts of the tectorial membrane of the pig have I been able to distinguish any longitudinally running fibers.

The normal markings readily detected on the under surface of the tectorial membrane of the pig when removed intact and unshrunken,

and viewed under surface upward, are four only: (1) The fine fibers of which the membrane consists, the prevailing course of which is obliquely transverse and which are embedded in the transparent, collagenous matrix; (2) the line of impress, the boundary of the zone of attachment, left by the edge of the labium vestibulare; (3) Hensen's stripe, always present, whose variations and significance will be mentioned below; (4) a line on the outer zone which, in passing from the apical to the basal end, gradually approaches and comes to coincide with the outer edge of the membrane, and which constitutes the outer edge or back of the *accessory tectorial membrane* to be described below, and from which may usually be detected short fibers extending obliquely towards Hensen's stripe. Some of the descriptions for Lowenberg's border plexus, some of the claims of attachment of the outer zone of the tectorial membrane to the cells of the organ of Corti, and some of the descriptions of extra lines on the surface were very probably dealing with this accessory membrane, for it seems to be easily displaced, and, in shrunken preparations, is diminished and distorted beyond recognition.

All the papers dealing with the appearance of detached pieces, seem to agree that the upper surface of the membrane is smooth and more or less evenly convex. Beyond the effect given by the component, obliquely transverse fibers of the membrane, the upper surfaces of my preparations showed no markings that could not be interpreted as due either to injuries from manipulation, adherent debris or coagulum filaments. The highest point in the convexity of this surface remains throughout in about the same relation to the organ of Corti.

The fibrous structure of the tectorial membrane is very evident in teased preparations, though the exact internal arrangement of the fibers is somewhat difficult to determine. As mentioned above, the fibers are imbedded, or distributed throughout, in a transparent matrix, seemingly having the character of a glutinous or collagenous semi-solid. It is the nature of this matrix that allows of that most remarkable flexibility and sensitiveness possessed by the membrane and probably determines its low specific gravity. The matrix is stiffened but slightly by fixing agents, shrinks severely in dehydration and stain tests indicate that it is not of a mucous nature. It is due to its shrinkage that the membrane so often appears in sections as an irregularly shaped, deeply staining, amorphous mass lying in various positions above the organ of Corti, and it is with this appearance the investigators have had frequently to deal.

Lowenberg, '64, thought that the membrane consisted of layers, one above the other; Göttstein, '72, pictured it as structureless, and many others after these failed to comprehend its character. Most of the physiological and theoretical papers giving it any attention assume rather than study its anatomy. All the more recent anatomical studies admit the membrane to be fibrous. Shambaugh, '07, assumed the membrane to be constructed of an immense number of delicate lamellæ, and on the basis of this, propounds a very interesting theory of tone perception. Coyne and Cannieu, '85, were, I think, the first to make tangential sections of the cochlea, passing through the membrane transverse to its fibers, and to picture the transverse sections of the fibers as fine dots, as shown here also in Fig. 9. They also tried to analyze the course and arrangement of the fibers, and, with Barth, '89; Dupuis, '94, and Kishi, '07, made, I think, a mistake in describing the fibers as coursing from the labium vestibulare in two layers, one on the upper surface and one on the under, with a less compactly assembled layer of fibers between the two. They probably mistook the peripheral condensation, explained above, as due to the action of the reagents, as special upper and lower layers of fibers.

Seen from the *upper surface*, the fibers appear to course from the attached or inner zone outward, but, instead of coursing radially, they always slant from the labium vestibulare toward the apex of the cochlea. This slant is greater in the region of the inner zone, and deviates slightly toward the radius in the outer zone as shown in Fig. 4, the general course showing a slight tendency toward the shape of the letter *S*. This general course was also noted by Dupuis, '94, in his preparations. Kishi notes an oblique direction tending toward the apex in the animals he studied, and Von Ebner states that the inclination is about 45° from the radius.

Kishi claims to have noted fibers of varying size and length, and Kolmer, '07, states that the fibers have a thickness of ¼ micron. From casual observation the impression is very readily obtained that the fibers course individually across the entire width of the membrane, but closer study of the membrane of the pig under higher power convinces that they are far more numerous than first supposed, and that they are too fine to be followed individually or to be measured by the ordinary means.

Comparing the surface view with the *transverse section* (Figs. 2, 6 and 4) shows that, instead of all the fibers extending from the labium

vestibulare across to the outer edge of the membrane, the greater number of them at least course varying distances across, then curve downward and, still curving, reach the under surface, where they terminate, many running a short distance parallel to the under surface, prior to termination. The shape of the bluntly rounded, outer edge of the membrane is determined by the curvature downward of the outermost of the fibers. The outline of this edge is never perfectly even, but always appears finely and irregularly scalloped, as shown in Fig. 3, suggesting that the fibers may have a tendency to course and curve around the edge in bundles. In some of my preparations the under surface of the outer edge of the sections at the apex (similar to Fig. 6) appeared thickly studded with the down-hanging ends of fibers as though the under surface had been frayed either by the tearing away of the peripheral condensation or by partial liquefaction of the matrix. Along the inner edge, the sections show that all the fibers by no means are continuous from the inner, attached zone, but that the rapid increase in the thickness of the free portion results from an enormous increase in the number of fibers concerned. The interior fibers of this region course and curve parallel in the main with those of the upper surface, till those nearer the under surface gradually come to sweep downward and then outward and parallel for short distances with the under surface which they form and in which they terminate.

Fig. 9 is made from a horizontal section of the cochlea, and represents a tangential section of the tectorial membrane passing about parallel with the surface of the labium vestibulare and splitting Huschke's teeth. It is taken from the neighborhood of the third half-turn, and a comparison of it with a line drawn in the same plane through Fig. 7 will make clear the relations and appearances shown by it. The plane passes through the dorsal aspect of the membrane, and, as is to be expected from the evident course of the fibers shown in Fig. 7, near Huschke's teeth (Ht) the fibers are cut transversely and obliquely in the zone indicated by *a*, while the fibers in the outer zone, indicated by *b*, course more nearly in the plane of the section. In this section the fibers do not appear to run wholly parallel with each other. Apparently they even anastomose, and where they are cut transversely, they appear to be connected with each other by fine collateral filaments. How much this specimen was shrunken and how much this appearance is due to the reagents cannot be determined. The tangled appearance is no doubt due largely to shrinkage and coagulation effects. The fine filaments

may represent the individual fibers, while the heavier lines and dots may consist of agglutinated bundles of them.

The *under surface* of the main body of the membrane is thus given a transversely fibrous appearance when viewed on the flat, not by continuous fibers coursing across it individually, but by the general direction of the curved ends of many fibers. Beginning on the under surface, the fibers first lie parallel with this surface and form it, and then curving outward, upward and then inward, contribute to the upper surface. The summation of the course of these ends gives to the under surface the appearance of being striated in a direction oblique from the radial and, like the upper surface, the slant is from the labium vestibulare toward the apex of the cochlea. But the direction on the under surface is more nearly radial than that on the upper, as may be seen by comparing Fig. 4 with Figs. 2 and 3. On both surfaces, the direction of the fibers in the inner or attached zone of the membrane is inclined more toward the apex than that of the fibers in the main body and especially the outer edge. An examination of the under surface showed that the most nearly radial direction of the fibers occurs in the second and third turns, and an attempt is made to show this in Fig. 1.

Fig. 4 represents a drawing of the broken end of a piece of membrane from a cochlea fixed in Zenker's fluid. The preparation showed that the fixed specimen, at least, in breaking, has a tendency to break parallel with the direction of the fibers, and it suggests that the difference in the course of the fibers above and below may contribute to the strength and elasticity of the membrane by a sort of interlocking arrangement. In a break like this, the portion of the fibers intervening between the under and upper surfaces must of necessity be broken across. In the break pictured, there were evident clumps of fibers which seemed to have been partly split off from the remainder before breaking, and which appeared something as slivers, each a mass of fibers held in a corresponding amount of the glassy matrix (Fig. 4, S).

From a careful comparison of the surface views with the sections one may conclude that the fibers contributing to the under surface of the tectorial membrane make their immediate approach (or, rather, considered from the standpoint of their origin, they leave this surface) from two general directions: (1) Most of those on the outer side of Hensen's stripe contribute first to the striation of the upper surface, then curve downward and then inward to contribute to the striation of the

under surface; (2) most of those on the inner side of Hensen's stripe curve from the inner zone, first slightly outwards, then sharply downwards, and finally inwards to contribute to the striation of the under surface, thus following an S-shaped course. Apparently, these two general directions would result in a midregion either free from fibers, or, in which the general direction would be neither the one nor the other; but, in the sections, the transitions of curvature seem to be so gradual that this region is never definitely marked. Further, the two directions should result in a zone of the under surface in which the ends of the fibers from the two directions intercross. The sections show this intercrossing, and that, while it occurs to some extent in the body of the membrane, the greater part of it, as to be expected, occurs in the immediate under surface, and by no means all in one line (see Fig. 7).

The cut ends of the segments of the membrane represented in Figs. 2, 3, 4 and 5 were, of course, not possessed by those segments, but were outlined upon them and the arrangement of the fibers drawn in accordance with the arrangement apparent from the study of the sections, in order to illustrate the relation between the fibers of the upper and under surfaces. The intercrossing of the ends of the fibers in the under surface is seldom apparent in the ordinary sections because such sections are usually more shrunken than those represented in Figs. 6, 7 and 8, and the intercrossing, and indeed the whole parallel arrangement, is involved in the more deeply staining peripheral condensation of the substance produced by the reagents. In Fig. 7, Pc, for some reason or other during the manipulation, probably in the sectioning, this peripheral condensation seems to have partially peeled off from the under surface of the inner side of the membrane and the strip to have become stuck to the inner supporting cells of the organ of Corti.

Looking down upon and into the under surface of the freed membrane, with the compound microscope and with transmitted light, this surface, and all focal planes near it, appear studded with numerous fine dots which manipulation of the focus shows to be the ends of fibers. These ends are most numerous in and along either side of Hensen's stripe.

Hensen's stripe, or streak, in my preparations has a structure, and, I think, a significance. Hensen, who discovered it, and Retzius and Schwalbe, who named it and described it as a hyaline, transparent strand on the under surface of the "middle zone," probably had to do with preparations shrunken at the periphery at least. Transparent

preparations examined from the ventral surface, by transmitted light, show it to be fibrous and to be largely composed of a dense linear series of the intercrossing ends of the fibers approaching each other in the ventral surface from the two directions. In fact, the stripe occupies approximately the position of the dividing line between the fibers coursing in this surface from the two directions. It is most probably distinguishable because it is a linear accumulation of these intercrossing ends which, as such, behave toward the light differently from the other regions. For the same reason, it was distinguishable in my preparations by reflected light, that is, when viewed over a black surface, as well as by transmitted light. It is strong enough to appear quite distinctly through the membrane when studied from the upper surface.

Von Ebner, '02, notes that Hensen's stripe may show from the upper surface, and thinks that it is produced by a thickening or bunching of the substance of the membrane, and he accepts the statements of others that it lies over the line of the inner hair cells of the organ of Corti. He, Coyne and Cannieu, '85, and Dupuis, '94, state that it is absent in some animals. The latter notes that it varies in different species, and that it may be modified by pressure of the cover glass, not leaving one to feel positive that the stripe is ever normally absent. Hensen himself thought the stripe a line of connection with the inner hair cells, and Shambaugh, '07, describes it as "a sort of fascet where, normally, the membrane is attached to the supporting cells just internal to the inner row of hair cells." The latter description is based upon the appearance of the membrane in sections, largely one section, manifestly distorted. In none of the sections of the pig's cochlea used here was it possible to locate Hensen's stripe by any means as positively as Dr. Shambaugh was able to do with his sections. It is of necessity always involved in the peripheral condensation. Denser, or more condensed, spots were often seen cut across in the under surface, but these were too numerous and too variously placed to be interpreted as other than sections of crimps in the peripheral condensation produced by the further shrinkage of the membrane during the preparation for sectioning.

In removing two of the preparations used here from cochleæ fixed and decalcified in Zenker's fluid, the tectorial membrane was found to be stuck down to the organ of Corti in the regions of the first and second turns of the spiral. By careful use of the needle one of these was freed, and, though finally broken, the pieces were stained in fuchsin and mounted, under surface upward. Though disappointing and practi-

cally useless for the purpose in mind, this preparation was of interest with reference to the position of Hensen's stripe. Cells and portions of cells of the organ of Corti were adhering to the region involved, and, in one place, nearly the whole organ, including both rods, for a stretch of several cells. The ends of the hair cells could be distinguishel as such by means of the crescentic lines of the exit of their hairs, and it could be seen that the outer and inner rows of hair cells extended one on each side of Hensen's stripe. In other words, both by actually distinguishing it at times in their midst and by tracing it from the clean regions into the region involved, it was evident that, in preparations of the pig fixed in Zenker's fluid at least, Hensen's stripe lies between the inner and outer rows of hair cells, and therefore over the relatively smooth line occupied by the enclasped phalanges of the rods of Corti.

It is difficult to say whether or not Hensen's stripe exists as a ridge projecting beyond the general level of the under surface. A number of investigators have described it as such; others, less definite, mention it as a thickening or bunching of the material, and I remember none to have specifically denied its being ridge-like. Sections should be practically the only means by which this can be determined, but sections have proved very untrustworthy, because, even if a ridge is indicated in them, one is never sure it is not due to inequalities of surface shrinkage, and also because Hensen's stripe cannot be positively located among the variable thickenings and markings that different sections show. When viewed from the under surface, one gets a very decided impression of a ridge, but, under magnification, allowing the whole width of the membrane in the field, the greater part of the under surface appears roof-like with Hensen's stripe as the highest part. Careful focussing up and down under high power shows that the stripe is higher than the adjacent surface, but much less so than was to be expected, and that the roof-like appearance under low power was an optical effect, explained as due to the ends of the fibers converging, in the glassy matrix, from the two directions toward and into Hensen's stripe.

If the stripe runs along between the inner and outer rows of hair cells, one might infer that it is a ridge which represents a strip of the membrane never in contact with the projecting hairs, but which fits into the groove walled on either side by the hairs, and that it should have a width throughout corresponding to the width of the line of the exposed surfaces of the phalanges of the rods of Corti. The exposed

surface of the phalanges is widest at the apex of the cochlea and grows narrower towards the base of the coil, just as the rods and the angle they form decrease in size, and it was found that the stripe is somewhat wider at the apex and decreases in width toward the base, but at no level was it found to be as wide as the groove floored by the phalanges, nor does it vary in width as much as the groove. The only inference drawn from this study is that Hensen's stripe probably has the form of a low ridge the existence of which may be protected by the groove over which it lies.

In looking over papers dealing with the development of the tectorial membrane and the sections from pig fœtuses prepared here for the purpose, the possibility was suggested that Hensen's stripe may have an embryonic significance; namely, that it represents that area or line on the under surface which is last to become detached from the cells which give origin to the membrane.

On the Development of the Membrane.

It is not the object of this paper to describe in detail the development of the tectorial membrane. All the essential stages of the process have already been worked out quite thoroughly. Kölliker, '61, Middendorf, Rosenberg, Göttstein, Nuel, Retzius, Schwalbe, Böttcher, Hensen, Prichard, Exner and Rickenbacher, '01, all agree that, in vertebrates, the membrane is a cuticular structure arising from the thickened epithelium of the inner side of the floor of the embryonic cochlear canal, and Kuhn and Hasse have described a similar origin for invertebrates. I find that in pigs of 2.5 cm. there has begun the marked thickening of the epithelium of that side of the cochlear canal which will become the portion to line the spiral sulcus and overlie the inner portion of the basilar membrane. At 3 cm. the thickening of the epithelium has increased and there appears above the entire thickening a cuticular film of quite appreciable thickness and decided fibrous character. The later stages, up to about 12 cm., show increase in the width of the epithelial thickening corresponding to the increase in the diameter of the cochlear canal, consequent increase in the width of the developing tectorial membrane and marked increase in the thickness of the epithelium concerned. At 12 cm., or shortly before, there is differentiated a second and much smaller epithelial thickening along the immediate outer edge of the first one, thus giving the greater and the lesser epithelial thicken-

ings, "pads," noted by Kölliker, '61, and more fully described by Böttcher, '69, and Rickenbacher, '01. The lesser thickening is the first indication of the differentiation of the organ of Corti, while the cells of the greater give origin to the tectorial membrane and later gradually retract and sink back into the low, indifferent cells lining the spiral sulcus. Böttcher thought that the tectorial membrane takes origin from both the greater and the lesser thickenings. This can hardly be claimed, for the pig, for while the edges of the two thickenings are, of course, quite close together, the early membrane does not begin to extend over the lesser till there are evidences of the beginning of retraction on the part of the greater thickening. Evidences to the contrary of this are sometimes seen in the form of a thin, frayed reticulum sticking to the inner edge of the lesser thickening and continuous with the membrane, but serial study suggests that such appearances are due to distortion and to coagulum films produced by the reagents. Two years after its publication, Hensen showed that Böttcher's conclusion was based in part upon artifacts.

As Rickenbacher pointed out, the membrane, throughout its elaboration, undergoes no active growth whatever, but is purely a passive product of the continued activity of the epithelial cells below it. Not till pigs of about 14 cm. do my preparations show evidences of differentiation of the cells of the lesser thickening into what will become the different cells of the organ of Corti (Fig. 10), and at that stage none of the cells of the organ are in the least recognizable until traced backward from the more advanced stages. The contention of Ayres, '91 and '98, partially supported by Czinner and Hammerschlag, '97, that the tectorial membrane consists of a segregation of continuations of the hairs of the hair cells of the organ of Corti, is shown in my preparations to be fully met by the statement of Rickenbacher, namely, that the tectorial membrane is considerably developed some time before the hair cells are differentiated as such. Rickenbacher showed further that much of the findings of Czinner and Hammerschlag in this relation were artifacts, and cites Hensen in suggesting the same to have been true with Böttcher.

By a process of retrogression and displacement, first suggested by Kölliker and described later by Exner, '97, the tectorial membrane developed wholly from cells at the inner side of the organ of Corti, finally becomes so left that its outer part extends over the organ. At first, when the lesser epithelial thickening is not apparent in the prepa-

rations used here, a thin fibrous film may be discovered overlying the entire surface of the greater thickening and inward upon what will become the labium vestibulare. At the very beginning, the then very short fibers stand vertical to the epithelium and are even then agglutinated by a seemingly fluid-like stage of the transparent matrix. From pigs of 3 cm. up to 15 cm. the more important changes taking place in the floor of the cochlear canal are a marked increase in both the thickness and the width of the greater epithelial thickening and the appearance and differentiation of the lesser thickening.

At the stage when the labium vestibulare is evident, the greater thickening wholly occupies the area of the future spinal sulcus and consists of a high, pseudostratified epithelium whose surface is level with the upward pointing tip of the labium itself (Fig. 10). As to be inferred from this condition, the continuation of the epithelium upon the labium is very much lower than that of the thickening proper. In fact, this portion comprises the inner, tapering edge of the thickening at the stage before occurs the differentiation of the mesodermal tissue into the limbus spirale and its labium vestibulare and when the whole is covered by the delicate beginning of the tectorial membrane. The epithelium upon the labium is thus thin from the first, remains so throughout, and takes part in the production of only the thin, tapering, permanently attached, inner zone of the tectorial membrane. In reality, it ceases as an epithelium, and probably altogether, in the adult cochlea, for then the only superficial cells of the labium are those which are situated between and level with the horizontal connective tissue bundles comprising the auditory (Huschke's) teeth (see Fig. 9). Probably it ceases quite early to produce tectorial membrane, for, from pigs of 12 and 14 cm. upward, the inner, attached zone of the membrane gains apparently very little in thickness.

As the greater epithelial thickening increases in width during the earlier stages of the development, the fibers of the tectorial membrane, standing vertical to the epithelium at the very first, are gradually drawn outward from the more firmly attached inner zone, so that, by the time a membrane has gained a more appreciable thickness, 10 cm. pigs, the first formed portions of the fibers come to lie horizontal or nearly parallel to the surface of the epithelium while their continuations curve downward till the growing ends of the fibers only are vertical to the cells of the parent epithelium. In this way is produced the transverse striations apparent in the upper surface of the adult membrane and

the curved course of the fibers apparent in sections of it. All sections of fœtuses show that the stages of development advance from the basal coil toward the apical, and so in the increase in thickness and width of the greater epithelial thickening, beginning at the base and advancing toward the apex of the cochlea, must lie the explanation of the fact that the outer direction of the fibers is inclined from the radial toward apex. Measurements from my preparations show that between 10 cm. and 15 cm., the width of the greater epithelial thickening increases from 124 microns to 174 microns. This increase consists of a very evident increase in the number of the epithelial cells concerned.

At about 14 cm., the lesser epithelial thickening, the future organ of Corti, has considerably advanced in form and appears as if it acts as a block to the further increase in width of the greater thickening, for, at that stage, the outer edge of the latter becomes bluntly rounded and bows upward (Fig. 10) with the result that in this edge, adjacent to the lesser thickening, there is formed the thickest part of the greater thickening. The outer edge of the developing tectorial membrane necessarily bends downward around this bluntly rounded edge of its parent epithelium. Up to this stage, the membrane never overlaps the lesser thickening and in confirmation of the statement of Rickenbacher, it must be said that at no stage is there good reason to assume that the cells giving rise to the organ of Corti ever have any thing to do with its development.

The order of the development of the membrane seems to be, first, the fibers and then the matrix, both being subadded gradually at the under surface. In all stages, from the very first, there always exists upon the immediate surface of the epithelium a thin, clear, parallel layer in which the matrix is either in a soluble stage of its development or wholly absent, and across which course the ends of the fibers from the epithelial cells into the body of the membrane above. In sections the thus unembedded ends of the fibers appear exceedingly tender, are often broken free and usually appear in agglutinated bundles (Fig. 10).

The stage of retrogression of the greater epithelial thickening, and the resultant displacement of the parts, begins with a cessation of growth of the epithelial cells, followed by their exhaustion and finally by a liquefaction of their remains, till, in the adult cochlea, the cells of the greater thickening are represented by the very low, indifferent epithelium which lines the spiral sulcus from the inner supporting

cells of the organ of Corti to the edge of the labium vestibulare. The exhaustion begins along the inner side of the greater epithelial thickening, at the edge of the labium vestibulare and gradually proceeds outward. Thus the first portion of the tectorial membrane to become free from its parent epithelium, that is, to cease growing, is the strip adjacent to the labium vestibulare. Sections from pigs of 15 and 17 cm. usually show a beginning recession of the epithelium in this region, and it is probably indicated in Fig. 10. (More strictly speaking, the portion of the membrane which first ceases to increase in thickness is, as mentioned above, the inner zone, attached upon the surface of the labium vestibulare.) The exhaustion of the epithelial thickening gradually passes outward till the last region of it that is active and attached to the tectorial membrane is its outer edge, or the region adjacent to the organ of Corti, which region, in the previous growth changes as noted above, became its thickest region. Finally this region recedes, the remains of the cells liquefy and the tectorial membrane is left entirely free from the cells which give rise to it. Transverse sections of the cochlear duct of pigs from 20 to 25 cm. often show a mass of disintegrating epithelial cells lying against the inner supporting cells of the organ of Corti, which mass represents the vestige of the greater epithelial thickening.

By the above processes of increase, recession and disintegration, the disposition of the fibers within and in the under surface of the tectorial membrane may be explained as well as the position which the membrane finally attains with reference to the organ of Corti (the lesser epithelial thickening).

The retrogression of the epithelial cells undoubtedly results in a decrease in the width of the space occupied by the greater thickening (the space which becomes the floor of the spiral sulcus), and this decrease results in the inward displacement of the organ of Corti to its final position under the outer zone of the tectorial membrane. Counts of the cells comprising the greater epithelial thickening in the third half-turn of several cochleæ from pigs of 14 to 15 cm. gave an average of 93 cells per transverse section. Counts of the cells lining the spiral sulcus, up to the inner supporting cells of the organ, in the same region of several fully developed cochleæ gave an average of only 21 cells, the averages showing that the space in the fœtal cochlea contains four times as many cells as the developed. Measurements of the width of the floor of the spiral sulcus of the developed cochlea gave

an average of only 75 microns, while measurements of the width of the greater epithelial thickening in the 15 cm. pig gave an average of 174 microns, showing the space in the fœtal to be more than twice as wide as in the developed cochlea. (The measurements indicate, further, what is shown in the specimens, that the epithelial cells of the fœtal cochlea, though much higher, are thinner than those of the developed.)

The direction of the fibers of the inner region of the body of the membrane is outward and almost parallel throughout. In this region multitudes of fibers are added to the body of the membrane, contributing to its sudden increase in thickness. The practically uniform outward direction here is due to the fact that these fibers were produced before the epithelium began to recede and the width of the thickening to decrease. Further outward, as far as Hensen's stripe, the fibers are directed outward, then downward, but still outward. At the region of Hensen's stripe, many fibers curve downward from their outward direction above and approach the under surface vertically. In fact, Hensen's stripe seems to be an expression of the period at which the retrogression of the epithelial thickening began. It also represents the line along which the thick, outer edge of the thickening was last attached and along which growth was last contributed to the membrane.

With the exhaustion and retrogression of the cells of the inner portion of the thickening began the decrease in the width of the space occupied by it. Consequently, the portions of fibers produced by it after the decrease in width began were no longer directed outward or vertically, but inward, drawn inward, as it were, by the now receding outer edge of the thickening. As a result, there is in Hensen's stripe a crossing of the ends of fibers approaching it from the two directions, as noted above, in describing Hensen's stripe.

And also as a result, the fibers coursing in the membrane on the outer side of Hensen's stripe are directed outward in the upper surface (the portions earlier formed), then curve downward (as do those on the inner side) and finally curve inward to approach the under surface at acute angles or to run short distances parallel with it. The tectorial membrane, firmly attached along its inner zone and sustained by its semi-solid matrix and its consequent elasticity, holds the position and shape in which it was molded; while the organ of Corti, during its elaboration, appears to follow the receding greater epithelial thickening and finally comes to be situated under the outer zone of the tectorial

membrane in such a position that the line of the phalanges of the rods of Corti about coincide with Hensen's stripe.

The greater width and thickness acquired by the tectorial membrane as its apical end is approached may be explained as due to the longer persistence and greater width attained by the apical portion of the greater epithelial thickening, noticeable in sections of fœtal cochleæ. All signs of the thickening may have disappeared in the basal coil when the coil of the apex may show considerable of the epithelium, and, in the adult, the floor of the spiral sulcus, as well as the entire spiral lamina, is left considerably wider in the apical than in the basal coils.

An Accessory Tectorial Membrane.

Though this structure as I shall describe it is undoubtedly present in my preparations, its description is entered into with some hesitancy because of the fact that in none of the papers I have been able to examine is such a structure noted for either the pig or other animals. The only explanation of why it has not been described before now is offered in the fact that it is so thin and fragile and so susceptible to the action of reagents that, with its existence not realized, it is impossible to distinguish in the ordinary preparations anything suggesting such a structure. Even after noting it in the unshrunken teased preparations, in only two of my transverse sections of the tectorial membrane, the best I have been able to get, could there be distinguished anything which might be interpreted as sections of this structure, however distorted. It was not evident on some of the broken teased preparations, because of the fact, soon learned, that it is apparently but very slightly attached to the main body of the tectorial membrane and is easily displaced or lost in the removal from the cochlea. In the teased preparations after reagents found to produce shrinkage, the "accessory membrane" was usually unrecognizable, appearing, from the under surface, as an irregular belt of very delicate zig-zag lines which might be interpreted equally well as crumplings and shrinkage disarrangements of the surface and fibers of the main body.

The structure was first noted in a piece of tectorial membrane removed after Zenker's fluid and broken on the slide while mounting it in glycerine. Under low light, it appeared as an exceedingly thin transparent ribbon extending far beyond the broken end of the main body, in places slightly twisted, but for the most part flat and showing

parallel edges. Traced to the main body, it was found to be lifted off for some distance and to lie upon the main body much as a ribbon would appear if lifted by the end from slight adherence to a surface. Fig. 3 is an attempt to imitate this appearance of the structure, as seen in the preparation, the end of the main body, however, not being shown as broken, but being utilized to show the arrangement and relations of the fibers of the body. When viewed in its undisturbed position, it appears lying upon the under surface, as shown in Figs. 1 to 5, Ac, and so delicate it is, that one unaware of its presence, especially upon unstained or darkly stained pieces of the membrane, might consider the appearance produced by it as due to mere disturbances in the arrangement of the fibers of the under surface of the main body. That it lies practically free or, at least, very lightly adherent to the under surface of the main body is indicated by the apparent ease with which it comes away and by its occasional total absence from broken pieces. During its further study upon various preparations, short extents of it were at times seen crumpled away and free from the under surface, and at times deviating inward or outward from its general alignment. In several cases the deviation outward was sufficient for a small portion of its outer edge to project beyond the outer edge of the main body. Because it seemed to have a practically separate existence, it is referred to here as an Accessory Tectorial Membrane. Its structure, its delicacy, and its position explain the difficulty with which it is distinguishable and suggest that the probable reason it has not been noted before is because none of the investigators using teased preparations happened to obtain pieces of it isolated, extending free and undistorted, in the field of the microscope.

In *shape and structure* this accessory membrane somewhat resembles a long comb, the tapering teeth of which, however, are in the form of a net consisting of two sets of parallel fibers all continuous into the "back of the comb" which is the outer edge of the membrane. The direction of one set of the fibers coincides with the direction of the fibers in that zone of the under surface of the tectorial membrane over which they lie. Thus, this set of the fibers cannot be distinguished when the accessory membrane is in position (Fig. 3). The other set of fibers crosses the first set obliquely, arising at acute angles to outer edge of the membrane and coursing in a decided slant pointing toward the apex of the cochlea. The fibers are embedded in a thin film of transparent matrix of the same character as that supporting those of the

tectorial membrane proper, and it is this matrix that maintains the shape of the accessory membrane and holds the two sets of fibers, and the fibers of each set, in their relative positions.

The inner edge of this membrane consists of nothing but the crossing inner ends of the fibers and is so exceedingly thin that it could not be distinguished at all when lying in position but for the optical effect produced by the obliquely coursing set of fibers. The outer edge (the back of the comb) is thicker than the inner, apparently resulting from a gradual increase in the amount of the supporting matrix. In the outer edge, the fibers of both sets seem to curl upward so as to produce a short abrupt curl in this edge of the membrane with the convex side toward the under surface of the tectorial membrane proper, as indicated in the drawing of the end in Fig. 3.

The question of the *attachment* of the accessory to the main body of the tectorial membrane could not be definitely settled. The accessory membrane was found so delicate that it would not stand manipulation; in more deeply stained preparations it could not be studied in its relations to the main body because of the light being obscured in passing through the whole structure; transverse sections, necessarily from dehydrated and embedded specimens, were entirely impossible, and, in the unstained and lightly stained mounts, if attaching fibers exist, they could not be distinguished in the maze of other fibers present on both sides of their probable locality. From the study made here, only this can be said: If the accessory membrane is attached other than by light surface cohesion to the main body, it is most probably attached along its outer, and thicker, edge. In several of my mounts, the inner edge appeared folded over for short distances as though it had been waving free in the fluids preliminary to the cover glass, while the outer edge retained its normal position as though it had behaved as a hinge. Further, the curled disposition of the fibers in the outer edge suggest that their ends may be continuous into the under surface of the tectorial membrane and that they may be broken, ripped asunder, in cases in which portions of the accessory membrane appear entirely free.

As to its *position,* the accessory membrane lies under the outer zone of the under surface of the tectorial membrane proper and to the outer side of Hensen's stripe. It exists throughout the length of the tectorial membrane.

Like the tectorial membrane proper, it is widest at the apical end and decreases in width toward the end of the basal coil. The decrease

in the width of the tectorial membrane proper occurs chiefly in the decrease in the width of the zone or strip on the outer side of Hensen's stripe. The decrease in the width of the accessory membrane is relatively much more gradual than that of this zone under which it lies. At its greatest width, in the apical turn (Figs. 1 and 2), its outer edge is considerably within the outer edge of the tectorial membrane proper, but its decrease is so much more gradual that by the time the seventh half-turn is reached, the outer edges of the two membranes coincide (Figs. 1 to 5). Also, at the apical end, its inner edge extends not quite to Hensen's stripe, but below, this edge comes to coincide with Hensen's stripe, and, at the basal end, the tips of its fibers may occasionally overlap the stripe. If Hensen's stripe coincides throughout with the line of the enclasped phalanges of the rods of Corti, then the accessory membrane can only come in contact with the hairs of the outer series of the hair cells.

Of the illustrations given of transverse sections, Fig. 7 alone shows a structure whose position warrants its being interpreted as a section of the accessory membrane. The structure is naturally attacked severely by the reagents, being very thin and fragile, and distortion renders it unrecognizable and often invisible in sections. One unaware of its existence would never discover it in even the best of sections.

Some of the observations recorded in the literature of the tectorial membrane may refer to this accessory membrane. It is somewhat probable that the irregular, transparent, reticular fringe described by Lowenberg, '64, as existing along the outer edge, and since referred to by some as "Lowenberg's border plexus" and by others as the third or outer zone of the tectorial membrane, may have been nothing more than the displaced outer edge of the accessory membrane projecting irregularly beyond the outer edge of the tectorial membrane proper. Coyne and Cannieu, '85, may have used this in their claim that the tectorial membrane is attached as far over as the cells of Claudius; Dupuis, '94, notes that Lowenberg's border plexus is very irregular and not always present; Von Ebner, '02, in Kölliker's Gewebelehre, notes and illustrates it as filamentous; Kishi, '07, considers it an artifact. Hensen, '63; Böttcher, '72; Ferré, '85, and several others since them deny the existence of the border plexus. The latter may have been dealing with more nearly normal conditions. Further, several observers, to be mentioned below, claim filamentous attachments between the under surface of the tectorial membrane and the hairs of the hair cells and

various other elements of the organ of Corti. It is probable that some of these attachments consist of crumpled bits of the distorted accessory membrane, augmented by coagulum filaments. Also some of the descriptions of various lines and markings on the under surface of the tectorial membrane, noted above, may have been dealing with appearances produced by the distorted accessory membrane as well as with crumplings of the peripheral condensation of the main body.

The processes by which the accessory tectorial membrane is developed from the greater epithelial thickening have yet to be worked out. Evidently it is one of the last structures formed, and probably its individual character may be due to its being formed during a period of rapid displacement of the parts.

The Attachment of the Tectorial Membrane.

All the observers invariably agree that the tectorial membrane is attached along its inner thin zone upon the surface of the labium vestibulare. This attachment is developed early in the development and is the line of fixation instrumental in the final course and arrangement of the fibers of the membrane resulting from, first the widening of the greater epithelial thickening and then followed by its retrogression and decrease in width.

Numerous investigators claim other attachments, but there is lack of agreement as to their location. There are to be found in the literature claims for attachment of the under surface of the membrane varying from attachment to the epithelium of the spiral ligament (Corti) and the cells of Claudius (Coyne and Cannieu), all the way across the lamina to attachment upon the inner supporting cells of the organ of Corti (Shambaugh). The majority of the claims are for attachment to the structural elements comprising the organ of Corti alone, especially to the hairs of either the inner or outer hair cells or both. Of the more recent papers, Kishi, '07, agreeing with Böttcher, '69, states that the membrane is connected with the lamina reticularis and with the hairs of both the inner and outer series. Siebenmann, '00, denies connection with the lamina reticularis in either the embryo or the adult. Von Ebner, '02, holds the membrane was attached to the lamina during development, but, in the adult, after the displacement of the parts, this attachment is necessarily lost and the membrane extends free over the spiral sulcus and organ of Corti. Rickenbacher, '01,

thinks, from his studies of the development of the membrane, that it is improbable, *á priori,* for the membrane to float freely in the cochlear duct. He did not carry his studies through the processes of the displacement. Shambaugh, '07, assumes that the membrane is attached to the inner supporting cells and that Hensen's stripe serves as a fascet for this attachment. Kolmer, '07, often found the membrane attached to various of the cells of the organ of Corti, but thinks these attachments were artifacts. As early as 1872 Göttstein described "transparent filaments" extending between the membrane and the inner supporting cells of the organ of Corti of fœtal cochleæ, but considered these as remnants of liquefying processes. Hensen, '07, in elaborating a theory for tone perception, assumes and pictures the tectorial membrane as extending free over the organ of Corti so that the hairs may brush against it during the agitations of the endolymph, resulting in auditory stimuli. The hairs have been described as sticking into the under surface of the tectorial membrane.

All the claims for the attachments of the membrane to any portion of the epithelium of the spiral lamina (including the organ of Corti) are based upon appearances presented in sections, and all describe the connections as filamentous. The studies made here tend strongly to the view that the membrane is attached only along its inner side and only upon the labium vestibulare.

(1) During the teasing away of the upper wall of the membranous labyrinth to expose the membrane preparatory to its removal, the outer portion could at times be easily seen under the dissecting microscope to wave upward and downward in response to agitations produced in the fluid with which it was covered during teasing. These movements seemed to occur along its entire course. They occurred within very small arcs and were suggestive of a certain amount of elasticity in the membrane, causing it to retain its horizontal position because of the attachment along its inner zone. If attached to the elements of the organ of Corti, or even to the hairs alone, while individually such attachments would be delicate and easily broken, it is hardly probable that the necessarily great multitude of such attachments would so readily disappear and allow the movements.

(2) Sections of fixed and dehydrated material are but little more suggestive of attachment of the membrane than they are of its being free from the organ of Corti in the adult condition. The membrane is always more or less shrunken and distorted, and these effects of the

manipulation may result either in its being drawn in contact with the organ below or in its being lifted well away from the organ. Sections often show it even pressed upon the organ, but the *majority* of sections show it directed in various angles, entirely free from the organ, and many of the older pictures of it are thus drawn. When caught more nearly in its normal position with its under surface parallel with and near the surface of the organ of Corti, delicate filamentous connections are often apparent, but such connections can be justly explained as brought about by crumplings or abrasions of the fibers in the under surface, or by bits of the very thin accessory membrane coming in contact with the auditory hairs or other elements, the appearance of continuity being accentuated by adhering coagulum filaments precipitated from the albumins and globulins of the endolymph.

(3) From the process of its development, it seem probable, contrary to Rickenbacher, but in accord with Von Ebner, that, *á priori,* the membrane is free from the underlying epithelial structures. During its development it is attached only to the epithelial cells giving origin to it, and since its outer zone acquires its adult position over the organ of Corti only by the recession of the parent epithelium and the consequent displacement of the organ, one must at least assume that, if attachment to the organ exists, it must be developed after the development of both the organ and the membrane. This is hardly probable and, moreover, it is hardly necessary to an explanation of the rôle of the organ in the phenomena of hearing.

On the Anatomy of Hearing.

It may be said that the tectorial membrane is comparable and analogous to the otolithic membranes of the cristæ and maculæ acusticæ, except that it is neither developed by nor upon cells belonging in the group of special sensory cells with whose stimulation it is concerned, and except, further, that in the higher animals it is not beset with calcareous products.

Lavdowsky, '77, and others, including Ayers, '91, have called attention to the fact that, from the nature of the stimuli, the function of hearing must require three mechanisms: (1) A vibratory mechanism; (2) a regulation mechanism, and (3) a mechanism for the perception of sound stimuli.

Hensen, '63, was the first to advance the idea of the hairs of the hair cells being brushed against the tectorial membrane for the origin

of the stimuli in the perception mechanism. Lavdowsky, Hensen, Nuel and others describe the basilar membrane, in the spiral lamina, as being composed of independent, radially disposed fibers. This and the further observations that the basilar membrane is considerably wider (and therefore its fibers longer) at the apex than in the basilar coils of the cochlea, led Helmholtz to advance the theory of hearing which bears his name. This theory involves the sympathetic vibration of the different "fibers" of the basilar membrane in resonance with the atmospheric waves as transmitted to the endolymph by the tympanic membrane and auditory ossicles, and it assumes that the vibrations of those fibers involved by a given stimulus cause the hairs of the hair cells overlying the fibers to rub upward against the tectorial membrane. It thus assumes, further, that the cochlea has the power of analysis of sound or that the perception of tone is mediated by different parts of the cochlea. Ter Kuile, '00, in a purely theoretical paper dealing with the transmission to the hair cells of energy from the supposedly vibratory basilar membrane, shows that the hairs do not rub against the tectorial membrane, but strike its under surface vertically. Ewald, '99 and '06, accepts the idea of the basilar membrane and experiments with thin rubber membranes placed under fluid, finding that vibrations may be induced in them in response to atmospheric waves. In fact, with but two exceptions that I know of, all of the investigators of physiological acoustics since Helmholtz have accepted the assumption that the basilar membrane is the vibratory mechanism, and in their writings have merely put forth various modifications of the original conception. The two exceptions are Kishi, '07, and Shambaugh, '07, both of whom assume that the tectorial membrane is the vibratory mechanism, both claiming the power of resonance in it, as will be mentioned below.

As noted by Gray, '00, the explanations of hearing as now offered may be divided into two general theories: (1) The Resonance Theory, suggested by the work of Hensen, Nuel and others, propounded and elaborated by Helmholtz and variously modified ever since in its application to the cochlea by different investigators, and (2) The Telephone Theory.

The latter theory was suggested by Rinne in 1865, supported by Voltolini in 1885, more fully elaborated by Rutherford in 1886, modified by Waller in 1891, and further modified by Max Meyer in 1898. It assumes that the transformed sound waves as imparted to the endolymph affect the structures of the cochlea as a whole.

Rutherford first advocated that all the hairs of the hair cells vibrate equally to every note and that the nerve impulses thus aroused are mere vibrations similar in frequency, amplitude (intensity), and character (quality) to the sound vibrations, and that, therefore, sound analysis is wholly cerebral.

Waller and Meyer assumed that the transformed sound vibrations in the endolymph act upon the basilar membrane as a whole, repeating the vibrations of the tympanic membrane. Meyer supposes that each wave, as it passes up the scala vestibuli, presses the basilar membrane downwards and does this just in the proportion in which amplitude of the wave is not decreased by the resistance it meets in passing upward toward the apex. Thus each wave will produce irritation of a certain number of hairs and the intensity of the irritation will diminish as the amplitude of vibration is diminished by resistance; and therefore a wave of greater amplitude will involve a greater extent of the basilar membrane, and of auditory hairs, than a wave of lesser amplitude. Certain waves, sooner than others, in passing up the scala will become too faint to sufficiently press down the basilar membrane. According to this view, pitch depends upon vibration frequency or the number of stimuli per second, while intensity depends upon the total number of nerve endings irritated. It allows a certain amount of analysis in the cochlea.

The telephone theory differs from that of Helmholtz in that it assumes that the basilar membrane, instead of certain of its fibers vibrating in sympathy with given notes, vibrates as a whole to every note in so far as the original amplitude of the wave and resistance to propagation will allow, and that the auditory nerve fibers transmit to the brain stimuli of frequencies and intensities of the note or notes concerned. The resonance theory supposes analysis of sound by the cochlea; while the telephone theory supposes distinctions of sound, perception of tone, etc., to be accomplished by the brain, made possible of course by the varying quality of the stimuli in the peripheral organ, the cochlea. The resonance theory of necessity requires that each fiber of the basilar membrane and each arch, or pair of rods, of the organ of Corti be able to vibrate or move upward and downward independently.

Numerous objections to the resonance theory have been made, both physiological and anatomical. Of the physiological objections, two may be cited as examples of those the obviation of which has been recently undertaken by adherents of the resonance theory.

(1) A mixture of notes of closely approximate beats, even having varying intensity, cannot be analyzed by the auditory apparatus; rather, only the maximum stimulus in the mixture is perceived. Gray, '00, attempts to obviate this with a modification of the resonance theory, in which he compares the sense of hearing with that of touch. He supposes that the basilar membrane does not vibrate as to its individual fibers, each in response to a given note, but rather in areas of its extent for each note, and thus he assumes that the mixture of approximate notes involves a given small area of the basilar membrane from which only the maximum stimulus is appreciated by the brain, all others of the mixture being neglected, just as when a small area of the skin is stimulated by a very bluntly pointed instrument and the "mind only pays attention" to the point of maximum stimulation; or, just as when two points on the skin, close enough together, cannot be distinguished from a single point when stimulated simultaneously. Evidently this modification also obviates the requirement of the resonance theory that each arch or pair of rods of the organ of Corti, as well as each fiber of the basilar membrane, must be able to move or vibrate independently.

(2) It is generally conceded that sensations of "noise" as distinguished from the perception and analysis of tones cannot be adequately explained by the resonance theory. Hensen, '07, has recently put forth an elaborate modification of this theory in which he tries, among other things, to account for this inadequacy. It is unnecessary here to discuss his ingenious paper further than merely to state that he retains the assumption that the basilar membrane is composed of fibers with the power to vibrate individually, allowing that probably several adjacent fibers, being of approximately the same length, may vibrate together with the respective note. To do this, he finds it necessary to add the assumption that the cochlea mediates only musical tones, and he calls it the "musical organ." This makes it needful for some other structure to mediate sensations of noise, etc., and for this he finds the cristæ of the semi-circular canals and the maculæ acusticæ adequate.

While, strictly speaking, the two objections or inadequacies cited are anatomical as well as physiological, there are some which may be considered more purely anatomical, and therefore physical, objections to the resonance theory.

From the nature of available information, the intangibility of the apparatus, it has been the rather common custom in discussing the physiology of hearing, to first assume the existence of anatomical

characters and then to base explanations of the phenomena, many of which may be largely psychic, upon the results of the application of excellent mathematics and physics to the structures assumed. The resonance theory must depend essentially upon the character it assumes for its vibratory mechanism. Therefore the anatomical objections to it must deal with these assumed characters. Among these objections may be enumerated the following:

(1) Supposing the basilar membrane to be composed of individual fibers capable of vibrating independently, its environment in the lamina spiralis is such that its vibration in response to many of the transferred sound waves, and certainly with any degree of sensitiveness, seems very improbable. The basilar membrane, the fibrous portion of the spiral lamina, is closely invested by two continuous layers of tissue on each of its sides. On its tympanic side, there is first the layer of endothelium lining the scala tympani (see Fig. 7), and second, the much thicker layer of epithelioidal cells which contains further, that anastomosing plexus of blood vessels known as the vas spirale, which is only approximately a single vessel in the end of the basal coil, but which elaborates with increasing complexity toward the apex of the cochlea. On its vestibular side, it is covered first by a "homogeneous" and well developed membrana propria of the neuro-epithelium (see Von Ebner, loc. cit., page 927, Fig. 1450), and lastly, the whole is covered by, or supports, the neuro-epithelium including that comprising the thick organ of Corti. Outside the animal body, structures of such relative thickness adhering throughout to a system of strings would effectually damp at least their resonant vibration. Further, if the basilar membrane were vibratory in the degree supposed by the theory, the circulatory pulsations in the vas spirale would very probably tend to at least confuse agitations produced by resonant vibrations of its directly overlying fibers, even with the habitual neglect by the auditory apparatus of the blood pulsations themselves.

(2) The resonance theory requires, and, truly, the earlier pictures of it assume (Neuel, '72, for example), that the basilar membrane be composed of a single set of radially disposed fibers. Ayers, '91, describes it in man as composed of four layers of fibers, three of which run radially from the lamina spiralis ossea into the ligamentum spirale to terminate at the base of the stria vascularis, and the fourth, a thin layer, running at right angles to the other three. If these four layers exist, there is nothing to be observed in either sections or teased prepa-

rations, indicating that they do not lie in direct contact and probably adhere to each other, and such an arrangement must tend to interfere with sensitive resonant vibration.

(3) Assuming that any or all parts of the basilar membrane proper consist of independent fibers, the question may be asked whether the membrane is capable of being thrown into vibration at all by sound waves. Ewald, '99, constructed a model in which he was able to so stretch a very thin rubber membrane that he succeeded in getting pieces as small as 0.5 mm. broad to vibrate when suspended in water by sound waves in the air. The recent measurements of the assumed vibratory width of the basilar membrane by Kolmer, '07, show this width to vary from only about 0.2 mm. (168 microns) in the basal turns to only 0.3 mm. (304 microns) in the apical turns. Shambaugh, '07, thinks that Ewald's model falls far short of proving that the basilar membrane, which he describes as being "much shorter, thicker and more rigid" than Ewald's rubber membrane, vibrates in response to sound waves transferred to the endolymph, and he mentions the fact that Helmholtz himself appreciated the doubt as to whether fibers so short as the width of the basilar membrane can be thrown into vibration by sound waves. Certainly its relative width and thickness, coupled with objections 1 and 2 above, make its vibration reasonably doubtful. Shambaugh describes the basilar membrane, in his preparations of the cochlea of the pig, as becoming so thick and rigid in the basal coil, "a considerable distance" from its basal termination, as to preclude the idea of its being a vibratory structure. In one specimen he found complete absence of the basilar membrane in the basal end of the coil, but instead the perfectly formed organ of Corti, with its tectorial membrane, rested upon a direct junction of the crista of the spiral ligament with the labium tympanicum of the spiral limbus. In another specimen, he found the perfectly formed organ of Corti resting upon a solid bony plate bridging the width between the lamina spiralis ossea and the outer wall of the cochlea. Such absences of the basilar membrane under a completely formed organ of Corti, suggest that it is not essential to the sense of hearing either as a structure vibrating in accordance with the resonance theory or in accordance with the telephone theory.

(4) To the above anatomical objections to the resonance theory may be added evidence that the basilar membrane is not composed of individual and independent fibers at all. The idea of resonant vibration as implied in the theory demands the existence of such. Some of the

older papers illustrate the fibers as separately distinct, and even counts of them are claimed, varying from 15,000 to 25,000. And measurements of their thickness have been given, varying from 1.5 to 2.3 microns. One of the most recent modifications of the theory, that of Hensen, is founded wholly upon the existence of separate fibers.

After becoming convinced by micro-chemical tests that the basilar membrane consists of white fibrous connective tissue, some horizontal sections of pig cochleæ were prepared here and stained by Mallory's method for white fibrous tissue. The sections were necessarily cut quite thin in order to get areas containing the basilar membrane alone, exclusive of its coverings, so that its actual construction might be studied. Fig. 11 is an attempt to show the appearance of flat sections of the membrane as brought out by Mallory's method. From these preparations, and afterwards even from the pieces obtained from the teased cochleæ stained with fuchsin, it became evident that the basilar membrane is nothing more nor less than a thin flat tendon, and that its so-called "fibers" correspond exactly to the well known fiber-bundles in tendon fasciculi, being by no means independent of each other even as bundles. Each bundle is, of course, composed of multitudes of fibers so fine that, even under oil immersion, one can never separate them with certainty as to the divisional units of the structure, much less measure them. The bundles (fibers of the basilar membrane), just as the bundles in a tendon fasciculus, are abundantly connected or continuous with each other by myriads of fine, silver-like collateral fibers inserted at all conceivable angles, the majority slanting in the direction of the bundles. In other words, the basilar membrane, instead of being formed of independent fibers, is a sort of a feltwork or modified reticulum of interwoven fibers, the general direction of most of which is radial to the axis of the cochlea, but withal, the resulting structure is such as to wholly preclude the idea of the independent vibration of adjacent fibers. True, in itself, it does not preclude the telephone theory of hearing. This radial or parallel tendency is no doubt due to the fact that, as the cochlea grows, the basilar membrane is developed from the mesenchyme under tension, just as tendons are, and thus it becomes stretched taut as the floor of the ductus cochlearis and merely serves for the support of the neuro-epithelium in the position for its functioning. The membrane differs from an ordinary flat tendon in the distribution of its nuclei. These, instead of being arranged throughout in the varying columns of tendon cells, are absent under the region of the organ of Corti. As

shown in Fig. 11, they appear between the bundles, in a belt near the beginning of the spiral ligament in the outer edge, and, in the inner edge, the nuclei of the labium tympanicum encroach but little further than the foramina nervosa of the habenula perforata. The membrane no doubt grows at the edges, and the midregion being oldest, its cells are probably exhausted.

(5) The resonance theory, with its assumption of individual fibers in the basilar membrane, as mentioned above, carries with it the idea that the different elements of the organ of Corti, including the arches, or pairs of rods of Corti, must be capable of moving separately. Not only do anatomists agree that the neuro-epithelium forms a continuous membrane throughout the cochlea, but the component cells of the organ of Corti are easily seen to be intertwined and interwedged among themselves. Further, the rods of Corti's organ are probably more firmly adherent to each other in their series than are any other elements of the organ. This may certainly be said of the series of outer rods. In teasing the cochlea for the tectorial membrane, I found in several preparations when mounted, considerable extents of the outer rods adhering to each other, appearing on the flat as a grill-work, and wholly free from other elements of the organ. From one specimen, fixed and decalcified with Perenyi's fluid, which has a macerating effect upon tissues unless followed by washing in alcohol, I succeeded in obtaining a tier of the outer rods more than 5 mm. long and so firmly coherent that it floated about in the teasing fluid and withstood manipulation sufficient to mount it entire. Occasionally short tiers were found in the mounts of the tectorial membrane, sometimes adhering to its edge and lying out flat and otherwise free so as to be easily studied. Fig. 12 represents an end of one of the latter, and was chosen because it had been torn from the series in such a way that it afforded an excellent illustration of the shape, interrelations and character of the outer rods. This preparation was fixed in Zenker's fluid. The inner rods are manifestly not so resistent as the outer, for, while distorted scraps and fragments from their dissolution were found in the mounts, tiers of them alone were never found intact. The ends of the phalanges of the outer rods often showed frayed bits of the phalanges of the inner adhering to them. All appearances indicated, however, that the rods of Corti, both inner and outer, must be quite firmly coherent both the inner to the outer and to each other in their series.

(6) The resonance theory applied, as it has been from the beginning, to the basilar membrane, requires not only that the rods (and the other

elements) of the organ of Corti resting upon the vibratory fibers should be able to move up and down independently, but it is usually inferred that both rods of the arch must rest upon the basilar membrane throughout the extent of the cochlea. In all of my vertical sections of the cochlea of the pig, and Shambaugh notes the same in his preparations, usually throughout the basal coil the feet of the inner rods of Corti do not rest upon the supposedly vibrating basilar membrane, but reach over to stand upon the thicker edge of the labium tympanicum. Ter Kuile, '00, recognized this, but made use of it to assume that contact of the hairs of the hair cells against the tectorial membrane during stimulation is not in a vertical direction, but occurs as a lateral, inward brushing motion, the outer rods alone being moved by the vibrations of the membrane while the inner rods merely act as fulcra in producing the brushing motion. This assumption gains nothing but an increase in the complexity of the resonance theory, since, above the basal coil, the feet of both rods do rest upon the supposedly vibrating portion of the basilar membrane. It is fairly well indicated from clinical evidence that the nerve fibers from the basal coil mediate sensations of notes having the higher pitch, and ter Kuile's assumption merely adds the anatomically improbable condition that the neuro-epithelium is agitated by these higher notes in a different way than it is by the lower notes supposedly affecting the coils toward the apex.

(7) To the anatomist, given structures in a given species of animal are strikingly identical in character. For example, all cochleæ of normal individuals of a given species are strikingly alike in all details.

The power of tone perception and tone distinction by different individuals is not as constant and uniform as would be expected with the apparently constant anatomical mechanism for the mediation of sound. Individuals without special training (habits) differ markedly, and it is well known that the "trained ear" in any special direction shows a far greater power of analysis of sound and distinction of smaller differences of tone than the untrained. Most of the investigators of the physiology of hearing, including Helmholtz, recognize this and usually try to obviate it by assuming modifications in the mechanism of the cochlea.

More probably, as in all the other senses, the whole question of analysis of stimuli and the power of finer perception, inherent or acquired by education, must be transferred from the peripheral or receptive mechanism to the central nervous organ. Just as in touch or smell or sight, so in hearing, all being physiologically similar, the variety of

the sensation experienced depends only upon the quality and intensity of stimulus applied to the peripheral nerve endings. The specialization of sensation is doubtless with reference to general groups only, and this specialization dependent upon the locality of the cerebrum to which the impulses aroused by external stimuli are borne. The optic nerve, stimulated by touch (pressure) conveys impulses which are interpreted as sensations of light; the acoustic nerve, stimulated by touch (tumors, etc.) gives rise to sensations of sound. And it is very probable that within the general groups, most manifest in touch, identical nerve terminations acted upon by external stimuli varying in quality, give rise to sensations varying according to the quality of the stimuli.

It is considered neither possible nor necessary in this paper to consider fully the numerous modifications and additions to the resonance theory. Many of the papers are merely attempts to explain away the physiological (and psychological) difficulties and anatomical objections to the theory as applied to the basilar membrane and the action of the organ of Corti. It seems to the author that these objections, taken collectively, are such that neither the resonance theory nor the telephone theory as applied to the basilar membrane are any longer tenable.

The fact has been frequently noted, and especially by ter Kuile, that the tectorial membrane, in all species, is always entirely coextensive with the organ of Corti, and is always sufficiently wide to cover the hair cells, whether these are in linear series on either side of the rods, as in mammals, or whether they are scattered throughout the entire epithelium of the organ of Corti, as in birds and reptiles. Since the same cannot be said of the basilar membrane, it seems very probable that the tectorial membrane is more essential to the sense of hearing. Further, because of its shape, its more logical position, above the auditory hairs, and its far more delicate sensitiveness, the tectorial membrane seems much better qualified to serve as the vibrating mechanism than the basilar membrane.

Siebenmann, '00, seems to have been the first to suggest that the tectorial membrane is the structure agitated by sound waves, though the inference drawn by Ayers, '91, amounted to something similar. Quite recently Kishi and Shambaugh, realizing the anatomical disqualifications of the basilar membrane, have attributed the power of resonance to the tectorial membrane.

Kishi, '07, after citing four anatomical objections, concludes that the basilar membrane is not qualified for the vibrating mechanism of either

the resonance theory or of any other theory of hearing. He substitutes the tectorial membrane as being more suited to the purpose, and then, from some rather distorted sections of the cochlea (illustrated with photographs), he assumes that the tectorial membrane is attached along its outer edge to the laminea reticularis of the outer supporting (Hensen's) cells of the organ of Corti, and thus claims that it is held down firmly upon the organ and always at right angles to the auditory hairs. Being also firmly attached along its inner edge, as all admit, Kishi describes and diagrams it as a membrane stretched tautly over the organ from the labium vestibulare of the spiral limbus to the lamina reticularis of Hensen's cells. He then assumes that the length of the fibers composing the membrane ocrresponds throughout to the breadth of the membrane in the respective turns of the coil. Admitting that his assumed absolute length of the fibers (the breadth of the membrane) cannot be determined because of shrinkage and distortion produced by the technique, he finds, from measurements of the width of the membrane in his sections, that the relative length of the fibers in the apical region is at least three times greater than those of the basal coil. Therefore he assumes that the fibers have different spans, vibrating lengths, in the different regions of the cochlea with all conceivable variations between the longest in the apex and the shortest in the basal end, and thus it is to be inferred that the tectorial membrane is a resonant structure composed of fibers capable of sympathetic vibration to all sound waves of lengths between and including those which may affect its longest and shortest fibers. He realizes that the fibers course obliquely across the membrane, slanting toward the apex, and that, therefore, their actual lengths are greater, especially in the apical region than the width of the membrane as seen in radial sections.

Against Kishi's conception of the tectorial membrane, three objections may be urged:

(1) From the processes of development of the membranes, it is very improbable, if not impossible, that any of its fibers in any region extend across the entire breadth of the membrane.

(2) From the processes of its development, it is probable if not certain that the great majority of the fibers are attached at neither of their ends, but merely lie embedded in the transparent matrix.

(3) From the studies made here and by others mentioned of preparations as nearly normal as possible, it is concluded that the tectorial membrane has but one attachment in life, namely, its inner edge upon the

labium vestibulare of the spiral limbus. In the apical turn, at least, its outer edge cannot be attached to the lamina reticularis, for this edge in the first half-turn (Fig. 6) may extend into the space of the ductus cochlearis a distance of nearly half its width beyond the organ of Corti.

Shambaugh, '07, urges the objections, accredited to him above, against the possibility of the basilar membrane being a resonance mechanism, and, from appearances in some of his sections, concludes (1) that the tectorial membrane does not lie free in the endolymph over the organ of Corti, but is attached along Hensen's stripe to the inner supporting cells of the organ; (2) that "the hairs of the hair cells project normally into the under surface of the tectorial membrane"; (3) that "the size of the membrana tectoria near the apex of the cochlea is many hundred times its size near the beginning of the basal coil"; and (4) he concludes further that, in structure, the tectorial membrane consists of "an immense number of delicate lamellæ taking their origin from the portion of the membrane which rests upon the labium vestibulare." From these conclusions and the conclusions generally accepted as to the relation of the tectorial membrane and the hair cells to stimulation of the acoustic nerve terminations, he advances a theory that the tectorial membrane consists of a series of resonators (the lamellæ) which are capable of responding to the most delicate impulses passing through the endolymph, claiming that the great variation in size of the membrane from one end to the other, suggests the possibility that, by acting the part of a resonator, it is capable of responding in different parts to impulses (tones) of different pitch. Shambaugh, in applying his theory, claims with reason that all the observations by Helmholtz and his followers supporting their resonance theory apply more readily to the tectorial membrane as a resonator than to the basilar membrane, and proceeds to explain the pathological phenomena of *"tone islands," "diplacousus binauralis dysharmonica"* and *"tinnitus aurium"* on the basis of a resonating tectorial membrane.

Some of the observations both made and cited in this paper are not in accord with the premises from which Shambaugh's theory follows. In the first place, it is considered probable that the tectorial membrane does lie free over the organ of Corti and that the auditory hairs do not project into it. In the second place, it is not a lamellated structure. Ever since 1869, when Böttcher teased portions of it and found them to contain fibers, the fibrous structure of the membrane has been conceded by all who have studied it with reference to its structure. Sections in

different planes, as made by Coyne and Cannieu, '85, and here (Fig. 9), indicate clearly its fibrous nature.

It is not the intention of the paper to elaborate another theory of hearing and to enter into a necessarily prolonged application and defense of it. Leave is asked to merely suggest a modification of a theory already advanced, namely an application to the tectorial membrane of the telephone theory, heretofore applied exclusively to the basilar membrane. Some of the considerations upon which this suggestion is based are the following:

(1) The prevailing acceptation is that the cochlea is the peripheral organ of the auditory apparatus, and that the construction of this organ is such as to be especially capable of serving, in conjunction with the central nervous system, in the analysis of sound.

(2) From their anatomical relationship, it is conceded that auditory impulses are aroused in the acoustic nerve through the mediation of the hair cells of the organ of Corti about which they terminate.

(3) It is usually conceded and here accepted that the hair cells are stimulated through the agitation of their hairs, but that the hairs are neither suitably constructed, long enough, nor vary sufficiently in length to be themselves acted upon selectively by the sound waves as transferred to the endolymph.

(4) All the recent conceptions of the process of hearing accept the idea that the hairs of the hair cells are agitated by contact with the under surface of the tectorial membrane, either by brushing against it or by perpendicular impingement, produced either by vibrations of the basilar membrane below or movements of the tectorial membrane above.

(5) The numerous physiological and anatomical objections to it are considered sufficient to render untenable the idea that the basilar membrane is the vibrating mechanism either of the kind demanded by the resonance theory or in accord with the telephone theory.

(6) While experimental investigation has not yet been able to ascertain the exact form of the wave motion in the endolymph of the cochlea, it has been determined by observation of the action of the tympanic membrane and auditory ossicles that the force of the motion produced in the tympanic membrane by the atmospheric sound waves may be increased thirty times in the transformation and transference of the motion to the basis of the stapes and the membrane of the fenestra vestibuli, and that the amplitude of the atmospheric waves may be reduced as much as seventy-six times (or more). In this transference

of the energy to the endolymph, the reduction of amplitude, as well as the increase of the force, depends not only upon the lever arrangement of the ossicles, but upon the tensity of the tympanic muscles and the pressure of the air in the tympanic cavity. Therefore, the wave motions imparted to the endolymph by the basis of the stapes *correspond* to the atmospheric sound waves, of which they are transformations, but *resemble* them only in frequency of vibration. The quality of the motion imparted to the endolymph depends of course upon the quality or form of the atmospheric waves acting upon the tympanic membrane, but the quality of the two may not be identical in detail. While the canals of the cochlea are probably entirely filled with endolymph normally, and under a pressure which depends largely upon the blood pressure of the different conditions of the body, the membrane over the fenestra cochleæ (rotunda) and the direct continuation of the endolymph of the cochlea with that of the vestibule are considered sufficient to allow compensation for the incompressibility of the fluid and to allow propagation of the motion in the form of true compression waves. Pressure applied by the stapes to the endolymph in the cochlea may not only be compensated or relieved by the membrane below and by the ductus reuniens connecting it with the sacculus, utriculus and semi-circular canals, but, by way of the sacculus, such periodic pressure may be compensated through the ductus endolymphaticus into the cranial cavity. Furthermore, the layer of softer tissue between the epithelium lining the scalæ and the solid walls of the bony labyrinth may aid in maintaining the form of the wave motion. Therefore there is reason to conclude that the motions imparted by the stapes at the basal end of the cochlear coil are propagated in the endolymph toward the apex of the cochlea in the form of compression waves, however short, with longitudinal direction and transverse vibration. The waves are very probably similar in many respects to pulse waves.

(7) That the agitation of the hairs of the hair cells is brought about through the activity or actual movements of the tectorial membrane induced by the wave motion transferred to the endolymph is suggested by the peculiarities of that membrane.

(*a*) It is in the logical position for such action. It lies above the hair cells adjacent to the portion of the endolymph to which the waves are first imparted by the basis of the stapes. The basilar membrane is situated below the tectorial and is both covered and obstructed.

(*b*) In the mammalia and in all animals possessing it, the tectorial

membrane is entirely coextensive with the organ of Corti. The basilar membrane as such is not entirely coextensive.

(*c*) From its specific gravity, its evident lateral elasticity and from its most remarkable transverse flexibility and sensitiveness to agitations in a fluid surrounding it, the tectorial membrane appears to be far more admirably qualified to serve as the vibrating mechanism than does the basilar membrane.

(*d*) From the evidence that the tectorial membrane is attached along but one of its sides; from the fact that, even if it were attached along both sides, none of its fibers are coextensive with its width; from the fact that it is so constructed that relatively very few of the fibers, even if vibrating, can in any way come in contact with the hairs of the hair cells, and from the fact that the great majority of its fibers are evidently attached at neither of their ends, it is very improbable that the membrane is capable of acting as a sympathetic resonator.

(*e*) In addition to its suggestive consistency and structure, the tectorial membrane is so shaped and proportioned as to suggest that it may act with reference to vibrations in the endolymph in a way by which the peripheral components of the phenomena of hearing may be explained; namely, the membrane may be acted upon as a whole, the extent, region, amplitude and quality of its vibrations depending upon the force, frequency, amplitude and quality of the vibrations acting upon it.

From the various pathological phenomena, observation of which have been followed by post-mortem examinations of the cochlea, it is quite generally accepted that sensations of the higher pitches are mediated by the structures of the basal coil of the cochlea, and from this it has been assumed, naturally, that the sensations of lower pitch are mediated by the apical coil.

The tectorial membrane is narrowest and thinnest in the basal coil and gradually increases in both width and thickness to acquire its greatest proportions in its apical end. Being attached along its inner edge throughout, it must be affected by sound waves in the endolymph very much as a very flexible ribbon so attached would be by agitations running parallel with its length in a fluid in which it floats.

The extent to which the tectorial membrane can be agitated must depend (1) upon the energy of the wave motion, or upon the extent and point at which the wave motion in the endolymph is neutralized by overcoming the inertia of the fluid and by the resistance offered by the

walls of the cochlea, and (2) upon the breadth and thickness of the membrane and thus upon the extent to which the wave energy is exhausted in overcoming the inertia of the membrane itself.

That notes of higher pitch or greater vibration frequency are more apt to produce vibrations in the thin, narrow, basal coil of sufficient amplitude to stimulate the auditory hairs than they are to produce such vibrations in the apical coil is considered probable for the following reasons:

(1) The thin, basal end of the membrane lies nearer the fenestra vestibuli (ovalis) or the point at which the waves are imparted to the endolymph. Of sounds of equal intensity, or amplitude of vibration, but of different pitch, those of higher pitch or greater vibration frequency are sooner overcome by the resistance of the medium (do not travel so far) as those of lower vibration frequency. In the atmosphere, sound waves of high frequency are damped out before those of low frequency and their speed of transmission continuously decreases as they become fainter. This damping out must occur much more quickly in a medium like the much more viscous endolymph. Therefore it is possible that sound waves of the highest perceivable pitch may affect only the end of the basal coil of the tectorial membrane and be damped out wholly before reaching the upper coils, or at least to such an extent as not to agitate the upper portions of the membrane sufficiently for stimulation of the hair cells.

(2) The natural vibration period of the thin, narrow strip is of greater frequency than that of the thicker wider strip. It is possible to subject a strip of material to vibrations of such frequency, either above or below its natural vibration period, that it will not vibrate at all or vibrate weakly or irregularly. It is probable that no portions of the tectorial membrane, when subjected to sound waves transferred to the endolymph, will undergo vibrations of sufficient excursion to impinge upon the auditory hairs except those portions whose natural periods correspond to the vibration frequencies of the waves affecting the endolymph. Portions adjacent to these, having approximately the same natural periods (thickness and width), would of course be also affected, but to a degree decreasing as the distance from the portion most affected increases. Or, again, the effect of loading a vibrating body is to lower its vibration frequency or pitch. If the body be of uniform proportions and the load be distributed uniformly, the vibration frequency of all its components will be lowered; if the load be placed at one part of the

body, one of the resulting complications will be a lowering of the vibration frequency of that part. Should the tectorial membrane be considered a vibrating body carrying a load so distributed as to gradually increase toward its apical end, then its vibration period or frequency must decrease as this end is approached. Therefore, it is possible that the thin, narrow basal coil of the tectorial membrane may be sufficiently affected by waves of high frequency to stimulate the auditory hairs when other portions of the membrane are not. Several waves, of course, may pass in a medium simultaneously in the same direction.

This idea suggests a sort of resonance quality in the tectorial membrane when the latter is considered as a whole, and thus it is not fully in accord with the idea originally suggested in applying the telephone theory to the basilar membrane. It is slightly analogous to some of the features of Waller's and Meyer's modification of the telephone theory.

(3) The natural consistency of a strip attached along one edge determines in considerable measure the extent and form of movements induced in it by wave motion in the medium surrounding it. The basal end of the tectorial membrane, being narrower and thinner, though of the same material, is more flexible than the end at the apex. Therefore, it must offer less resistance to waves of high frequency (is more easily crumpled into abrupt and frequent folds) than the thick apical end. The viscosity of a vibrating body, while it may affect the vibration frequency (pitch) but little, aids materially in causing the amplitude of vibration, the excursion or intensity of movement of the body, to gradually decrease and dwindle away as the waves pass along the body. It is therefore possible that waves of high frequency are capable of throwing the thin basal coil of the tectorial membrane into waves of considerable excursion or amplitude, while, as they pass along toward its apical end, they may be gradually absorbed in overcoming the inertia of the membrane; first, becoming too faint to throw it into vibrations, or folds, of their frequency and of sufficient amplitude to agitate the auditory hairs below, and finally, as the broad, thick end is approached, a region is reached in which the waves of high frequency wholly dwindle away.

In the same way, for the above reasons, it may be suggested that waves of lower frequency than those which sufficiently agitate the basal end of the membrane only, can, according to their frequency or length, affect respectively the remaining regions sufficiently to stimulate the auditory hairs, because such longer waves travel farther in the given medium, are less rapidly overcome by friction of the walls of the scala

of the cochlea, and because the broader and thicker portions of the membrane probably can be thrown into vibrations by the waves of lower frequency. In other words, the vibrations of higher frequency are more rapidly absorbed and dwindle away in passing along the membrane, while waves of greater length or lower frequency may throw the thicker portions of the membrane into undulations of sufficient amplitude for impingement upon the auditory hairs. Thus the first half-turn of the cochlea would be a portion of the peripheral organ of the auditory apparatus which is thrown into activity only by sound waves of the lowest frequency to which the mechanism is capable of reacting.

Aside from the possibility that the different widths of the tectorial membrane possess different natural vibration periods and therefore may exercise a sort of synchronous selection or resonance with reference to the waves passing in the endolymph, there is nothing in the above suggestions to claim it improbable that the thin, basal coil is not made to undulate by waves of low frequency also. It very probably is, and under the following conditions:

There is little information available as to the properties of sound waves traveling in a substance whose elasticity is not the same in all directions. It is known that in strips of wood the waves travel more rapidly, are less impeded, in the direction of the fibers than across them. The tectorial membrane is most elastic in the direction of its fibers, that is, it is more resistant to stress applied transversely to them. It is exceedingly flexible and sensitive to motion applied transversely to its long axis. Such motions are, in the main, parallel to the direction of its fibers and thus can meet less resistance from them. Since, as shown above, the fibers are not so arranged nor so attached as to act as a system of resonators, and since the membrane is attached only along one side instead of at each end or along both sides, it is very probable that it is largely a passive structure. Attached along its inner edge and held in its position over the organ of Corti by its elasticity, it extends, suspended in the endolymph and subject to be acted upon by whatever motion may be imparted to the latter. Sound waves transferred to the endolymph by the stapes at the fenestra vestibuli must travel along the membrane from basal end to apex with excursions of amplitude transverse to its long axis and thus in the direction which may bring into play its remarkable flexibility. Waves of a given frequency of vibration will affect corresponding vibrations in the membrane to just that extent and amplitude to which they are not damped

out by the endolymph and resistance of the walls, and not absorbed in overcoming the viscosity and bulk of the membrane itself. The waves of lowest frequency, or greatest length, may produce corresponding undulations in the *entire* membrane; waves of the highest frequency may produce in the thinner, and therefore most flexible, end of the membrane *alone* corresponding undulations of sufficient excursions for the necessary impingement upon the auditory hairs. Undulations of high frequency would result in a greater number of impingements per unit of length of the organ of Corti than would waves of low frequency, and thus both the nature and the locality of such stimulation would be different. Waves of higher amplitude, or intensity, would produce impingements of greater intensity and thus give sensations interpreted in degrees of intensity.

Functioning in this way, the peripheral organ of the apparatus is functionally as well as morphologically comparable to the so-called otolithic organs, the cristæ and maculæ acusticæ. And, further, it is comparable with the other organs of special sense. The varieties of optic sensations, for example, depend upon the intensity and quality of the stimuli, that is, upon the number and variety of waves of light impinging upon a unit area of the retina. The various sensations obtained by touch depend upon the number, intensity and quality of the stimuli applied to the skin. Differences in quality of stimuli at the periphery are perceived and interpreted as differences by the central nervous organ. A number of stimuli applied to a unit area of the skin gives rise, within the possibilities of skin-innervation, to a different sensation or interpretation than does a single stimulus applied to that area. The same stimuli applied with different intensity give rise to interpretations of different intensity. So, in general, for taste and smell, all being dependent upon contact, whether the energy applied be simply mechanical or more strictly chemical.

In the auditory organ the stimuli arousing the sensations are thought to be mechanical. The greater numbers of stimuli applied to unit areas of the organ of Corti result from waves of high frequency and give rise to a sensation interpreted and named by the central nervous organ as high pitch. It happens that the region of the cochlea anatomically adapted for mediating sensations of highest pitch is its basal coil. Conversely, smaller numbers of stimuli applied to the unit area are interpreted as low pitch, the stimuli from waves of the lowest frequency being distributed most sparingly, but throughout the extent of the cochlea,

including the basal coil. Greater amplitude would mean intensity of impingement and interpretations of intensity of sound. Physical reinforcement of wave motions would mean reinforcement of tones; quality of impingement upon the auditory hairs would mean quality in the sensations as interpreted; the number of a given variety of stimuli applied to the unit area of hair cells would determine the predominant variety of the sensations resulting.

If the *accessory tectorial membrane* described in previous pages of this paper should prove to be a true and constant structure, it would be considered capable of separate vibration. Varying slightly in width, being narrowest at the basal end, this membrane suggests a considerable increase in the possibilities of function of the cochlea. It would undulate in accord with waves in the endolymph too faint to agitate the main body of the membrane at all, while its vibrations would be subject to the same conditions and would vary much as those of the main body. With waves of greatest amplitude it would act in conjunction with the main body. It is interesting to note that from its position it would act alone, only upon the outer and wider series of the auditory hairs.

In all the preparations showing the coherent series of the outer rods of Corti's organ, an interesting interrelationship of the rods was suggested. As seen on the flat, the shafts or slender mid-portions of the rods invariably showed a tendency to be grouped (Fig. 12). From those preparations in which the locality of the coil could be determined, this grouping seemed to be different in different regions. In the first turn of the organ of Corti, the shafts were grouped in twos and threes; in the second turn (Fig. 12) they were grouped in threes and fours; in a longer strip of them, fully five millimeters, which, during the teasing process, was seen to float out from the region of the fifth turn, the shafts were arranged in groups of from five to eight. None were obtained as coming from the basal coil.

We have no information as to whether or not the rods stand in this relation during life. They possibly stand straight and equidistant and cohere into groups during the manipulation before and during the mounting on the slide. In forming the arch bounding the tunnel of Corti, the shafts of the rods stand approximately straight in profile view, while the portions braced by the foot-cells always curve as they approach their rest upon the basiliar membrane (Fig. 12). It was thought possible, then, that the grouped appearance of the shafts on the slide might result from the straightening of the curved foot-portion

when the series comes to lie flat on the slide. However, if this were true, one would expect all of the shafts to be curved, whereas those in the middle of each group are usually straight. Again, if the shafts stand straight and equidistant during life, noticeable depressions in the surface of the phalanges opposite the spaces between the groups would probably result from the bending of the shafts in forming the grouping. In all the preparations, the outline formed by the cohering phalanges appeared straight. Further, in the grouped conditions shown in the preparations, the granular protoplasm dispersed between the rods appeared continuous throughout the smaller spaces between the rods of each group, but in the spaces between groups it appeared above and below with a thin film along the sides of the bounding rods, leaving a definitely bounded vacant space in the center (p., Fig. 12). In the split shown in Fig. 12, the upper area of this protoplasm appeared split also. Since this preparation came from a cochlea fixed in Zenker's fluid, the protoplasm must have been hardened while in position in the cochlea and therefore was firm enough to be broken, as shown when the rod-series was split by the teasing process.

Whether equidistant or grouped in life, the preparations suggest an anatomical arrangement which may increase the functional possibilities of the organ. As shown by Joseph, '00, and by Held, '02, and as shown in Fig. 12, the rods proper consist of bundles of longitudinally placed fibers held together by a seemingly hyaline matrix, and therefore may be distinguished from the granular protoplasm distributed between the rods and forming the foot cells. From all appearances, the rods are relatively rigid, the outer more so than the inner series, and their presence is generally conceded as serving for the support of the neuro-epithelium at each side. If they are grouped during life, then the two phalanges which come together opposite the larger spaces between the groups (a., Fig. 12), might be less resistant to vertically applied force than would the phalanges of the rods of the middle of the groups, b, and thus, also, would the hair cells immediately supported by these phalanges be held in varying degrees of rigidity against the impact of the tectorial membrane. On the other hand, a separation of the rods, as shown in the groups, into straight and equidistant relations would produce slight bulges in the outline of the coherent phalanges, and thus, if the rods are straight and equidistant during life, this condition probably results in hair cells at intervals standing higher than others and more apt to be stimulated by slight undulations of the tec-

torial membrane, and to be stimulated more strongly by undulations of greater amplitude. Either relation (that is, if the hair cells do not lie in the same plane), would be a factor in determining the number (and also the intensity) of the stimuli applied to a unit area of the organ of Corti. Such conditions are merely suggested by the slides. Though constant in my preparations, the grouping may be artifact and may mean nothing at all.

As evident in the above pages, I have entered very lightly into an application of the laws of physics to the anatomical rôle suggested for the tectorial membrane. Many features must be subjected to further anatomical investigation and must receive further substantiation before a wise application of the known can be made. For the same reason, the physiological phase of the question, which, based upon the many auditory phenomena, could be prolonged indefinitely, is touched upon but little. Just how far the cochlea, in itself, takes part in the analysis of sound is the difficult question. In the physiological literature the cochlea is spoken of as *analyzing, noticing, appreciating phase, distinguishing and perceiving tones, etc.* It is well known that several waves may pass, in the same direction, simultaneously through a medium. In the cochlea, acting as above suggested, their resulting stimulation of the auditory hairs would be somewhat segregated as to pitch. A mixture of sounds of different qualities but of approximate pitch would act upon approximately the same area of the organ of Corti, complicate the process and probably be interpreted as *"noise."* The matter of the finer analysis of sound is no doubt almost wholly cerebral. It certainly is largely a matter of education. It is of course probable that cochleæ, as other organs of the body, may differ as to their anatomical excellence in different individuals. I wish to suggest that most of the phenomena of hearing which are actually peripheral may be explained on the basis of the relationships suggested.

Impulses borne by the cochlear division of the acoustic nerves are conveyed to given localities of the cerebrum. Probably any stimulus aroused in these fibers gives rise to sensations of sound. Gray, '00, reports a case of deafness and "singing noise in the ear" in which the post-morten examination showed all the divisions of the ear to be in perfect condition, but, on further search, a tumor was found in the medulla oblongata encroaching upon the entering trunk of the acoustic nerve. *Tinnitus aurium* could be produced not only in this way, but, if produced temporarily, or permanently as sometimes happens, by a

violent auditory stimulation (explosions, etc.), it might result from the tectorial membrane being thrown by the excessive amplitude of the vibrations so violently upon the auditory hairs that it becomes stuck to them for a while by means of its glutinous matrix and thus would give rise to continuous stimulation. When teased out in the fresh condition, the membrane adheres to the needle point with a readiness very embarrassing to the operator, and sections often show it adhering to the hair cells upon which it has evidently been crumpled by the manipulation.

Calcareous deposits in the matrix of the membrane would not be surprising, considering the developmental analogy it bears to the otolithic membranes. If uniformly distributed, these would produce a stiffening of the membrane and a general impairment of the hearing; if localized they would result in *"tone islands."* Calcification may be the cause of some of the peculiarities of the "failing ears" of old age.

Hensen, '07, in his recent paper upholding the resonance theory as applied to the basilar membrane, claims that the tectorial membrane, considered free by him, cannot be made to impinge upon the auditory hairs by wave motion in the scala vestibuli, assuming that waves in this canal would produce simultaneous depressions of the whole spiral lamina below and thus of the hair cells, so that the usual space separating them from the tectorial membrane when the cochlea is at rest would be maintained. And he thinks, therefore, that sensations of sound do not arise till the wave motions have passed through the scala vestibuli and, therefore, only on their return in the scala tympani below does the resonance action of the fibers of the basilar membrane force the hair cells upward to impinge upon the under surface of the membrane. This idea seems to me subject to the following suggestions:

(1) It seems probable that confusion would result from the anatomical necessity, involved in his idea, that the two sides of his resonant membrane would be subjected simultaneously to different sets of waves, those passing above and those below a given point.

(2) Or, if the basilar membrane is capable of undulating so freely to the waves in the scala vestibuli, these waves would be imparted through it to the endolymph in the scala tympani below, and the same waves passing in the same direction in both canals would meet at the helicotrema and would either be reflected there by the wall of the labyrinth and return towards the middle ear, meeting other waves traveling in the opposite direction, or they would be damped out in the confusion at the helicotrema.

(3) The scala tympani increases in diameter in passing from the helicotrema to the fenestra cochleæ (rotunda). Therefore, supposing that the sound waves passing in the scala vestibuli return without interference in the scala tympani, they would not only be fainter because of the resistance of the endolymph and walls of canal through which they have passed, but their amplitude would be further decreased because of their being dispersed over the increasing space of the scali tympani. So, Hensen's idea must assume that the stimulating resonant action of the basilar membrane is accomplished with waves of less amplitude than when entering the cochlea.

(4) Anatomical studies of the basilar membrane suggest that it is wholly incapable of moving as sensitively as the tectorial membrane to waves in the scala vestibuli. Not only is the basilar membrane firmly continuous along its either edge with the walls of the labyrinth and invested above and below by layers of other tissue, but even when torn away as a free strip, it is far more stiff than the tectorial membrane. When teased free in fresh preparations it is rigid enough to more than retain its shape, and its flexibility, compared with that of the tectorial membrane, is as a wooden board compared with a strip of tissue paper. It must at least resist wave motion in the endolymph far more than the tectorial membrane which lies suspended in the endolymph, one edge free, and by position is the first to receive the impact of the waves.

To these objections to Hensen's idea may be added the objections enumerated on another page against the idea that the basilar membrane is a resonance mechanism at all.

From the anatomical standpoint, the basilar membrane may be considered as nothing more than a thin, flat tendon, thicker along its edges, whose purpose is to so strengthen the floor of the cochlear duct that it may firmly support the organ of Corti and at the same time be thin enough to allow the presence and necessary caliber of the scala tympani below it.

The *vestibular* (Reissner's) *membrane* is considered as having little to do with the function of the organ of Corti. By development, it is the remains of the outer wall of the embryonic cochlear canal, after the liquefactions of the mesenchymal tissue resulting in the scala vestibuli. It may serve as a protection to the organ below, damping violent agitations in the scala vestibuli and preventing upward displacement of the tectorial membrane. It is weakest along its edges, which condition gives, in teased cochlea, somewhat the impression of its being hinged to

the walls of the labyrinth. Grasped in the forceps, long strips of it can be removed intact, so easily does it come away. Therefore, sound waves passing in the scala vestibuli may be readily imparted to the endolymph in the cochlear duct.

Summary.

(1) The tectorial membrane of the pig, occupying a cochlea of about four turns, has an average length of 25.5 millimeters. It is about three times as broad and five times as thick in the apical half-turn as it is in the last half-turn, its dimensions decrease gradually from its apical toward its basal end, and its ends terminate bluntly.

(2) Its specific gravity is but little greater than that of the fluid in which it lies.

(3) It possesses a small amount of elasticity, barely sufficient to cause the thicker, apical region to resume its normal coils while the membrane is suspended in fluid after being freed from its attachment. Its greater elasticity is in the direction opposed to stress applied longitudinally. It is remarkably flexible to stress applied transverse to its long axis.

(4) Its structure consists of multitudes of delicate fibers of unequal length embedded in a transparent matrix of a soft, collagenous, semisolid character with marked adhesiveness. The general transverse direction of the fibers inclines from the radius of the cochlea toward the apex, which inclination is greater in the upper than in the under surface. Most of the fibers, by coursing and curving through the membrane, take part in producing the fibrous appearance of both the upper and under surfaces.

(5) From the study of both its adult structure and the processes by which it is developed, it is concluded that none of its fibers extend the entire width of the membrane, none are attached at both ends, and the greater number of them are attached at neither of their ends.

(6) Hensen's stripe is explained as a line of the intercrossing ends of the fibers of the under surface resulting from the processes by which the growth of the membrane terminates.

(7) From its study in both the fresh condition and in preparations considered least shrunken and distorted, it is concluded that the tectorial membrane projects free over the organ of Corti and is attached only along its inner zone upon the labium vestibulare of the spiral limbus.

(8) A thin, exceedingly delicate, accessory tectorial membrane is described lying along the under surface of the outer zone of the main body to which its outer edge is lightly attached. It varies in width somewhat as does the main body and its fibers extend inward toward Hensen's stripe, but only extend over the outer series of hair cells.

(9) To the several objections advanced by others to the assumption that the basilar membrane performs resonant vibration, there is added evidence that the basilar membrane is nothing more than a flat tendon composed of a lamina of interconnected bundles of white fibrous connective tissue whose purpose is merely to strengthen the floor of the ductus cochlearis and the position of the organ of Corti, and which are too rigid and firmly associated to allow of resonant vibration. And, further, even if resonance were anatomically possible in the membrane, the two layers of tissue on each of its sides would be sufficient to damp such action.

(10) To the evidence adduced that the different elements of the organ of Corti are incapable of being moved separately by vibrations in the basilar membrane, there is added evidence that the outer series of the rods of Corti are especially so associated as to be incapable of separate motion. The outer rods are more resistant to maceration than the inner rods.

(11) The theories in which the basilar membrane is considered the vibrating mechanism in the cochlea are considered untenable, and an application of the telephone theory to the tectorial membrane as the vibrating mechanism is suggested on the basis of its logical position, its extent, shape, proportions, consistency and structure, and the probable character of the transformed and transferred sound waves in the endolymph of the cochlea.

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EXPLANATION OF FIGURES.

Abbreviations in common.

Ac., accessory tectorial membrane.
Hs., Hensen's stripe.
Iz., inner zone of tectorial membrane.
Lv., Labium vestibulare.
Mb., Basilar membrane.
Mv., Vestibular (Reissner's) membrane.
St., Scala tympani.

Fig. 1.—Representing unshrunken appearance of an entire tectorial membrane teased from the cochlea of a pig two weeks old. Under surface upward. Shape constructed from measurements from several specimens and from study of specimen represented. Drawn with coil more open than normally to avoid overlapping of edges in apical turns. Arrangement of fibers drawn in from specimen.

Fig. 2.—Block from first half-turn of whole specimen. Viewed from under surface. Cut end showing course of fibers is added from study of sections of other membranes. *Li.*, line of impression of edge of labium vestibulare.

Fig. 3.—Block from third half-turn of whole specimen, under surface upward, showing course of fibers and appearance of accessory membrane as torn loose from main body. *Li.*, line of impression of edge of labium vestibulare; *Lr.*, portion of lamina reticularis removed from labium with inner zone of tectorial membrane.

Fig. 4.—Block from fifth half-turn of whole specimen, showing the general course of the fibers as viewed from the upper surface, and indicating the character of cleavage in a broken end of the membrane. *S.*, slivers of fibers and matrix formed in the breaking.

Fig. 5.—The end of the basal coil of the tectorial membrane, showing the outer edge of the accessory membrane coinciding with the outer edge of the main body, and showing how the inner zone (*Iz.*) or the attached portion of the membrane curves so as to constitute the tip of the termination.

Fig. 6.—Vertical section of the tectorial membrane in position and through the first half-turn of its coil, showing the extent to which its outer edge projects beyond the organ of Corti and the course and arrangement of its fibers. *Pc*, peripheral condensation interpreted as produced by the shrinkage action of the reagents; *Vs.*, vas spirale, here a plexus instead of a single vessel; *Ss.*, spiral sulcus.

Fig. 7.—Vertical section from third half-turn of same cochlea as Fig. 6. with the organ of Corti represented entire and showing the character of the epithelium of the spiral sulcus (*Ss.*) and an appearance on the under

surface of the outer zone of the tectorial membrane, *Ac.*, which is interpreted as representing the much shrunken accessory membrane in section. *Pč.*, below, shows what seems in the section to be a strip of the peripheral condensation torn off in the manipulation and adhering to the inner supporting cells of the organ of Corti. *E.*, endothelium lining scala tympani, *St.; Vs.*, vas (plexus) spirale. The curved shape of the section of the tectorial membrane is due to shrinkage.

Fig. 8.—Vertical section from seventh half-turn of same cochlea as Fig. 7. The curve in the upper surface of the outer zone of the tectorial membrane is explained as due to shrinkage produced by the techique as well as the fact that the membrane does not appear to extend entirely over the organ of Corti. From the size of the tectorial membrane, as compared with Figs. 6 and 7, it is assumed that the section passes some distance from the basal end. Lettering same as in Figs. 6 and 7.

Fig. 9.—Horizontal section of tectorial membrane at region of second turn of coil, showing appearance and arrangement of fibers as cut transversely, obliquely and longitudinally. Irregularities of course of fibers explained as due largely to collapsed condition produced by reagents. *a.*, region of transversely cut fibers; *b.*, longitudinally cut fibers; *Ep.*, "Epithelial cells" inserted between the white fibrous tissue bundles; *Ht.* (Huschke's teeth) of the labium vestibulare.

Fig. 10.—Vertical section from the third half-turn of a cochlea from a fœtal pig of 14 centimeters, showing a stage in the development of the tectorial membrane just before the beginning, along the inner edge, of the retrogressive changes of the greater epithelial thickening, *Get. Let.*, lesser epithelial thickening, enlarging to form organ of Corti; *Mt.*, tectorial membrane; *Ss.*, cells in region of what will become spiral sulcus; other lettering same as in Figs. 6 and 7.

Fig. 11.—From thin horizontal section of basilar membrane, stained by Mallory's method for white fibrous tissue, showing the structure to be composed of bundles of white fibers, *Fb.*, connected with each other by numerous fibers less compactly arranged. *Ls.*, side toward spiral ligament; *Lt*, side toward labium tympanicum of spiral limbus; *Fn.*, foramina nervosa in habenula perforata.

Fig. 12.—Portion of a line of the outer rods of Corti, adhering together and showing grouping as appeared in teased specimen from second turn of cochlea. *a.*, phalanges assumed to be less resistant to downward pressure than those designated by *b.; f.*, fibrous portion of curved foot of rod which rests over basilar membrane; *Ir.*, fragments of inner rods left in their separation from the outer; *P.*, granular protoplasm between rods and probably continuous with that forming the foot cells.

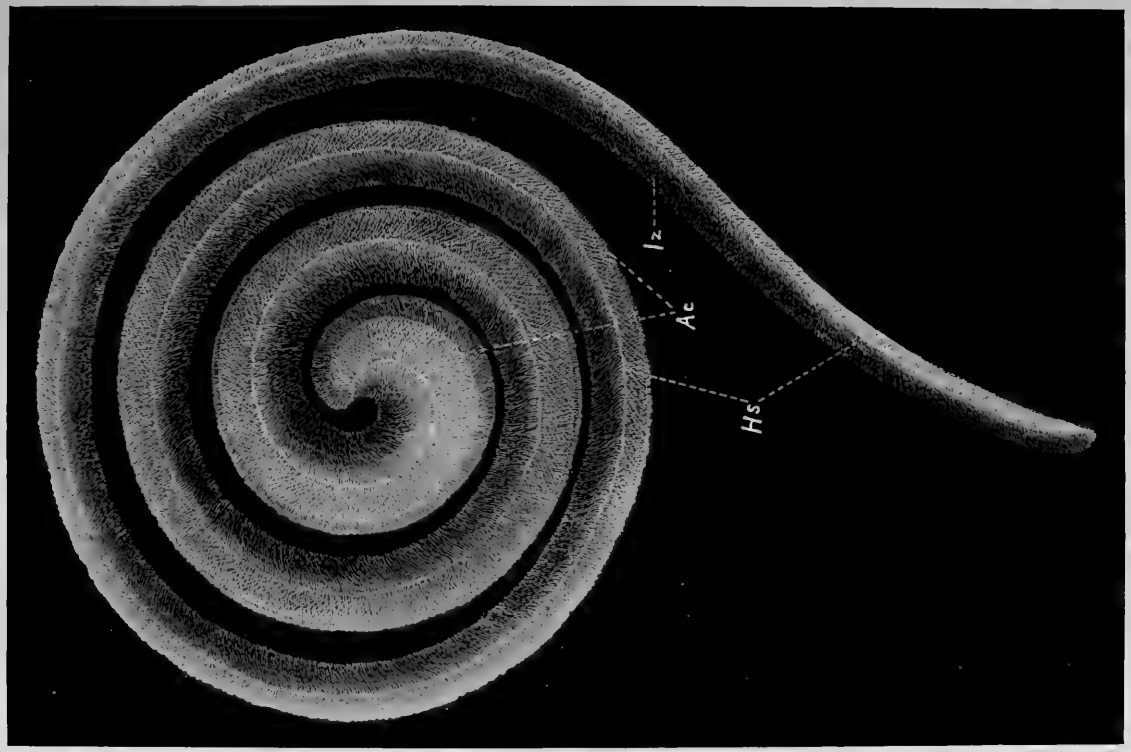

FIG. 1

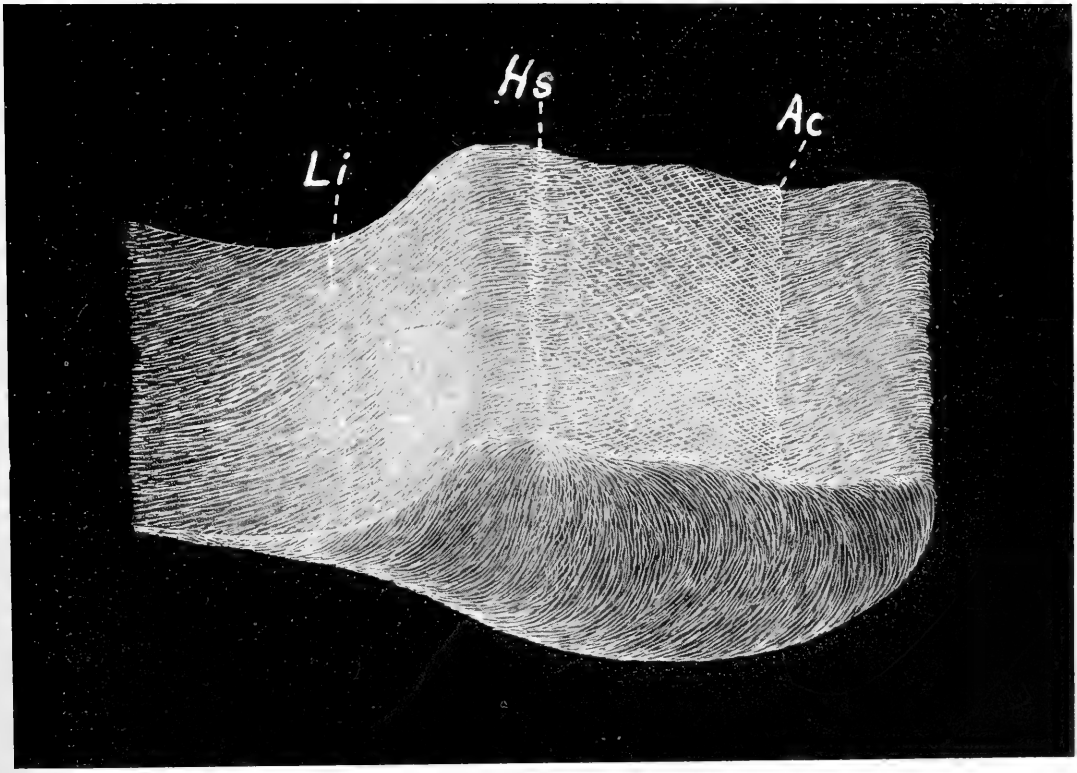

FIG. 2

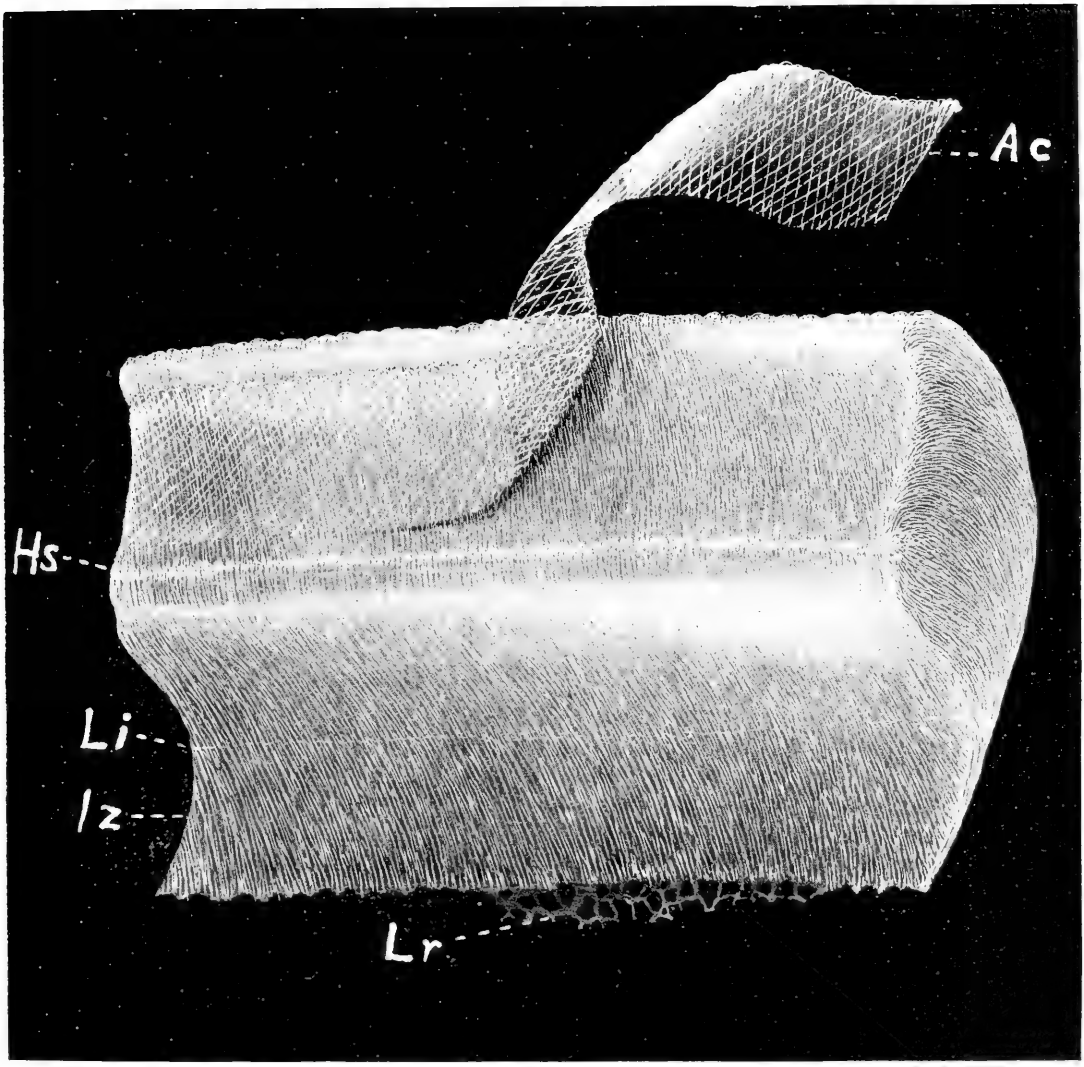

FIG. 3

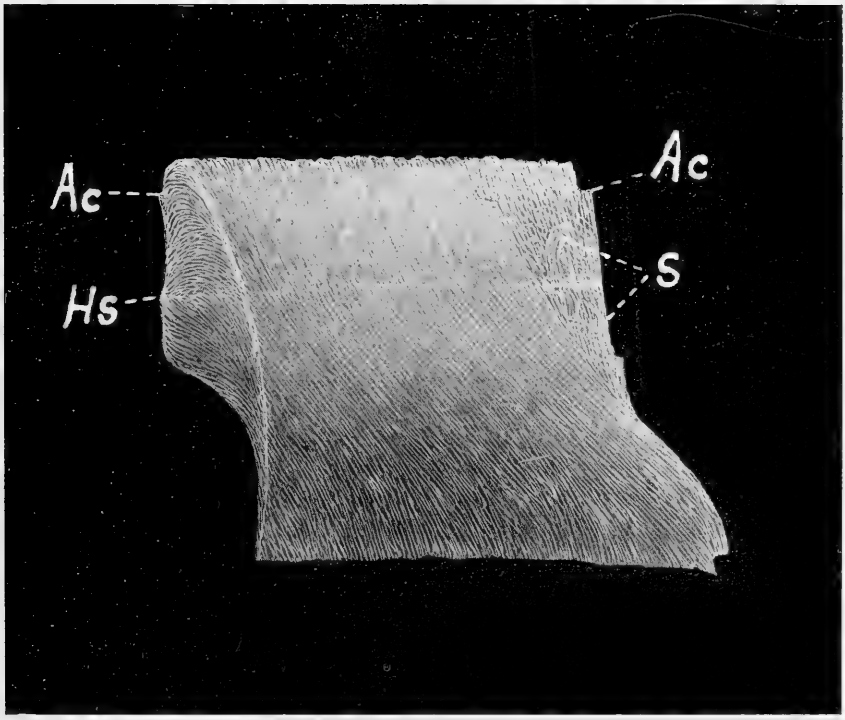

FIG. 4

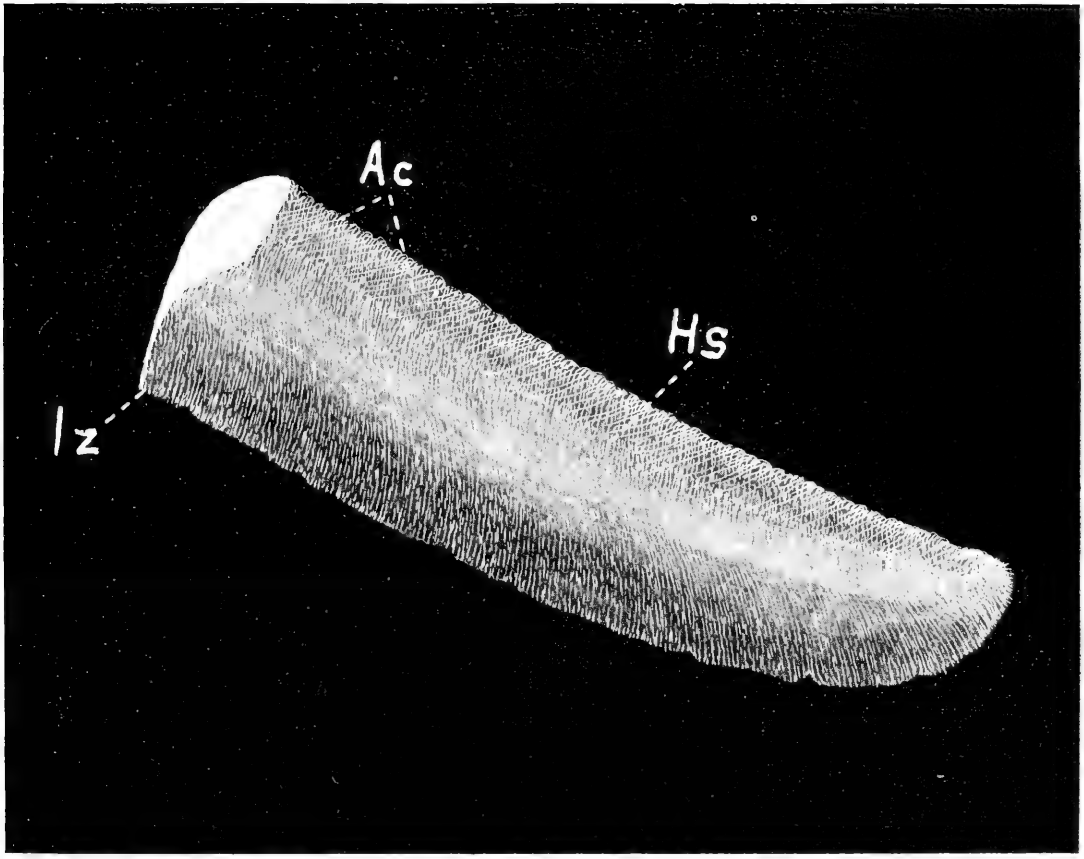

FIG. 5

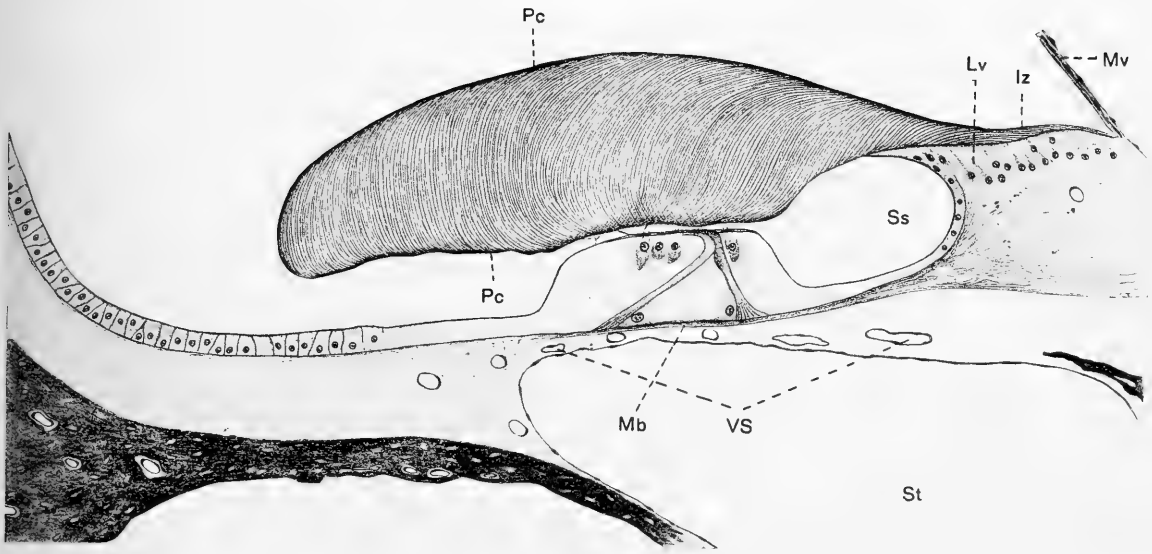

FIG. 6

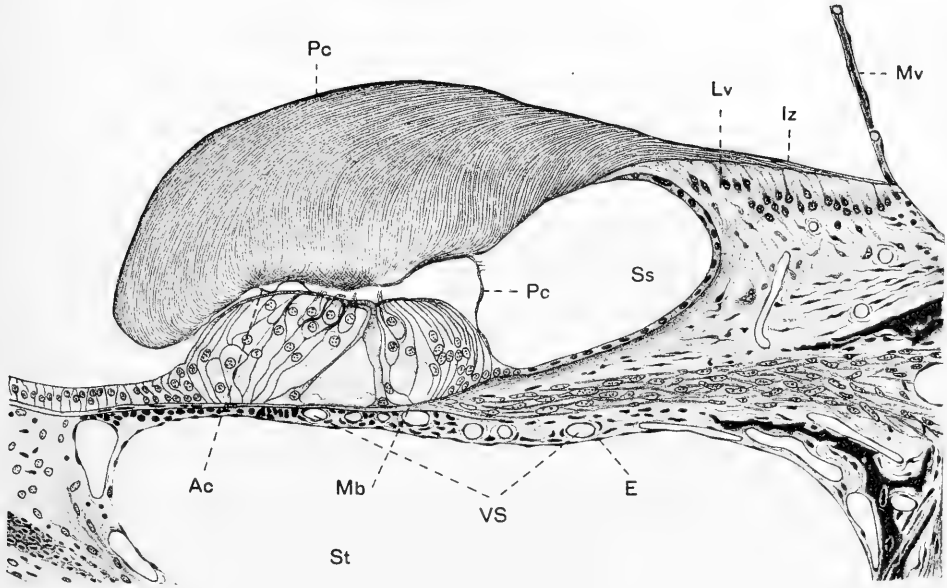

FIG. 7

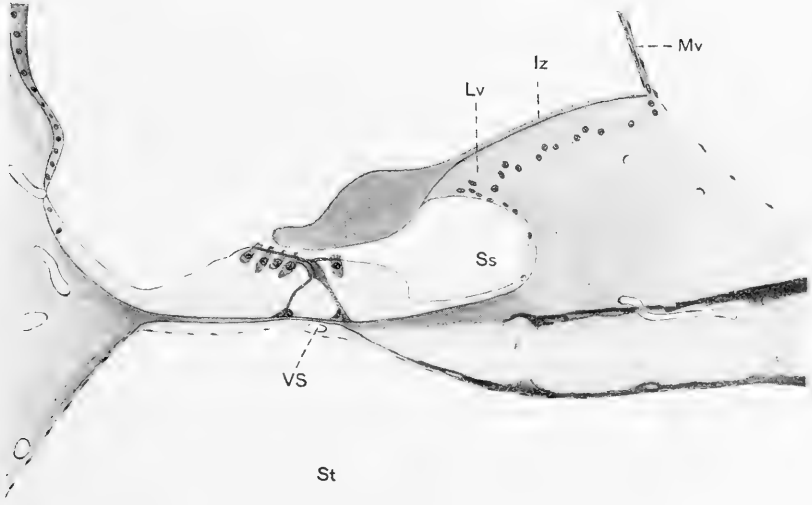

FIG. 8

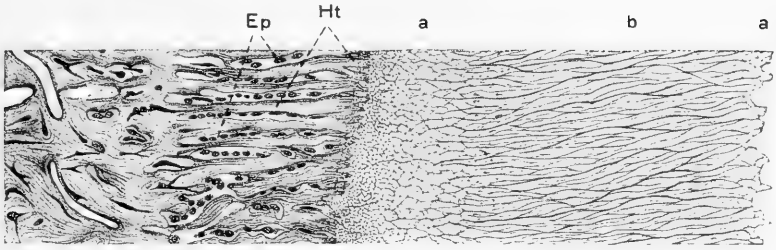

FIG. 9

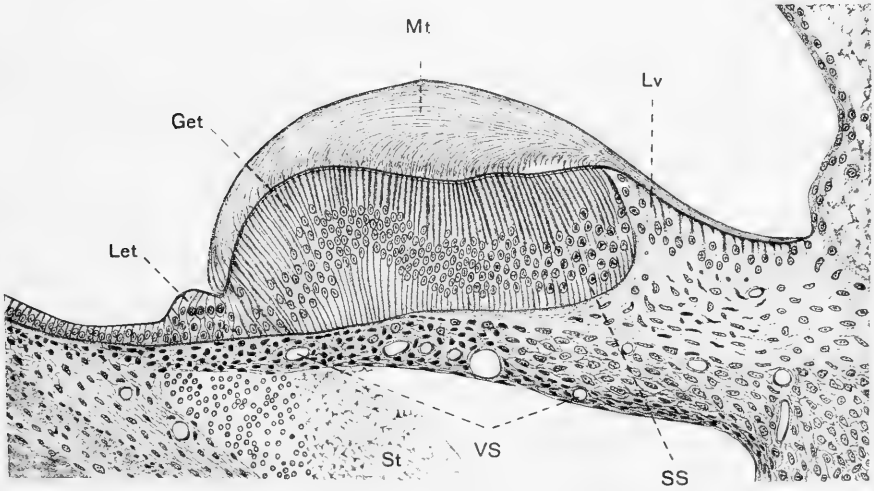

FIG. 10

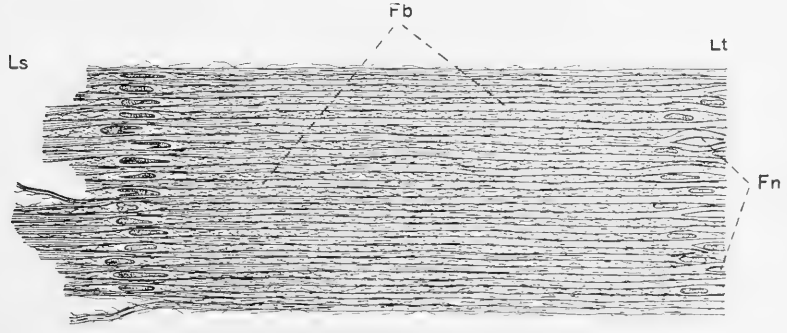

FIG. 11

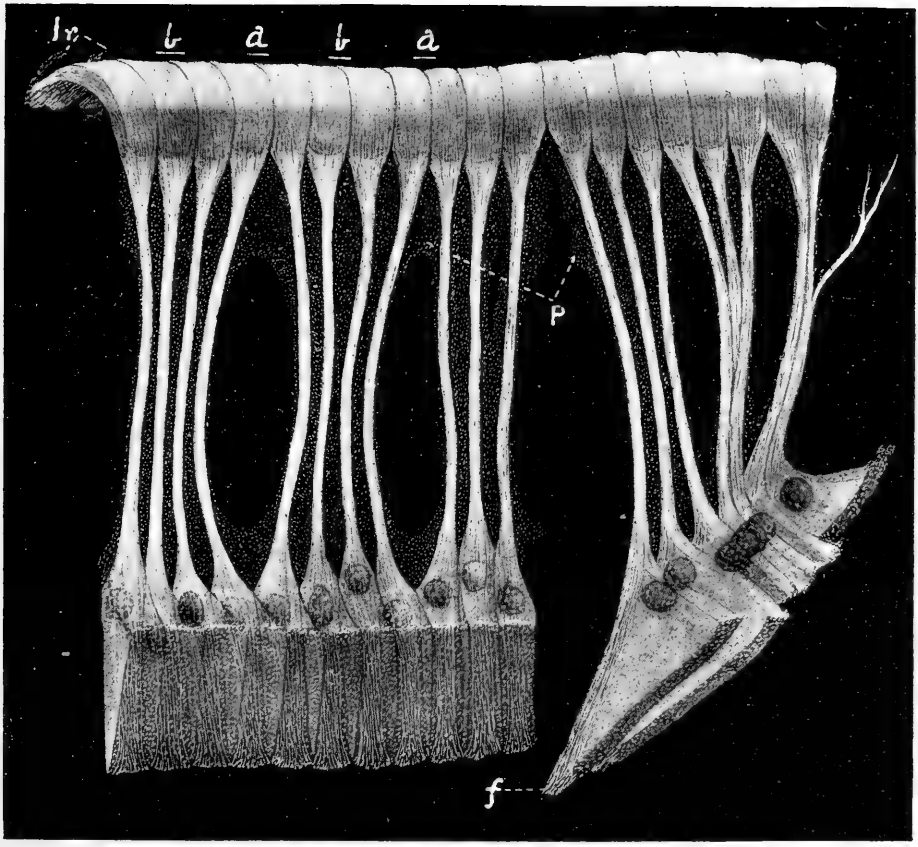

FIG. 12

EARLY DEVELOPMENT OF THE CERVICAL VERTEBRAE AND THE BASE OF THE OCCIPITAL BONE IN MAN.[1]

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University of Wisconsin.

WITH 3 FIGURES.

During the earlier stages of development the cervical vertebræ resemble those of the thoracic region. The two regions soon become differentiated from one another by the much greater development of the costal processes of the thoracic region. The seventh cervical vertebra alone, as a rule, has a large costal process, and this does not extend far beyond the transverse process of the neural arch (Fig. 1). In the cervical, as in the thoracic vertebræ, the development of a region of loose tissue in the base of the primitive ventral process serves to separate the costal element from the transverse process. In this loose tissue an anastomosing artery extends from the intersegmental artery on the posterior to that on the anterior side. The anastomosing artery between the costal element and transverse process of the seventh cervical vertebra remains small, but the more anterior anastomosing arteries give rise to a large continuous vessel, the vertebral artery, which extends anteriorly between the costal processes and transverse processes of the root of the vertebral artery.

In the costal processes of the seventh cervical vertebra centers of chondrification are found at the period when similar centers appear in the ribs. Centers of chondrification in the costal processes of the rest of the cervical vertebræ appear much later, usually not until the embryo has reached the length of from 16-18 mm.

As in the thoracic vertebræ, there are two bilaterally placed centers

[1]The early development of the thoracic, sacral and coccygeal vertebræ has previously been described in THE AMERICAN JOURNAL OF ANATOMY, Vol. IV, 1905.

of chondrification for each of the vertebral bodies. These soon fuse with one another ventral and dorsal to the chorda dorsalis. In the first two vertebræ the ventral fusion takes place before the dorsal fusion.

There are separate centers of chondrification for the neural arches. In the more distal cervical vertebræ these centers are similar to those of the thoracic vertebræ. In the more proximal cervical vertebræ the centers of chondrification appear as basal plates lateral to the anterior end of the bodies of the vertebræ. With these they soon fuse. From the plate-like base chondrification extends rapidly into the main part of the arch. From the neural arches, laminar, articular and transverse processes are developed. The costal elements have separate centers of chondrification which soon fuse proximally with the bodies of the vertebræ and distally with the tips of the transverse processes of the vertebræ. The dorsal growth of the laminar processes and the formation of the spinous processes of the cervical vertebræ take place in the main like that of the thoracic. When fully formed, however, the cartilaginous cervical vertebræ have essentially the shape of the adult osseous cervical vertebræ. Even before the end of the second month of development distinct cervical characters may be distinguished (Figs. 1 and 2).

Some investigators hold that the neural arches of the mammalian vertebræ contain elements of both the ventral and dorsal arches found in the lower vertebrates (see Schauinsland, Hertwig's Handbuch, 1902). There are theoretical grounds for believing that the ribs primitively belong to the ventral arches. In the higher mammals and man, however, the presence of the ventral arch elements is manifest merely in the caudal region, where temporary hæmal processes are developed, and in the upper cervical region, where, in the membranous stage, there are differentiated from the ventral margins of the primitive discs bands of tissue which connect the bases of the neural processes. These bands of tissue have been called by Froriep the hypochordal braces (Spangen). In reptiles and birds the hypochordal brace becomes converted into cartilage and connects the cartilaginous arches of each side with one another. It finally becomes fused with the ventral portion of the proximal end of the vertebral body. In the primitive type of development the chondrification takes place from two bilaterally placed centers, each of which, according to Schauinsland, represents a ventral hemiarch. In other instances chondrification takes place from a single center situated in the median line. According to Froriep, in the cow a

median center of chondrification appears in all the hypochordal braces, but, except in the first two vertebræ, the brace disappears before cartilage is actually formed. In the hypochordal brace of the second

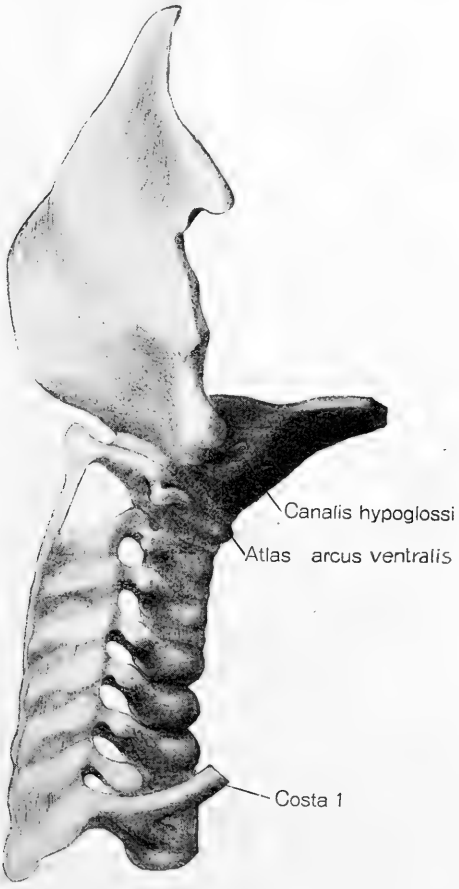

Fig. 1.—Lateral view of a model of the occipital cartilage, the cervical vertebræ, the first thoracic vertebra and the proximal end of the first rib in an embryo 20 mm. long. The costal elements of the cervical vertebræ are cartilaginous and are connected by ligamentous tissue with the transverse processes of the neural arches and with the vertebral bodies. The intervertebral discs are shown except between the fourth and fifth, and the fifth and sixth vertebræ. Dense interarticular tissue is shown between the articular processes from the second cervical to the first thoracic vertebra and, posterior to this, interlaminar connective tissue membranes and a ligamentous band running from the neural process of the atlas to the thoracic region.

vertebra the cartilaginous anlage is very transitory, in the first vertebræ it forms the anterior portion of the arch of the atlas. Weiss describes two bilaterally placed centers of chondrification in the hypochordal brace of the atlas in the white rat. No cartilage is found in the more distal hypochordal braces. In man a hypochordal brace becomes well

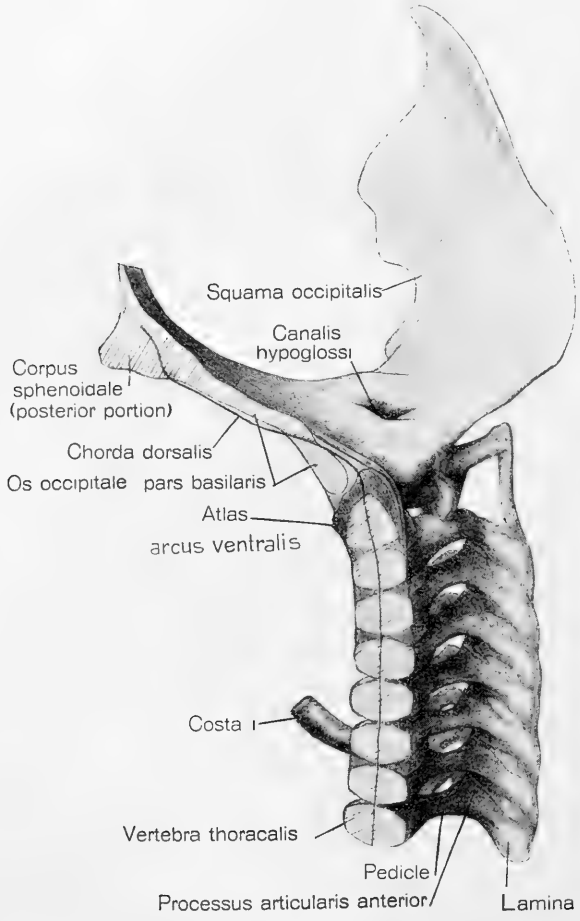

Fig. 2.—Postero-medial view of the model represented in Fig. 1. The anterior extremity of the base of the occipital and the posterior part of the body of the sphenoid are also shown. Between the posterior part of the base of the occipital and the epistropheus the intervening dense tissue has in part been removed so as to reveal the ventral arch of the atlas. The intervertebral discs are omitted between the fourth and fifth, fifth and sixth cervical, and between the seventh cervical and first thoracic vertebræ.

developed merely in connection with the atlas. It becomes cartilaginous later than the neural arch. There are indications of two bilaterally placed centers of chondrification, but fusion with one another and with the neural arches takes place as soon as chondrification is well under way.

Specific mention must be made of the mode of development of the epistropheus, of the atlas, and, in connection with the latter, of the base of the occipital.

Epistropheus.—The general mode of development of the epistropheus is like that of the other cervical vertebræ. Its marked distinction comes from its union with the body of the first cervical vertebra. This union

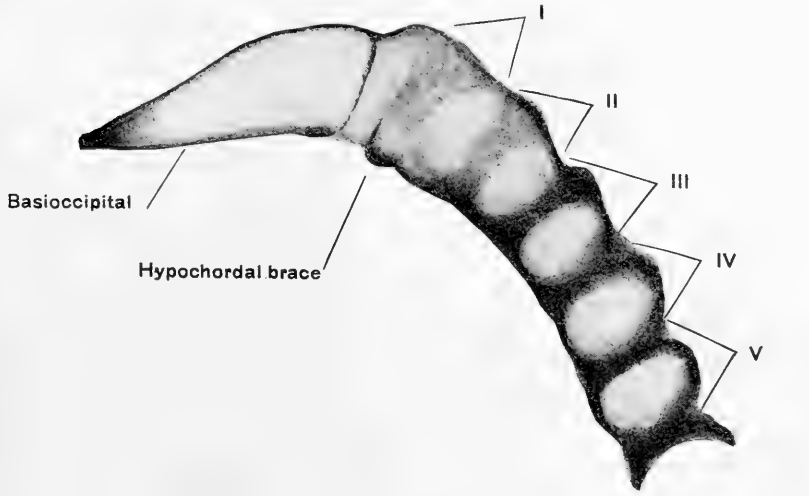

Fig. 3.—Sagittal section through the lateral part of the cervical region of the spinal column of an embryo 14 mm. long.

takes place through the transformation of the intervertebral disc into cartilage, first lateral to the mid-sagittal plane and later in this plane.

Atlas.—The base of each neural hemi-arch of the atlas becomes temporarily fused with the body (14 mm. embryo), but this fusion is incomplete and soon is followed by the development of dense fibrous tissue between the arch and the body (Fig. 2). At the same time the hypochordal brace becomes cartilaginous and unites the arches of the atlas in front of the body. Each costal process becomes fused medially to the basal process, laterally to the transverse process of the corresponding hemi-arch.

The articulation between the lateral mass of the atlas and the superior articular surface of the epistropheus seems to be formed rather in the interventral than, as in the other intervertebral diathroses, in the interdorsal membranes. This is also true of the atlanto-occipital diathrosis. For a brief period (14 mm. embryo) the bases of the neural arches of the atlas and epistropheus, together with the tissue intervening between the bases of arches of the atlas and the occipital, become fused into a nearly continuous mass of precartilage (Fig. 3).

Hagen, His' Archiv, 1900, gives a somewhat different account of the development of the atlas and epistropheus in man. He concludes (1) that the dens epistrophei arises from the region of the body of the epistropheus and a portion of the body of the atlas; (2) that the massæ lat. of the definite atlas arise from the rest of the primary anlage of the body of the atlas, and (3) that the short piece which unites them in front arises from the fusion of both neighboring septa.

Basi-occipital.—Opposite the last occipital myotome the axial mesenchyme is differentiated, like that of the spinal sclerotomes, into a light anterior half and a dense posterior half or scleromere. In the spinal region each scleromere joins with the light half of the sclerotome next posterior in giving rise to the body and arch processes of a spinal vertebra. In man the occipital scleromere is not thus associated with the light half of the first spinal sclerotome. On the contrary, it becomes associated with the lighter tissue of its own segment and with the tissue into which this is continued anteriorly. Laterally the tissue differentiated at the side of the anterior half of the first spinal sclerotome, the interventral membrane, becomes temporarily converted into a precartilaginous membrane (Fig. 3).

Chondrification of the base of the occipital begins in two bilaterally situated centers in the posterior portion of the occipital anlage. The union of these centers takes place posteriorly ventral to the notochord and anteriorly dorsal to the notochord (Fig. 2). The neural processes of the posterior part of the occipital anlage seems to have separate centers of chondrification, but these centers fuse almost immediately with the centers of chondrification of the body.

From the tissue derived from the first and second sclerotomes and not utilized in the formation of the atlas and the epistropheus are derived the various ligaments which unite these bones. The details of the formation of these ligaments are too complex for description here.

THE PHARYNGEAL POUCHES AND THEIR DERIVATIVES IN THE MAMMALIA.

BY

HENRY FOX, PH.D.

WITH 73 FIGURES.

The present paper is an outgrowth of an earlier unpublished article submitted to the Faculty of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Ph.D. The original article gave the results of a study of six or seven different stages in the development of the pig. Subsequently, through the kindness of Dr. C. S. Minot, I was enabled to study the extensive series of mammalian embryos in the collection of the Harvard Medical School. Of these I studied most thoroughly the series of pigs and cats, but also gave some attention to the later stages in the rabbit. The results of this additional study, along with those included in my former article, I now offer in the present paper.

My aim is to give a complete history of the pharnygeal pouches and their derivatives as typically exemplified in the mammalia. The main facts of this history had been largely determined previous to my starting the investigation, but the interpretations attached to these facts by various authors differed considerably, and, moreover, there remained a number of details about which there was much confusion. These unsettled matters seemed to me to warrant a full investigation of the subject.

Soon after I had begun my observations an important article by Hammar appeared treating of the development of the fore-gut in man. Hammar had in his possession a large series of embryos, and from these he made out a full and consistent history of the middle ear and Eustachian tube. He also compared with his own results the statements made by earlier authors, and, through the more abundant material at his command, was enabled to show how their conclusions were in most cases the result of mistaken interpretation based on an insufficient body of facts.

While primarily concerned with the development of the pharynx in man, Hammar also examined a series of rabbit embryos, and while he does not in his article treat of them particularly, he yet mentions that he finds an essential agreement in the formation of homologous parts in both forms. Accordingly, he is inclined to assume that the essential features of the development in man will hold good in the case of other mammals.

Hammar's first article was followed by a second on the fate of the second pharyngeal pouch. This is the last article of his I have seen, and, so far as I know, he has not published any articles on the fate of the last two pouches.

The appearance of Hammar's paper seemed to me at first to do away with the necessity of further study of the first two pairs of pouches, but as Gaupp had already expressed the idea—based upon the conflicting statements of earlier investigators—that the formation of these parts probably differed considerably in different species of mammals, I concluded that a further contribution on the subject in the three species examined by me would not be without value. Moreover, as Kastschenko, the chief authority on the process in the pig, had declared that the middle ear tube did not arise in any way from the first pharyngeal pouch, I considered this an additional reason for continuing my investigation.

The results of this investigation, so far as the first and second pharyngeal pouches are concerned, are largely confirmatory of the conclusions reached by Hammar in man and the rabbit. The probability therefore is that the development of these parts is essentially similar in the majority of placental mammalia.

In the case of the third and fourth pharyngeal pouches I have obtained results which clear up certain details about which there has been much conflict of opinion. Among these may be mentioned the determination of the origin and structure of the carotid gland, a reconciliation of the conflicting statements regarding this structure made by Kastschenko and Prenant, a confirmation of the ectodermal origin of the so-called thymus superficialis of Kastschenko, and finally the origin of a second structure—beyond doubt the glandule thyroidienne of Prenant—from the fourth pouch.

My earlier studies were made by the aid of the wax reconstruction method. Later, owing to the lack of facilities for continuing the use of this method, I adopted the method of graphic projection, making dorsal, ventral and lateral views of each stage studied.

During the progress of this investigation I received much assistance from a number of investigators. To Dr. E. G. Conklin I am greatly indebted for his kind encouragement and helpful suggestions, and for these I desire to express my hearty thanks. To Dr. C. S. Minot I am under special obligations for his kindness in allowing me to examine the fine series of embryos in his charge. I also desire to thank Dr. C. B. Davenport for permission to continue part of this work in the laboratory at Cold Spring Harbor, Long Island.

I shall present the results of my studies under the following headings:

I. The Formation and Structure of the Pharnygeal Pouches.

II. The Later Modifications and Fate of the Pharnygeal Pouches.

In this study I was enabled to examine the following stages, which I here present in the order of progressive development:

Pig.	Cat.	Rabbit.
(3) 6.5 mm., (M^2)	(1) 4.6 mm., No. 398	(13) 14 days, 10.0 mm., No. 157
(6) 9.0 mm., (M^5)	(2) " 413	(19) 16½ " 17.8 mm., " 576
(7) 10.0 mm., No. 401	(4) 6.2 mm., " 380	(20) 18 "
(8) 12.0 mm., " 518	(5) 9.7 mm., " 446	(25) 20 " 29.0 mm., " 172
(9) 13.5 mm., (M^1)	(14) 10.7 mm., " 474	(26) 21 "
(10) 14.0 mm., No. 65	(16) 15.0 mm., " 436	
(11) 17.0 mm., " 51	(21) 23.0 mm., " 466	
(12) 18.0 mm., (M^3)	(24) 31.0 mm., " 500	
(15) 20.0 mm., No. 542		
(17) 24.0 mm., " 64		
(18) 25.0 mm., (M^4)		
(22) 32.0 mm., No. 74		
(23) 35.0 mm., (M)		

I. The Formation and Structure of the Pharyngeal Pouches.

Under this heading I shall describe all stages leading up to the complete formation of the four pairs of pharyngeal pouches characteristic of the mammalian embryo. The stages here considered include Nos. 1 to 4, inclusive.

The earliest stage of development of the pharynx and its appendages was shown in a cat embryo of 4.6 mm., No. 398 of the Harvard collection (Figs. 55 and 56.) The embryo is approximately straight, the headfold is distinctly differentiated, but the posterior two-thirds of the enteric cavity opens widely into the yolk vesicle (at x in the figures). The neural tube is closed except anteriorly, where a narrow cleft still persists. The optic vesicles are present, but there is no sign of the optic cups.

The pharynx anteriorly is in contact with the stomatodeal plate (St.). As a whole it is a relatively wide, dorso-ventrally flattened sac. Only two pairs of pharyngeal pouches are present as wide lateral diverticula of the pharynx. Of these the first (Ph. P. I) alone reaches the ectoderm and joins with it for a short distance. The second pair (Ph. P. 2) are only barely indicated as faint outbulgings, the one on the left being the more distinct of the two.

The pericardium is of small size, in striking contrast to the enormous bulk it attains in later stages. It contains the inner portions of the great vitelline veins (v. v.), which are joined together only at their extreme anterior ends. Only one pair of fully developed aortic arches is present—the first or mandibular (ao. i). These extend dorsally in front of the first pouch and join the paired dorsal aortæ. Two prominent out-bulgings from the sides of the vitelline veins are probably destined to form the common trunk from which the remaining aortic arches subsequently arise.

A cat embryo, No. 413 of the Harvard collection, shows the next stage in advance (Fig. 57). The posterior part of the body is still approximately straight, but the head portion is strongly flexed upon it and is of relatively much greater extent than before.

Anteriorly the stomatodeal plate has disappeared. The pharynx is, as before, a wide flattened sac, but its width in its anterior portion is somewhat greater than in its posterior part. Its floor is somewhat deeper than before and close to the mouth is produced into a deep median groove— the median oral groove (M. GR.).

The hypophysis (HYP) appears as a blunt protuberance from the dorsal side of the pharynx close to its anterior extremity. Three pairs of pharyngeal pouches are now present. The first two pairs reach the ectoderm and join with it for a considerable extent (see light areas of Ph. P. 1 and 2, Fig. 57). Of the third pair, the pouch on the right side reaches the octoderm, while that on the left is still removed by a slight interval from it.

The first pharyngeal pouch forms a relatively large transverse fold. The greater part of its lateral margin is in contact with the ectoderm. The area of contact is widest dorsally and diminishes progressively in width toward the ventral side. The extreme ventral part of this margin extends a slight distance below the region of contact as a free edge, which then turns suddenly inwards as the ventral margin of the pouch. This part of the pouch projects slightly below the floor of the pharynx and thus forms a ventral diverticulum of the pouch.

The second pharyngeal pouch, although considerably smaller than the first, is essentially similar to it. It has a ventral diverticulum, which is somewhat less prominent than the same part in the first pouch.

The third pharyngeal pouch is considerably smaller than its two predecessors. It forms a finger-like outgrowth, which extends outwards and downwards and, in the case of that on the right side, joins the ectoderm. The left pouch does not quite reach the latter.

The fourth pharyngeal pouch is only barely indicated by a slight bulging of the walls of the pharynx behind the base of the third pouch.

The first three pairs of aortic arches are now fully developed and a fourth is beginning to develop.

In a pig embryo of 6.5 mm. (M^2 of my collection) and a cat of 6.2 mm. (No. 380, Harvard collection) all the pharyngeal pouches and their associated parts are typically developed. The two embryos show almost the same relative stage of development, but that of the pig shows a slightly more primitive condition. It will, accordingly, be considered first.

The pharynx (Figs. 1, 2 and 3) shows four complete pairs of pharyngeal pouches, all of which have a more or less extensive contact with the ectoderm of the corresponding grooves. Between the first two pairs of pouches the pharynx is considerably wider than in the region between the last two pairs. Anteriorly the hypophysis (HYP.) projects forward as a blunt protuberance, and immediately back of it arises a minute conical process, the representative of Seessel's pocket.

The pharyngeal pouches in general have the form of vertical wing-like expansions projecting outwards and slightly backwards from the side walls of the pharynx. Typically, they are joined to the pharynx by a relatively narrow base and only laterally dilate into the wing-like expansions mentioned. Each pouch is attached laterally to the ectoderm. The extent of this attachment is shown by the clear areas in Fig. 1. As these show, it varies greatly, being most extensive in the second, where it includes almost the entire lateral margin. A similar relation is noted by Hammar in the corresponding stage in man, and, as the figures of the next stage show (see Fig. 58), it holds in the cat.

A conspicuous feature—shown best in the second and third pouches—is the presence of deep ventral projections to the pouches (V.D. 1-4). They reach to a greater or less extent below the floor of the pharynx. Hammar calls them the ventral diverticula. They appear, from all published figures examined, to be constant at the corresponding stage in all mammals so far investigated.

A ventral view (Fig. 3) shows a number of important features. Projecting from each side of the pharynx are the four pharyngeal pouches, each with its ventral diverticulum. That of the first pouch (V. D. 1) forms a low narrow ridge extending from the infero-lateral angle of the pouch inwards and slightly backwards quite to the median line, where it joins the corresponding ridge of the opposite side. There is thus formed a complete transverse V-shaped fold, the apex of the fold being the meeting point of the two opposite limbs. The ridge corresponding to the median oral groove begins immediately in front of this apex. The shallow impression between corresponds to the tuberculum impar of His. Just behind the apex is the median thyroid. The latter consists of two lobules joined to each other and to the pharynx by a slender epithelioid cord.

The ventral diverticula of the next two pouches are much deeper than that of the first, but are largely confined to the lateral half of the pharynx. A faint ridge, however, extends from the base of the second diverticulum to the median line, where it is joined by a similar ridge from the third pouch (see Fig. 60 of the next series for this condition). The two sets of ridges thus converge to form a rather low protuberance immediately above the thyroid and in front of the tracheal ridge.

The presence of these inner low ridges connecting the opposite ventral diverticula of the second and third pouches shows their essential agreement in this respect with the first pouch. Only, in the case of the two former, the lateral half of each ridge is produced far below the level of the inner portion, while in the first pouch the depth (its height) of the ridge is throughout approximately uniform.

Owing to the form of the ventral diverticula of the second and third pouches there is left between their opposite lateral halves a considerable space, in which is lodged the apical portion of the heart along with the large arteries radiating from it (Fig. 3). The prominent aortic arches at this time are the third (carotid), fourth (aorta typica) and the fifth (pulmonary). The latter has a small posteriorly directed branch—the later pulmonary artery (Fig. 3, Pul.), The first aortic arch is much reduced in size and has lost all connection with the dorsal aorta. The second is also extremely reduced and is only connected with the dorsal aorta by an extremely narrow (apparently functionless) vessel.

Immediately back of the common origin of the aortic arches begins a sharp median ridge, which deepens posteriorly. It represents the future larynx and trachea.

The first pharyngeal pouch has a greater lateral extent than any of the succeeding. As the figures show, the lateral extension of the pouches decreases regularly from before backwards. The first pouch blends with the lateral portion of the pharynx by a broad base, so that it is impossible to draw any definite line between the two. The limits assigned by Hammar, whose usage in this matter I adopt, will be given presently. Laterally the outer extremity of the pouch is produced upwards as a blunt prominence—the dorsal diverticulum of Hammar—which projects considerably above the roof of the pharynx. The dorsal diverticulum terminates in a narrow apex—the dorsal apex (d. a. 1) (Recessus tympani anterior, Hammar).

Hammar includes in the first pouch the following parts: (1) The sulcus tubo-tympanicum. This is Moldenhauer's term for the prominent ridge (Fig. 2, S. T. T.) representing the antero-lateral border of the pouch. It begins externally at the dorsal apex and extends downwards, inwards and forwards, terminating close to the base of the hypophysis. (2) The latero-ventral ridge and its continuation, the ventral diverticulum. This is a narrow ridge which in its dorso-lateral portion is joined to the ectoderm. The connection includes the dorsal two-thirds of its lateral extent. The lower third forms a free edge, and this, at its lower outer angle, turns sharply inwards and backwards to form the ventral diverticulum. (3) The sulcus tensoris tympani (S. T. Ty.). This is a term applied by Hammar to the border extending from the dorsal apex backwards and inwards to join the next part along the inner border of the hyoid arch. (4) The sulcus tympanicus posterior (S. T. P.). This term, also given by Hammar, includes the longitudinal ridge forming the inner boundary of the hyoid arch and connecting the sulcus tensoris tympani with the base of the second pouch. (5) The impressio cochlearis. This Hammar defines as a conspicuous depression on the dorsal wall of the pouch close to its origin from the pharynx. The auditory sac lies immediately above this area.

The second pharyngeal pouch is characterized, as already mentioned, by the extensive contact of its lateral margin with the ectoderm. Only at its extreme lower end does this border have a free margin. So far as the present specimen is concerned, there is no communication between the lumen of the pouch and the exterior. The closing membrane is exceedingly thin, but examination shows no break in its continuity.

The ventral diverticulum of this pouch forms a prominent quadrangular fold. The mesial half forms only a faint ridge, but the lateral

portion is very deep. The deepest part is represented by the blunt angle immediately below the lower end of the lateral border.

Posterior to the region of the second pouch the pharynx diminishes considerably in width. Its lateral margin forms a low ridge connecting the second pouch with the third. Between this ridge and the median dorsal ridge of the pharynx is a shallow longitudinal furrow, in which is lodged the dorsal aorta.

The third pharyngeal pouch is slightly smaller than the second. It is joined by a relatively narrow base with the pharynx, but distally expands into a broad wing-like fold with a prominent ventral diverticulum. A slight dorsal diverticulum is also present. The lateral margin is in contact with the ectoderm for almost its entire length.

As in the case of the second pouch, the deep portion of the ventral diverticulum is limited to the lateral half of the pharynx. Its mesial portion is represented by a low ridge, which extends from the root of the lateral half forwards and inwards close to the median line, where it joins with the same part of the second pouch. The extreme ventral tip of the ventral diverticulum is turned toward the mesial side.

The fourth pharyngeal pouch is the smallest of the series. It is divided by a shallow constriction into two parts, a dorso-posterior portion (Ph. P. IV), which projects laterally and at one point comes into contact with the ectoderm, and a ventro-anterior bulge, which terminates blindly and corresponds to a ventral diverticulum.

From the base of the ventral diverticulum a low ridge extends forwards to the base of the third pouch. It corresponds to the mesial extension of the ventral diverticulum.

In the cat embryo of 6.22 mm. (No. 480, Harvard collection) the condition of the pharynx is essentially similar to that just described in the pig. As in the latter, four pairs of pharyngeal pouches are present.

The characteristic features of this stage are shown in Figs. 58, 59 and 60. Fig. 58 shows the lateral aspect. The clear areas on the lateral margins of the pouches show the extent to which these are attached to the ectoderm. It will be noticed that they are essentially similar to the same parts in the preceding specimen. The dorsal diverticulum of the first pouch is somewhat more elevated. The ventral diverticulum of the third pouch extends to a slightly lower level. The fourth pouch shows more clearly its division into two portions. The dorso-posterior portion is somewhat bulbous. Its more dorsal part is

flattened and is produced outwards as a thin process which reaches the ectoderm. The ventral diverticulum projects almost directly forwards.

The median thyroid is of a relatively large size. It has lost all connection with the pharynx and lies at a lower level than in the preceding specimen.

Owing to the more rapid growth of the mandibular and hyoid arches as compared with that of the arches posterior to them, the originally almost transverse plane of the second and third pouches becomes postero-lateral. Their originally anterior and posterior surfaces thus become antero-lateral and postero-internal, respectively. Their lateral margins thus come to project backwards.

The increased antero-posterior growth of the mandibular arch leads to a change in the direction of the tubo-tympanal border of the first pouch. The latter is at first almost transverse, but later assumes a more anterior direction. The more antero-mesial direction of this border in the present stage as compared with that in the preceding shows the beginning of the change. As growth continues the border progressively lengthens, thus giving an increased width to the basal portion of the pouch. These relations are clearly indicated in the dorsal view (Fig. 59).

Figs. 59 and 60 show the relations of the more posterior pouches to the now fully formed sinus præcervicalis—relations which are of considerable importance in view of later developments. Owing to the great increase in bulk of the hyoid arch the posterior border of the latter projects backwards. The third and fourth arches increase but slightly in bulk and thus remain at a considerably lower level than the arches in front. The sinus is thereby formed as a deep recess, the bottom being formed by the arches mentioned. Just within the anterior margin of the sinus opens the second pharyngeal groove. The third groove occupies the middle of the inner walls. Dorsally it meets the upper extremity of the fourth groove. From this point the latter turns strongly downwards, backwards and inwards to where it meets the fourth pouch. As the latter lies at a considerably lower level than the other pouches, this part of the sinus projects inwards as a prominent, pointed process.

The ventral view (Fig. 60) shows some additional features. On the right side the section is taken at a slightly lower level than on the opposite side, and accordingly it shows the entire exterior of the first two arches, together with the ventral extension of the first pharyngeal

groove. It also shows how the antero-internal angle of the sinus præcervicalis is continued ventrally into the ventral extension of the second groove. The latter has a decided anterior course, and at its mesial end meets the first groove.

On the left side the ventral wall of the sinus præcervicalis is represented as having been removed, so that its interior is clearly shown. The internal process of the sinus is less deep than the same part on the right.

The continuous transverse fold formed by the ventral diverticula of the first pouch is clearly shown in this view. As in the case of the pig, there is no contact between this fold and the corresponding ventral extension of the groove, the two being separated by a considerable thickness of mesenchyme.

II. The Later Modifications and Fate of the Pharyngeal Pouches.

Owing to the more or less independent course which the different pouches take in their later history, I think it will conduce to greater clearness if I consider them separately, and accordingly I subdivide the above topic as follows:

A. The Modifications of the First Pharyngeal Pouch.
  (a′) The Formation of the Primary Tympanic Pouch.
  (a″) The Differentiation of the Tympanic Cavity and Eustachian Tube.

B. The Modifications and Fate of the Second Pharyngeal Pouch.
  (b′) The Retrogressive Modifications of the Pouch.
  (b″) The Formation of the Tonsillar Fold.

C. The Metamorphoses of the Third Pharyngeal Pouch and its Derivatives.
  (c′) The Elongation of the Ventral Diverticulum and the Formation of the Thymus.
  (c″) The Origin and Structure of the Carotid Gland.
  (c‴) The Sinus Præcervicalis and its Relation to the Thymus.

D. The Fourth Pharyngeal Pouch and its Transformation into the Lateral Thyroid and Glandule Thyroidienne.

A. The Modifications of the First Pharyngeal Pouch.

(a′) The Formation of the Primary Tympanic Pouch.

The pharynx is essentially alike in a pig of 9 mm. (Series M^5, my collection) and in a cat of 9.7 mm. (No. 446, Harvard series). Fig. 61

gives a ventral view in the latter. The first pharyngeal pouch is wider in the antero-posterior direction than before—a change connected with the anterior growth and elongation of the oral cavity and the consequent prolongation in the same direction of the attached tubo-tympanal rim. The ventral diverticula are slightly less prominent. Together they form a low V-shaped elevation on the floor of the pharynx. Just external to the median apex formed by the convergence of the arms of the V each is joined by one of the pair of folds forming the outer line of the tuberculum impar (Tub.). Close to the lateral margin each arm is crossed by the broad alveolo-lingual fold (AL.F.). A slight distance in front the latter meets the vestibular fold (V.F.). Immediately back of the point of convergence a lateral fold (SM.F.). is given off, which extends obliquely outwards and backwards over the lateral ridge of the latter. The formation of this fold marks the initial step in the development of the later important submeckelian fold.

The tuberculum impar arises as a result of the bipartition of the median oral ridge. The crest of the latter widens and its middle part then becomes depressed to form a shallow concavity—the ventral counterpart of the tuberculum.

In the pig of 10 mm. (No. 401, Harvard series, Figs. 4-6) the pouch is joined to the ectoderm by only the dorsal third of its lateral ridge. The remainder of this border is now free and forms a low fold separating the antero-lateral and postero-lateral surfaces of the pouch. Ventrally it is continuous with the ventral diverticulum. Where the transition takes place the alveolo-lingual swelling cuts across it at right angles, forming here the line of demarcation between the pouch and the pharynx.

The ventral diverticula present no new points of interest. The swellings which marked the lateral boundaries of the tuberculum impar are now relatively inconspicuous, having been absorbed along with the adjacent parts of the pharyngeal floor in the broad depression (representing the anlage of the tongue) lying between the alveola-lingual ridges.

Dorsally the pouch projects relatively higher than hitherto and terminates in a more acute apex. This condition is not due to the growth dorsalwards of the pouch, but is a result of a ventral displacement of the pharynx. As a comparison of the figures shows, the formation of the neck of the animal is attended with a ventral (caudal) flexure of the posterior half of the pharynx. The flexure also affects to a minor

degree the remainder of the pharynx, tending to displace it to a lower level. This tendency, however, is checked by the fact that the first pair of pouches is still attached to the ectoderm by their lateral extremities. These points are accordingly relatively fixed in position, and, as the basal portion of the pouch sinks in response to the general lowering of the pharynx, the structure attains the pronounced ascending course characteristic of it at this stage.

In consequence of this change the basal portion of the pouch has assumed an almost horizontal plane, while its peripheral part ascends almost vertically. Where the two parts meet there is on the lateral surface a slight ridge extending from the lateral ridge to the base of the vestibular fold. It corresponds with the fold mentioned in the preceding stage as forming the beginning of the submeckelian fold (Fig. 6, S.M.F.).

This fold subdivides the antero-lateral wall into two surfaces, an external, dorso-lateral and a mesial ventro-lateral surface. The former forms an elongated triangular area limited dorsally by the tubo-tympanal crest and posteriorly by the lateral ridge. The latter forms a smaller triangle bounded internally by the alveolo-lingual fold and posteriorly by the lateral ridge.

The anterior prolongation of the tubo-tympanal ridge is more pronounced than in the preceding stage. The difference is due to a continuance of the process, already mentioned, of anterior elongation of the oral cavity.

A pig of 12 mm. (No. 518, Harvard series, Figs. 9-11) shows the pharynx only slightly larger than in the stage just described. The continued anterior elongation of the oral cavity has given the tubo-tympanal crest a decided antero-posterior course. The pouch retains its connection with the ectoderm only at its dorsal apex. The lateral ridge forms only a low prominence extending from the dorsal apex to the ventral diverticulum.

The dorsal apex appears broader and more depressed than in the preceding stage. This condition, I think, results from the lateral flexure of the apex in consequence of the general growth in width of the head.

At this stage the pouch has the essential features of the primary tympanic pouch of Kastschenko. This investigator considered the pouch as merely a widened diverticulum of the lateral wall of the pharynx and regarded the lateral ridge as alone representing the first pharyngeal

pouch. As Hammar shows and my observations confirm, Kastschenko's conception of the pouch was entirely too limited and was doubtless due to his not examining earlier stages in which it is more typically developed.

The primary tympanic pouch at this stage is a dorso-ventrally flattened triangular fold which arises by a broad base from the pharynx and terminates peripherally in the dorsal apex. The pouch as a whole lies almost horizontally, but towards the lateral edge it turns sharply upwards. Its walls are medio-dorsal and lateral. The former is limited laterally by the tubo-tympanal crest, dorsal apex and posterior tympanal borders. All below these limits is embraced in the lateral wall. This is divided by the lateral ridge into two surfaces, antero-lateral and latero-posterior. The antero-lateral surface is further subdivided into two areas—dorso-lateral and ventro-lateral—by the submeckelian fold.

The ventral diverticula now form a pair of low swellings. Mesially they are interrupted by a shallow longitudinal groove connecting the tongue concavity with the deep hollow in front of the larynx.

In a pig of 13.5 mm. (Series M[1] of my collection) the condition of the pouch is intermediate between that last described and the next. The only feature that calls for remark is the presence at the dorsal apex of a short narrow process by which the pouch retains its last connection with the ectoderm (Fig. 37).

In the pig of 14 mm. (No. 65, Harvard series, Figs. 14-16) the primary tympanic pouch has separated entirely from the ectoderm and now lies some distance below it—a condition due to the greater lateral growth of the head compared with that of the pouch.

The pharynx at this time begins to show modifications due to its own differential growth. The increase in width of the anterior half is considerably greater than in the posterior portion. Thus, while the distance between the apices of the first pair of pouches has increased appreciably since the last stage, that between the same parts in the second pair remains approximately the same. In consequence of this the pouch now shows a more pronounced lateral projection. The tensor-tympani crest turns sharply inwards and joins the posterior tympanal border at an obtuse angle. The latter border also shows a tendency to assume a more transverse trend. The second pouch appears as a rounded prominence at the postero-internal angle of the tympanic pouch.

The ventral half of the lateral ridge and its continuation, the ventral diverticulum, have disappeared. Their former position is only indis-

tinctly indicated by low swellings on the under side of both pouch and pharynx. The dorsal half of the lateral ridge, however, is continued into the submeckelian fold, and these are now slightly more prominent. Together they now form a continuous crescent-shaped fold extending from the dorsal apex to the base of the vestibular fold. It underlies, for the greater part of its length, Meckel's cartilage. For this reason I have called it the submeckelian fold. The shallow depression in the lateral wall which it subtends I call the Meckelian fossa.

The paired ridges which formerly limited the tuberculum impar laterally have now become blended with the epithelium covering the tongue *anlage*. The formation of the latter has been accompanied by the progressive downgrowth of the surrounding alveolo-lingual crests, particularly in their anterior portion. The deep space thus enclosed is filled with the tissues of the organ. Posteriorly this space is now connected by a deep groove with the space in front of the larynx.

An early stage in the formation of the external auditory meatus is shown by the conical indentation projecting under the pouch. Its inner angle terminates a short distance below the latero-posterior surface. The two structures are nowhere in contact, a moderately thick layer of mesenchyme intervening between them.

In the pig of 17 mm. (No. 51, Harvard series, Figs. 19-21) the primary tympanic pouch is slightly more expanded and depressed. The dorsal apex has become flattened out to a low rounded prominence and has sunken to a lower level, so that it scarcely projects above the level of the pharyngeal roof. The tubo-tympanal crest in consequence is almost horizontal. Anteriorly it turns sharply inwards to form the relatively short tubal portion, the remainder forming the tympanic part (see Fig. 20).

On the lateral wall the submeckelian fold forms a prominent, projecting ridge. It extends from the dorsal apex downwards and forwards to the latero-inferior edge, when it projects as a convex ventral pocket. In front of this region it suddenly dies out, forming only a low fold (Fig. 19, y.), continued to the base of the vestibular fold. The interval outside of this part is occupied by Meckel's cartilage. The latter ascends from the mandibular arch in the angle between the submeckelian and the vestibular folds and thereby comes to lie in front of and above the former. The presence of the cartilage in the angle mentioned has probably some close connection with the separation of the two folds. Its presence would inhibit continued lateral extension

of the connecting portion, while it would not interfere with such growth in the remainder of the fold. The latter would then continue to expand laterally and would thus give rise to the prominent projection which it forms at this stage.

The form of the pharynx is essentially the same in a pig of 18 mm. (Series M^3, my collection) and a rabbit of 14 days (No. 157, Harvard series, Fig. 70). It differs but slightly from that last described. The greater part of the tympanic pouch lies in an almost horizontal plane, only its extreme lateral portion being slightly upturned (Figs. 41-46). The dorsal apex forms only a low eminence, the meeting point of tubo-tympanal border, submeckelian fold and tensor tympani border.

The most important feature of this stage consists in the definite segregation of the neighboring skeletal structures, particulary Meckel's cartilage and the auditory capsule. Their formation is so intimately associated with certain later modifications of the pouch that a short description of their essential characteristics is necessary. Meckel's cartilage (Mck.) is a stout rod, which, as already mentioned, rises from the mandibular arch in the angle between the submeckelian and vestibular folds and then turns obliquely backwards above the former fold (Figs. 41-43). Close to the posterior margin of the fold it sends down the stout manubrium which curves around the back of the fold and terminates in a slight depression—the manubrial fossa—immediately beneath (Figs. 43-44). The submeckelian fold is thus wedged in the angle between Meckel's cartilage and the manubrium and is thus relatively fixed in position (Fig. 43). This relative fixity of the fold is an important factor in the final transformation of the pouch into the definitive tympanic pouch and Eustachian tube.

The auditory capsule occupies the depression (Impressio cochlearis) between the dorso-internal surface of the pouch and the roof of the pharynx.

(a″) The Differentiation of the Tympanic Pouch and Eustachian Tube.

In a pig of 20 mm. (No. 542, Harvard series, Figs. 23-27) we observe the beginning of the changes leading to the final transformation of the primary tympanic pouch into the definitive pouch and Eustachian tube. The transformation appears to be closely connected with a continuance of the processes already indicated. Of these we may recall (1) the ventral (caudal) flexure and elongation of the posterior half of the pharynx in connection with the formation of the neck, (2) the

anterior extension and flexure of the mouth, and (3) the relative fixation of the primary tympanic pouch by the differentiation of the surrounding cartilages.

As a result of the flexures of the pharynx and mouth the common structure now has the form of an arch (Fig. 23), the apex of the arch being that part lying between the primary tympanic pouches. From . . side of this part each pouch projects as a broad, flattened fold, which towards its periphery turns strongly upwards so that the apex again extends some distance above the roof of the pharynx. Together the tubo-tympanal and tensor tympani borders form an arched curve, the apex being formed by the dorsal apex (Fig. 23). The submeckelian fold (S-M.F.) has much the same appearance as before. It is completely separated from the vestibular fold. It, however, no longer projects below the ventral line of the pouch, but lies a slight distance above it on the lateral surface. This change has been effected by a process which only becomes noticeable in the region of the pouch at this time. This is the downward growth and posterior extension of the alveolo-lingual folds (A.L.F.). As these grow down they carry with them the adjacent ventro-lateral wall of the pouch, and thus the latter loses its original horizontality and assumes an inclined position. Its surface thus comes to be more nearly continuous with the plane of the dorso-lateral portion. Since the submeckelian fold forms the dividing line between the two portions, it comes, in consequence of this change, to occupy its present relatively higher level on the side of the pouch.

An important, but at this stage inconspicuous, feature is a shallow indentation on the posterior tympanal rim between it and the second pouch (see Figs. 26-27, z.). The latter pouch is now so small that the exact line of demarcation is not easily recognizable. A slight ridge (Fig. 26, p-m.f.), however, which extends from the indentation to the submeckelian fold, enables one to fix upon this point as being between the two structures. The same ridge, showing the same relations, is present in the immediately preceding stage when the second pouch was still clearly recognizable. This ridge later becomes the prominent elevation limiting the manubrial fossa posteriorly.

In the cat of 10.7 mm. (No. 474, Harvard series) the tympanic pouch shows a slight advance. The indentation between the pouch and the second pouch is slightly deeper and consequently the posterior tympanal crest now forms a rounded lobe projecting dorsally. In all other respects this stage is so similar to the preceding that further description is unnecessary.

The cat of 15 mm. (No. 436, Harvard series, Fig. 63, 64) presents the next stage in the modification of the tympanic pouch. The incision, which in the preceding stages had just begun to form between the tympanic pouch and the dorsum of the second pouch, is now much deeper. The postero-lateral lobe of the pouch in consequence protrudes more strongly in the dorso-posterior direction. As a result of the incision a new ventro-mesial border (V.M.R.) has begun to form between the base of the pouch and the pharynx. Posteriorly this border connects by a rounded angle with the posterior tympanal border (Fig. 64, s. t. p.).

The connection of the pouch with the pharynx is both relatively and actually of lesser extent than in the preceding stages. This condition represents the commencement of the gradual constriction of the connecting part as a result of the anterior extension of the incision.

Owing to the increased depth of the intervening incision the tympanic pouch is now completely separated from the second pouch. This condition is apparently produced in the following manner: It will be recalled that the pouch has now become relatively fixed in position by being included between Meckel's cartilage with its manubrial process and the auditory capsule. The neighboring lateral walls of the pharynx, on the other hand, are continuously being displaced to a lower level by the downgrowth of the alveolo-lingual margins. Among the parts thus carried down is the concavo-convex fold representing the dorsal remnant of the second pouch (Ton.F.). In consequence of this displacement of the second pouch and the relative fixity of the tympanic pouch, the incision (z) between the two spreads dorsally over the second pouch and reaches the longitudinal ridge (P-S.F.) lying immediately internal to the base of the pouch (cf. Figs. 26, 70 and 64). Thus the base of the tympanic pouch is placed in connection with this ridge, which is the external expression of the groove extending backward from the Eustachian opening between the levator cushion and the salpingo-pharyngeal fold. For convenience in description I shall speak of it as the post-salpingeal groove.

As a result of the process just described the dorsum of the second pouch comes to lie on the lateral surface of the pharynx below the posterior margin of the tympanic pouch. With the subsequent downgrowth of the alveolo-lingual folds it is carried farther ventralwards, and, as will be described later, is finally transformed into the tonsillar recess.

On the expanded lateral wall of the tympanic pouch two prominent outstanding folds are now present. The anterior is the submeckelian fold; it shows the now deep Meckelian fossa on its dorsal side. The posterior fold is less prominent; it corresponds to the ridge formerly mentioned as forming the posterior limit of the manubrial fossa. The latter now forms a depression of considerable depth.

A rabbit of 16½ days, 17.8 mm. (No. 576, Harvard series, Fig. 71) shows the constriction of the tympanic pouch still further progressed. The post-salpingeal fold (p. s. f.) is more convex. The dorsum of the second pouch (ton. f.) is separated by a short interval from the base of the tympanic pouch. The remaining features of the pouch are essentially like those in the following stage.

This stage is represented by a pig of 24 mm. (No. 64, Harvard series, Figs. 29, 30). The constriction of the tympanic pouch has now reached a stage where its connection with the pharynx embraces about two-thirds of its former extent. The ventro-mesial margin is accordingly of considerable length. The posterior half of the pouch projects strongly backwards as a wide, cup-shaped fold.

The submeckelian fold forms a wide, almost horizontal shelf (Figs. 47-50, s. m. f.). Laterally it reaches considerably beyond the dorsal apex, so that it is clearly visible from above (Fig. 30). On lateral view it appears at a considerably higher level than before. This position it has obtained partly as a result of its lateral extension and the consequent flattening of its dorsal surface and partly from the ventral downgrowth of that portion of the pouch lying immediately below it (cf. Figs. 48-50, with Fig. 43).

The manubrial fossa forms a shallow impression between the submeckelian (s. m. f.) and post-manubrial folds (p. m. f.). The latter is much less prominent in the pig than in the equivalent stage of the cat.

The pig of 25 mm. (Series M³, my collection), while slightly more advanced than the preceding, is essentially similar so far as the tympanic pouch is concerned. Figs. 47-51 give views of several transverse sections of the structure.

The next step in advance is shown by a cat of 23.1 mm. (No. 466, Harvard collection, Figs. 66-67). In this case the tympanic pouch and Eustachian tube are first clearly differentiated from each other. The former is a wide, cup-shaped expanse, concave dorsally. As a whole, it has a decided ascending direction. The postero-lateral border (P-L.B.) forms a highly elevated ridge. Immediately back of the

dorsal apex it is interrupted by a deep incision—the incissura tensoris (I.Tn.). Anterior to the apex is the submeckelian fold (SM.F.) facing at this stage in the antero-dorsal direction. Laterally its margin is so far upturned as to hide from view the adjacent part of the tubo-tympanal border.

The manubrial fossa (Mn.F.) is very deep. It lies immediately below the tensor incision, bounded anteriorly by the submeckelian fold and posteriorly by the post-manubrial fold (P-M.F.). The external auditory tube lies a short space below the fossa, but is still separated from it by a considerable thickness of connective tissue.

The most noteworthy feature of this stage is the initial division of the pharynx into its oral and nasal portions by the backward extension of the palatine incisions. The oral cavity has been entirely separated from the nasal tube, but the constriction of the pharynx has only begun in its more anterior part. The constriction, as the figures show, takes place in the part lying below the post-salpingeal fold, between it and the tonsillar fold.

The rabbit of 18 days (Harvard series), while showing a slight difference from the preceding, is yet so closely similar that a full description is unnecessary. Its general features can be seen by consulting Fig. 72. The most marked feature is the greater posterior extension of the palatal constriction. The broad grooves continued back from the latter over the sides of the pharynx represent the posterior palatine grooves (Arcus pharyngo-palatinus), p. pl.

In the pig of 32 mm. (No. 74, Harvard series, Figs. 32, 33, 52) the Eustachian tube is more constricted than in the preceding stage. The tympanic pouch projects sharply outwards and backwards. Close to where it joins the tube it gives off the still prominent submeckelian fold. Where the latter and the tubo-tympanal borders meet is the dorsal apex (Recessus anterior, D.A.1). Below the latter on the lateral wall is the now crescent-shaped post-manubrial fold. The latter arches around underneath the manubrial fossa (Mn.F.) and becomes continuous with the portion extending to the dorso-lateral margin of the pouch. Immediately below the fossa the ventro-lateral surface of the pouch is flattened and is adpressed against the inner part of the external auditory tube. Only an exceedingly thin layer of connective tissue intervenes between the two structures (Fig. 52).

The cat of 31 mm. (No. 500, Harvard series, Figs. 68-69) gives the final stage in its species. The Eustachian tube is very narrow, while

the tympanic pouch is widely expanded, particularly in its posterior part. It still retains its cup-like form, the concave surface fitting closely against the ventro-lateral wall of the auditory capsule. The submeckelian fold (S-M.F.) is relatively not so prominent as earlier. The dorsal apex or anterior recess (D.A.1) projects strongly outwards. The manubrial fossa (Mn.F.) forms a deep hollow on the more dorsal portion of the lateral surface. It is largely surrounded by the now high and conspicuous post-manubrial fold (P.M.F.). Below the fossa is the surface already mentioned as being in close relation with the external auditory tube. The remaining posterior extension of the pouch is simply applied to the neighboring part of the auditory capsule.

The latest stage studied is shown by a rabbit of twenty-one days. Fig. 73 shows the more important points. The manubrial fossa (Mn.F.) is still rather deep in its dorsal half, but vertrally becomes very shallow and there tapers out to a point. The area entering into the constitution of the tympanic membrane is more extensive than in the preceding stage. It now includes a considerable part of the surface in which the manubrial fossa is located.

The Meckelian fossa (Mk.F.) is almost obliterated; it persists as a very shallow impression on the antero-dorsal margin close to the union of the pouch with the Eustachian tube.

Review and Comparisons.

The foregoing results render it highly probable that the developmental history of the first pharyngeal pouch is essentially the same in the three species of mammals studied.

This history I have subdivided into three periods, as follows:

(1) The period of formation of the typical pouch.

(2) The period of transformation of the pouch into the primary tympanic pouch.

(3) The period of differentiation of the tympanic pouch and Eustachian tube and their subsequent modifications.

Period I. The formation of the pharnygeal pouches takes place in the usual manner—beginning with the most anterior and ending with the most posterior.

When typically developed the first pharyngeal pouch has the form of an approximately transverse vertical fold. At its dorsal lateral

angle it projects dorsalwards as a narrow prominence, the dorsal apex (recessus anterior). From this apex three prominent ridges diverge, *i. e.,* antero-lateral, lateral and postero-lateral. The first extends diagonally inwards and slightly forwards. It forms the sulcus tubo-tympanicus of Moldenhauer. The lateral ridge is that by which attachment to the ectoderm is effected. The area of attachment includes nearly its entire extent. Ventrally this ridge is continued into the ventral diverticulum. The postero-lateral ridge extends obliquely inwards and backwards from the dorsal apex to the dorsum of the second pouch.

The ventral diverticula of the first pair of pouches are at first more prominent than those of the succeeding, but they are soon outstripped by the latter. Typically they form a pair of low, but sharp folds, which at first are continuous across the median line of the pharynx.

Period II. The most important changes leading to the transformation of the first pouch into the primary tympanic pouch are the following:

The gradual separation of the pouch from the ectoderm. This process begins on the ventral side and progresses dorsalwards until complete separation has been effected. In consequence of this separation the lateral ridge becomes greatly reduced and partly absorbed into the neighboring walls of the pouch.

The tubo-tympanal border becomes prolonged in the anterior direction. This change is produced as a result of the elongation in the same direction of the adjacent part of the oral cavity.

The ventral diverticula first become interrupted in the mid-line, and later gradually disappear as a result of absorption into the floor of the pharynx.

The basal or mesial portion of the pouch is displaced ventralwards in consequence of a corresponding displacement in the adjacent part of the pharynx itself. This portion of the pouch thus assumes an almost horizontal position. At first the peripheral part, owing to its continued attachment to the ectoderm, retains its ascending course, joining the mesial portion at a sharp angle. Later, after complete separation from the ectoderm, the peripheral portion also sinks, and thereby assumes a plane more nearly like that of the mesial portion.

The submeckelian fold is formed by the union of the dorsal remnant of the lateral ridge with the diagonal fold separating the basal and peripheral portions of the pouch. At first the fold is continuous an-

teriorly with the lateral margin (vestibular fold) of the oral cavity. Subsequently this connection is interrupted and the submeckelian fold then grows out as a prominent shelf-like protuberance underlying Meckel's cartilage.

Period III. The transformation of the primary tympanic pouch into the definitive tympanic pouch and Eustachian tube is marked by the following features:

The peripheral portion of the pouch becomes relatively fixed in position by the segregation of Meckel's cartilage with its manubrial process and the auditory capsule.

The basal portion, on the other hand, continues to be carried down by the downgrowth of the alveolo-lingual fold.

The combined effect of these two processes is to give the pouch a peripherally ascending course.

An incision forms at the postero-internal angle of the pouch between it and the dorsum of the second pouch. This incision rapidly extends forwards as an ever-widening cleft between the base of the pouch and the wall of the pharynx.

In consequence of this process the connecting part of the pouch is progressively constricted until it forms a narrow tube, the Eustachian tube.

The remainder of the pouch retains its original wide extent and forms the tympanic pouch.

The later changes relate mainly to modifications in the detailed structure of the tympanic pouch. Among them are the formation of the manubrial fossa, the reduction of the submeckelian fold and the formation of the tympanic membrane.

The manubrial fossa lodges the ventral extremity of the manubrium. At first it is a shallow impression on the lateral surface immediately underlying the posterior part of the submeckelian fold. With the formation of the definitive tympanic pouch it rapidly deepens to form a cup-like depression. Subsequently this elongates at its ventral extremity to form the fissure-like groove characteristic of its final stage.

The submeckelian fold is at first very prominent and partly encloses a Meckelian fossa. The latter later assumes a more flattened form and the fold at the same time broadens until it is absorbed into the wall of the pouch. In the latest stage the submeckelian fold forms only an inconspicuous swelling on the outside of the tubo-tympanal border.

The tympanic membrane is formed by the progressive approximation of

the ventro-lateral portion of the tympanic pouch and the neighboring dorso-internal surface of the external auditory tube. At first the two surfaces are separated by a considerable interval filled with connective tissue. This interval later becomes narrower until it is reduced to an exceedingly thin layer—the membrana propria of the definitive membrane. The formation of the tympanic membrane begins on the ventro-lateral surface of the pouch, but subsequently it extends dorsalwards so as to include the portion containing the manubrial fossa.

After its differentiation the pouch as a whole increases in width both laterally and longitudinally. Its posterior portion extends backwards as a prominent projection (posterior recess). The margins become upraised and thus the pouch as a whole assumes a cup-like form. The concavity on the dorsal side, corresponding to the promontory, lies close to the latero-ventral surface of the auditory capsule.

As already mentioned, my results make it highly probable that the developmental history of the first pharyngeal pouch is in all important respects similar in the three types studied. This probability is still further heightened when the results are compared with those obtained by other investigators. Thus Piersol has described and figured the earlier stages in the rabbit. They agree in every important particular with the corresponding stages in the cat and pig.

The most complete comparison can, thanks to the work of Hammar, be made with the human species. Hammar figures nearly every stage from the typical first pharyngeal pouch to the end of fœtal life. I have carefully compared Hammar's descriptions and figures with mine and find that in every important particular they are applicable to the types examined by me. It is in fact difficult to recognize any important differences, at least as late as the stage when the tympanic pouch and Eustachian tube have been fully differentiated. In the case of the human species the tympanic pouch during the later fœtal life gives rise to several outgrowths from its dorso-lateral margin. From one of these the mastoidal cells arise as a complex series of buds. In the rabbit these outgrowths had not formed at as late a stage as that of an animal of 21 days. Whether they are present at the same stage of development in the other two forms I am, at present, unable to say. The latest stages of each, which I was enabled to examine, showed no trace of them.

Hammar does not lay as much stress as I on the submeckelian fold. He describes its formation correctly, but apparently fails to note its separation from the vestibular folds and its later lateral expansion. His figures, however, leave no doubt that in these particulars the human

species agrees with the other types. In some of his figures I am not certain whether Hammar means to include the submeckelian fold as a part of the recessus anterior or to limit the latter to the dorsal apex. His descriptions seem to me to favor the latter alternative. He applies, at any rate, no distinctive term to the fold, and accordingly I have felt free to call it the submeckelian fold.

The foregoing remarks make it apparent that the same essential type of development of the tympanic pouch and Eustachian tube holds in species belonging to four different orders of mammals, *i. e.,* Rodentia (Lepus), Ungulata (Sus), Carnivora (Felis), and Primates (Homo). So far as known, other species, which have been much less thoroughly investigated, agree with this type. Accordingly, it seems reasonable to suppose that the same type prevails in the majority of ordinary placental mammals and that it represents the typical development of the structures in the class. In forms which are adapted to a special environment (Cetacea, for example) or which are farther removed from the main phylogenetic series (Edentata) it may show important modifications. So far as I am aware, these forms have not yet been investigated in regard to this point. The Marsupials and Monotremes have also not been sufficiently investigated to allow of any assertions being made concerning them. It may be added that a figure by Maurer, showing an early stage of the pharynx in Echidna, bears a striking likeness to that of my 6.5 mm. pig and 6.2 mm. cat.

B. THE MODIFICATIONS AND FATE OF THE SECOND PHARYNGEAL POUCH.

(b′) The Retrogressive Modifications of the Pouch.

We left the second pharyngeal pouch fully and typically developed in a cat of 6.2 mm. (Figs. 58-60). Its form at that stage is that of a postero-laterally projecting, vertical fold, which is connected by its entire peripheral margin with the ectoderm of the corresponding groove. At its dorso-lateral angle it is produced into a slight elevation forming a dorsal apex (D.A.2) similar to that of the preceding pouch, but considerably less prominent. On its ventral side the pouch is continued as a prominently projecting ventral diverticulum (V.D.2). The deep portion of the latter is limited to the lateral half of the pharynx, its internal border forming a free edge (Fig. 60). At the base of this edge the diverticulum is continued mesially as a low fold similar to the same part in the first pouch. Like the first pouch, the second has four borders and three surfaces. The borders are antero-lateral, postero-internal, lateral and ventral. The surfaces are antero-lateral, medio-

posterior and dorsal. The antero-lateral border (Ton.F.) extends from the dorsal apex diagonally forwards and inwards to the postero-internal angle of the first pharyngeal pouch. It forms the dividing line between the dorsal and antero-lateral surfaces. The postero-internal border is approximately crescentiform. Laterally, owing to the posterior flexure of the pouch, its course is almost longitudinal, but basally it bends first inwards and then posteriorly and connects with the lateral ridge extending to the third pouch. It separates the dorsal and postero-internal surfaces. The lateral margin forms the part connected with the ectoderm. It separates the antero-lateral and postero-internal surfaces. Ventrally it is continued into the ventral margin, which forms the free edge of the ventral diverticulum.

In a cat of 9.7 mm. (No. 446, Harvard series, Fig. 61) the second pouch, beyond a slight increase in size, shows but few new features. For a short distance below the dorsal apex it has separated from the ectoderm—the initial step in the process which in this case begins at the dorsal end and progresses towards the ventral. The separation is accompanied by the ingrowth of mesenchyme into the intervening space.

The latero-ventral angle of the ventral diverticulum is produced into a slight projection. As a result the inner border of the diverticulum ascends more diagonally to the floor of the pharynx.

In the pig of 10 mm. (No. 401, Harvard series) a departure from the preceding stage is shown by the slightly lower level of the second pouch. In the preceding examples the dorsal line of the pouch lay a short distance above the same line of the pharynx, while in the present stage it lies below it. This condition is probably produced by the changes taking place in the neighboring parts. The hyoid region increases in thickness more rapidly in its dorsal portion than in its relatively passive ventral part. The dorsal portion thus projects outwards over the lower and consequently the second ectodermal groove assumes a more inclined direction than before. With the latero-ventral rotation which the dorsal half of the groove undergoes it naturally results that the attached dorsal portion of the internal pouch accompanies it, at least in part, in the same direction, and thus assumes a more lateral, as well as lower, position.

In the 12 mm. pig (No. 518, Harvard series, Figs. 9-12) the second pouch comes to a standstill so far as any lateral growth is concerned. Thus the distance between the lateral margins of the two opposite pouches remains the same as in the preceding stage. The first pharyngeal pouch, on the contrary, continues to extend rapidly in that direc-

tion, and at the same time carries with it the attached adjacent parts. As already mentioned, the antero-lateral margin of the second pouch is continuous anteriorly with the latero-posterior border (S.T.T.) of the first pouch. At first the two join at a considerable angle, but as this border of the first pouch is carried outwards by the growth of the pouch, the attached antero-lateral border of the second pouch (Ton.F.) follows it and thus the angle tends to become drawn out and the borders to form a continuum. Consequently at this stage the antero-lateral border extends diagonally outwards instead of inwards, as in preceding stages.

The lateral flexure of the antero-lateral margin causes it to arch outwards above the underlying antero-lateral wall. The latter thus forms a well-marked concavity, which is limited internally by the low fold (later part of the alveolo-lingual sinus) connecting the ventral diverticula of the first and second pouches. Owing to its inclined position, this surface will henceforth be called ventro-lateral (Fig. 12, c. v.).

Corresponding to the depressed condition of the ventro-lateral surface, the dorsal surface, which is everywhere closely adpressed against the underlying wall, is raised into a low dome-shaped convexity. The latter I shall call the dorsal prominence (Fig. 10, D.Pr.).

The ventral diverticulum (v. d. 2) is reduced to about three-fourths of its former vertical extent. This change I am inclined to attribute, in part at least, to the outward extension of the antero-lateral portion of the pouch. The latter would set up a tension in the remainder of the pouch which would lead to a partial absorption of the diverticulum into the adjacent portion of the pouch. A fact favoring the existence of such a tension is the presence upon the ventro-lateral wall of a narrow fold extending obliquely upwards from the base of the diverticulum (Fig. 12).

The lateral margin of the second pouch is now largely free from the ectoderm, the connection with the latter persisting only in its more ventral portion, where the corresponding ectodermal groove forms a deep, vertical pit (Fig. 11).

The pig of 14 mm. (No. 65, Harvard series, Figs. 14-17) shows the second pouch slightly reduced in vertical extent, but produced at its ventro-lateral angle into a long, fine process (Fl.P.), the distal end of which is attached to the ectoderm. Elsewhere the pouch is free and is removed by a wide interval from the ectoderm. This condition is the result of the rapid growth in thickness of the hyoid region. As the

figures (12 of last stage and 17 of this) show, this growth has not been accompanied by a corresponding increase in the pouch, which at this stage remains of the same width as in the preceding stage. Consequently, as the second pharyngeal groove is displaced more and more lateralwards, the attached ventro-lateral angle becomes drawn out into the process here shown. Owing to its form, I designate the latter the filiform process (fl. p.).

The lateral margin of the pouch is considerably less prominent than hitherto. This change appears to be produced by an actual regression of the margin. This is indicated by the fact that the distance between the lateral margins of the two opposite pouches is slightly less than in the preceding stage. The regression is probably attributable to the tension exerted upon this margin by the continued lateral extension of the adjoining antero-lateral margin with which it now joins at a wide angle.

As just mentioned, the antero-lateral margin (ton. f.) has continued to extend in the lateral direction. It thus has a decided antero-lateral course. For this reason it is inappropriate to call it by the term hitherto used, and accordingly I shall hereafter speak of it as the dorso-lateral margin.

The dorsal apex (D.A.2) of the pouch now forms only a slight protuberance at the posterior extremity of this margin (Fig. 15).

In consequence of the extension laterally of the dorso-lateral margin the underlying ventro-lateral surface has acquired the form of a deep concavity (Fig. 17, c. v.). The overlying dorsal wall is correspondingly raised as a broad dome-shaped prominence (Fig. 15, D.Pr.).

The ventral diverticulum (v. d. 2) has almost ceased to exist as a distinct feature. Only in its more peripheral part does it project to a fair degree below the ventro-lateral line of the pharynx. Its middle part has largely disappeared owing to the downgrowth of the alveolo-lingual ridge (Fig. 17, al. f.) and the union of the latter with the sinus piriformis (Fig. 17, s. pi.). The place of the original diverticulum is indicated by a widening of the continuous ventro-lateral fold thus formed.

The more internal part of the diverticulum persists as a slight ridge on the inner side of the ventro-lateral fold (Fig. 17).

In the 17 mm. pig (Figs. 19-22) the second pouch has entirely severed its connection with the ectoderm, leaving the filiform process terminating blindly in the mesenchyme.

Owing to the continued lateral extension of the dorso-lateral margin (Ton.F.), the original lateral border now forms a continuum with it. This leaves the dorsal apex as a minute protuberance at its posterior extremity.

The dorso-lateral margin shows no increase in length, but anteriorly it has been carried farther outwards in consequence of the extension of the tympanic pouch in that direction. It thus acquires a course almost in line with the postero-lateral margin (s. t. p.) of the latter. Only a slight notch remains to indicate the dividing line between them.

The ventral diverticulum (v. d. 2) has now nearly disappeared, having been absorbed by the downgrowth of the ventro-lateral margins of the pharynx.

The features of the second pouch in the pig of 17 mm. are essentially duplicated in cats of 10.7 mm. and 12 mm.

A rabbit of 14 days (No. 157, Harvard series, Fig. 70) shows a stage somewhat intermediate between that just described and the next.

The same remark is also applicable to an 18 mm. pig (Series M^3, of my collection).

In a pig of 20 mm. (No. 542, Harvard series, Figs. 23-27) the second pharyngeal pouch is chiefly modified as regards length and direction. As indicated by the figures, these modifications are related to the ventral (caudal) flexure of the posterior half of the pharynx. As already mentioned (see account of tympanic pouch), the tympanic pouch has at this time become relatively fixed in position by the formation about it of the related cartilages. Consequently, as the pharynx continues to bend toward the ventral side, the attached second pouch tends to be drawn out and flattened (Fig. 23). This process is also accelerated by the continued deepening of the ventro-lateral margin of the pharynx.

The hitherto prominent dorsal prominence is now reduced to a low swelling located at the postero-internal angle of the tympanic pouch. No lateral extension of this part of the pouch has taken place since the 17 mm. stage. Its middle and posterior portions, on the contrary, have shrunken slightly, due probably to the tension produced by its elongation in the ventral direction and the continued downgrowth of the adjacent ventro-lateral margin (A-L.F.) of the pharynx.

Posteriorly the second pouch thus forms a low ridge situated on the outer side of the ventro-lateral fold (= conjoined alveolo-lingual and piriform sinuses).

The shrunken filiform process is still recognizable.

The dorsal apex has been absorbed into the neighboring surface of the dorsal prominence.

The ventral diverticulum forms only an inconspicuous fold in the same situation as hitherto.

(b″) The Formation of the Tonsillar Fold.

The cat of 15 mm. (No. 436, Harvard series, Figs. 63-64) gives us the initial step in the transformation of the remnant of the second pouch into the tonsillar fold.

In this stage the dorso-lateral fold, representing the second pouch, no longer forms a continuum with the adjacent border of the tympanic pouch, but is separated from the latter by an indentation which extends quite across its dorsal side to the longitudinal ridge (P.S.F.), forming its mesial boundary.

The second pouch thus forms an arched lateral fold. The lateral margin (Ton.F.) of the fold lies on a level with the ventro-lateral line of the pharynx. The ventral side is concave; the dorsal correspondingly convex. Anteriorly the fold is continued immediately under the ventro-internal angle of the tympanic pouch and extends to the base of the vestibular fold. Internally the fold is limited on the ventral side by the alveolo-lingual fold, on the dorsal by the adjacent surface of the pharynx. The structure thus defined is the tonsillar fold (tonsillar sinus). The concavity on its ventral side corresponds to the tonsillar prominence (tonsillenhöcker).

There is no trace at this stage of the filiform process.

The rabbit of 16½ days (No. 576, Harvard series, Fig. 71) shows an essentially similar condition. The fold (ton. f.) is more strongly arched and its lateral edge lies some distance above the lower edge of the alveolo-lingual groove. The fold is widest immediately under the post-salpingeal ridge (p. s. f.). Its anterior continuation forms a low ridge, which probably represents an extension of the fold over the adjacent surface of the pharynx.

In the 24 mm. pig (No. 64, Harvard series, Figs. 29-30) the tonsillar fold is removed by a considerable interval from the base of the tympanic pouch (Fig. 30). Between them the surface of the pharynx is depressed, forming the palatal constriction. The present position of the fold is due to the formation of this constriction and to the continued downgrowth of the alveolo-lingual margin (A-L.F.) with which it is closely associated.

In form the tonsillar fold (Ton.F.) of the pig of this stage bears a greater resemblance to that of the cat than to the same structure in the rabbit. The tonsillar fold of the latter has a more decided ascending plane than the others.

In the cat of 23.1 mm. (No. 466, Harvard series, Figs. 66-67) the tonsillar fold (Ton.F.) has attained its definite position. The palatal constriction has now separated the nasal cavity from the mouth and has begun to encroach upon the pharynx. The tonsillar fold forms a wide, diagonally ascending arched fold on the side of the oral portion. Its ventro-lateral surface is, as usual, deeply concave.

The pig of 32 mm. (No. 74, Harvard series, Fig. 32) shows the tonsillar fold (Ton.F.) more nearly erect than in the cat. In outline it is approximately quadrangular and its outer (= ventral) surface is less concave than in the cat. Ventrally it is limited by the alveolo-lingual ridge (A-L.F.), which at this stage no longer forms the lower line of the pharynx, but lies on the outer side of the glosso-epiglottic fold (vallecula glosso-epiglottica).

In the 31 mm. cat (No. 500, Harvard series, Figs. 68-69) the tonsillar fold (Ton.F.) has essentially the same form as in the 23 mm. cat. As in the pig last described, its lower boundary—the alveolo-lingual ridge—now lies on the outer side of the glosso-epiglottic fold (G.Ep.).

The palatal constriction has now completed the division of the pharynx into nasal and oral portions.

The narrow cord shown in the figure parallel with the tonsillar fold is an epithelial structure which lies free in the connective tissue to the outer side of the fold. Its significance I have not been able to solve.

In none of the stages so far studied did I observe any clear indications of the formation of lymphoidal tissue in connection with the tonsillar fold.

In the rabbit of 21 days (Fig. 73) the tonsillar fold (Ton.F.) is approximately vertical. Its lateral surface is deeply concave and lies between a dorsal and a ventral fold. The former corresponds to the supra-tonsillar recess and evidently represents the derivative of the second pouch. The ventral fold I am inclined to homologize with the infra-tonsillar recess (V.T.) which is a derivative of the pharynx. Hammar, however, who describes a similar stage in the rabbit as well as in man and several other mammals, fails to mention this fold as the part in question. I regret that with the relatively few later stages at my disposal I have not been able to solve this problem satisfactorily.

Review and Comparisons.

My investigations make it probable that the history of the second pouch, so far, at least, as its earlier stages are concerned, is similar in the forms studied. Unfortunately, my rabbit and cat material was not sufficiently abundant to enable me to make this statement without qualification. However, the specimens I did examine agreed very closely with corresponding stages in the pig series. The later stages were not sufficiently numerous to enable me to make comparisons. In its general features the development of the tonsillar fold seems to agree in all forms; in details, there are undoubtedly considerable differences in the different species.

The history of the pouch, as mainly determined in the pig, divides itself in two periods—the first characterized by a series of retrogressive changes in the pouch, the second by a series of progressive changes converting the remains of the pouch into the tonsillar fold.

When typically developed the second pouch has the form of a postero-laterally projecting vertical fold. Dorsally the dorso-lateral angle is produced as a dorsal apex. Ventrally it shows a prominent ventral diverticulum. Connection with the ectoderm is more extensive than in any other pouch, the entire lateral margin taking part in the formation of the *verschlussmembran*.

The earlier modifications of the pouch are connected with the rapid lateral growth of the hyoid region. The pouch, on the other hand, remains stationary. Parts of it are, however, connected with adjoining structures, and, as these undergo displacement connected with subsequent growth, the pouch becomes profoundly modified.

Separation of the pouch from the ectoderm begins on the dorsal side and extends progressively toward the ventral. The last point to remain attached is the ventro-lateral angle of the ventral diverticulum, which becomes drawn out into a thin cord, the filiform process. The latter subsequently separates and then shrinks in length and disappears.

Largely as a result of the lateral extension of the adjoining tympanic pouch the dorso-anterior portion of the second pouch is drawn farther outwards. Its margin, which originally extended forwards and inwards, acquires an antero-lateral course and thus comes to form a continuum with the posterior border of the tympanic pouch. The underlying antero-lateral surface becomes ventro-lateral and its wall becomes depressed to form a deep concavity, which corresponds to the later ton-

sillar projection. The closely adpressed dorsal wall is correspondingly raised into a dome-shaped swelling, the dorsal prominence.

After its separation from the ectoderm the original lateral margin of the pouch recedes towards the median line. At first it forms a slight projection at the postero-internal angle of the pouch, but later this is absorbed and then forms a continuum with the dorso-lateral fold.

The ventral diverticulum early diminishes in size and later is absorbed by the downgrowth of the alveolo-lingual fold.

At the termination of the first period the remains of the second pouch form a laterally ascending arched fold, which lies at the postero-internal angle of the tympanic pouch. On its ventral side it is concave and on the dorsal correspondingly convex. Its inner boundary is formed by the alveolo-lingual ridge.

The second or progressive stage is marked (1) by the separation of the second pouch from the tympanic pouch, (2) its ventral displacement to its definitive position, and (3) its progressive modification to form the tonsillar fold.

The separation from the tympanic pouch takes place by the extension of the indentation between the two structures over the dorso-lateral surface. The second pouch thus comes to lie at a slightly lower level than the base of the tympanic pouch.

The ventral displacement takes place in connection with the continued downgrowth of the alveolo-lingual ridge and the accompanying formation of the palatal constriction. The latter forms between the base of the tympanic pouch and the dorsum of the tonsillar fold and as it enlarges the fold is pushed farther ventralwards, where it attains its final definitive position.

In its principal features the tonsillar fold in the later embryonic stages is similar in the species studied. It then forms a prominent arched fold on the lateral surface of the oral portion of the pharynx parallel to the alveolo-lingual sinus. Its ventro-lateral surface is concave, its dorsal convex.

The later modifications are concerned with the assumption of its definitive form. Owing to lack of materials, these modifications were not traced. The rabbit of 21 days shows that they may be considerable. I shall consider them further in the comparative part.

Contributions to the developmental history of the second pouch have been made by a number of investigators, chief among whom are Born, His, Rabl, Piersol, Kastschenko and Hammar. The results of these

authors, while agreeing in certain respects, are hopelessly discordant in others. The most satisfactory account is that given by Hammar of the development in man. Hammar also describes a few stages in the formation of the tonsil in several other species of mammals. In the main my results are in harmony with his. The only statement of his to which I cannot subscribe is that the *"kiemengang"* (= my filiform process?) is an ectodermal derivative. As his figures show, this structure occupies the same relative position as my filiform process. In Hammar's view this is formed by the passive deepening of the ectodermal groove produced by the growth of the hyoid region. He also pictures it as protruding above the margin of the pouch as a dorsal organ. In the pig, on the other hand, this structure is perfectly continuous with the ventro-lateral angle of the pouch and appears as a prolongation of the latter. In none of the specimens examined by me did I notice any communication between the lumen of the filiform process and the exterior. As for a dorsal organ projecting above the ventro-inferior edge of the pouch, I find no evidence of it. Accordingly, I am disposed to think that the filiform process and the "kiemengang" are independent structures. The latter would then be absent in the pig, while the former would be lacking in the human species. This view is supported by the observations of Piersol on the rabbit. He speaks of the ventro-lateral angle as continued in a blind tube. This evidently corresponds to the filiform process. He later speaks of the latter as cutting off from the pouch and undergoing changes reminiscent of the thymus. I find nothing of this in the pig. In the latter the process simply disappears—at least I have not seen any trace of it later than a 17 mm. animal. On the other hand, Piersol describes a long epithelial tube, which according to him arises from an insinking of the ectodermal groove. This corresponds to the *"kiemengang"* as described by Hammar. Piersol states that it originates while the filiform process is still present (twelfth day), but later (fourteenth day) it disappears without leaving a trace. If the facts as described are correct, the rabbit shows the filiform process and *"kiemengang"* as independent formations. The latter is evidently an extremely temporary structure. As already mentioned, I saw no trace of it in the pig, and in this I am in agreement with Rabl and Kastschenko, both of whom studied the same animal. The short duration of the "kiemengang" may perhaps have led to its being overlooked in this animal.

I may add here that the term *kiemengang* was first applied by Rabl to the endodermal structure here called filiform process. Hammar considers Rabl's account as contradicted by his results as determined in the human species, and accordingly applies the same term to the ectodermal structure. In case two independent structures, one endodermal and the other ectodermal, are found to exist in mammals, it will be necessary to return to Rabl's original use of the term.

My rabbit and cat series throw no light on this puzzling matter. In the former I did not examine sufficiently early stages, while in the latter the stages which would show the structures under consideration were lacking in the collection.

The remaining results agree fairly closely with those of Hammar. The form of the early tonsil in the forms studied by me differs somewhat from that in man, though the difference is a minor one. In regard to the rabbit of 21 days, Hammar does not speak of it as having an infratonsillar sinus. My specimen, on the other hand, shows a fold which, in my opinion, corresponds to this sinus. As, however, I was unable to examine forms in which the latter is undoubtedly present, I will not urge this homology.

The above comparisons would indicate that, although the chief features in the history of the second pouch agree in all species of mammals studied, there are considerable differences in detail. The matter of the filiform process and *kiemengang* would illustrate this. In later stages, as Hammar shows and as my specimens indicate, the tonsillar fold differs considerably in its structural details in various species of mammals.

C. THE METAMORPHOSES OF THE THIRD PHARYNGEAL POUCH AND ITS DERIVATIVES.

(c′) The Elongation of the Ventral Diverticulum and the Formation of the Thymus.

When typically developed, as in the cat of 6.2 mm. (Figs. 58-60), the third pharyngeal pouch bears a considerable resemblance to the second. Like the latter, it bears a deep ventral diverticulum (V.D.3), which likewise is limited to the lateral half of the pharynx, its inner half forming only an inconspicuous ridge. The deep part of the diverticulum is only slightly prolonged in a ventro-mesial direction.

The lateral margin is joined to the ectoderm for almost its entire extent, in this respect also resembling the preceding pouch (see clear area in Fig. 7).

In the 9.7 mm. cat (No. 466, Harvard series, Figs, 61, 62) the ventral diverticulum (V.D.3) of the third pharyngeal pouch is slightly more elongated at its ventro-internal angle. In other respects it is essentially similar to the stage last described.

The pig of 10 mm. (No. 401, Harvard series, Figs. 4-8) shows clearly the initial steps in the formation of the thymus duct. The ventro-internal angle of the pouch is now clearly elongated in a ventro-mesial direction and ends in an acute angle which is wedged in the angle between the roots of the carotid and aortic arches (Fig. 7). The downgrowths of the two sides are not quite symmetrical, the right being slightly larger and ending in a more acute angle than that on the opposite side. Laterally the lower part of the pouch has separated from the ectoderm, leaving only its dorsal half in contact with the latter. Below the point of contact the lateral border turns obliquely inwards and downwards and is continued into the ventro-lateral edge of the thymus downgrowth.

On the dorsal side the peripheral portion of the pouch projects slightly above the upper end of the *verschlussmembran* as a dorsal diverticulum (Figs. 4-8, D.A.3).

The carotid gland (Figs. 7-8, C.Gl.) lies closely adpressed against the anterior wall of the pouch and on its dorsal side projects slightly above the upper margin of the latter (Fig. 8). We shall defer further consideration of the gland until later.

In the 12 mm. pig (No. 518, Harvard series, Figs. 9-11, 13) the ventral diverticulum (V.D.3) is further elongated. In addition to the ventro-internal direction which it took in the earlier stage, it now shows a pronounced anterior trend, an effect of the ventral rotation of the adjacent part of the pharynx. At this time it has acquired a distinct tubular form.

The union of the pouch to the ectoderm is limited to a short stretch immediately below its dorsal apex. The rest of its lateral border is free and is continued ventrally into the outer edge of the tubular downgrowth.

The part connecting the pouch with the pharynx is considerably more constricted than in the preceding stage.

The tubular downgrowth is still further elongated in a 14 mm. pig (No. 65, Harvard collection, Figs. 14-16, Thy.). Its blind ventral extremity lies a slight distance below the level of the pericardio-cervical

groove and thus occupies the upper part of the pericardial region. It retains its tubular form, but shows a differentiation into two portions—a terminal, swollen portion and an intermediate, relatively narrow canal, which connects the former with the remaining dorsal body of the pouch. The latter now forms a compressed epithelial plate, bearing upon its anterior surface the voluminous carotid gland. It is still connected with the pharynx by a narrow connective.

The dorsal apex of the pouch has disappeared. The peripheral portion of the pouch is attached for a short distance to the anterior wall of the fundus præcervicalis (F.Pc.).

A lumen is present in the tubular downgrowth and in the pharyngeal connective, but has disappeared into the dorso-peripheral part by approximation of its anterior and posterior walls. The latter thus assumes the form of a vertical plate, connected with the fundus præcervicalis at its dorso-lateral angle and continuous with the intermediate cervical canal of the thymus at its ventro-internal angle.

In the 17 mm. pig (No. 51, Harvard collection, Figs. 19-21) the thymus downgrowth (Thy.) has still further elongated and now shows clearly its segmentation into three portions. These include (1) the considerably swollen thoracic vesicle, (2) the intermediate cervical connective (CV.C.), and (3) the dorsal plate (D.Pl.), with which is closely associated the carotid gland (C.Gl.) and fundus præcervicalis (F.Pc.).

Only a few fragments of the original lumen now remain, mostly confined to the thoracic vesicle.

Connection with the pharynx is still maintained by an extremely thin, solid connective (Fig. 45, of an 18 mm. pig.).

The dorsal body of the pouch, as already noticed, has become reduced to a flattened plate and now constitutes a part of thymus. It has separated from the ectoderm of the surface of the body, but remains attached to that of the fundus præcervicalis, which constricts from the superficial ectoderm and accompanies the thymus as the latter passively recedes from the exterior. The detailed account of this process will be reserved for later treatment. It suffices at this time to state that this ectodermal structure remains in close connection with the dorsal extremity of the thymus for a considerable period.

In an 18 mm. pig the thymus shows no essential deviations from that in the preceding stage. It is slightly longer and has a more vertical course than in the latter.

I shall at this stage treat of the factors which appear to be operative in producing the present condition of the thymus. So far as I have been able to determine, the modifications which the third pouch has undergone are referable, in large part at least, to the operation of purely mechanical factors. The pouch itself shows but little power of active growth. Compared with the surrounding parts, it is relatively passive. The first important factor is found in the unequal rate of growth of the neck and of the ventral tubular process. The former carries the roots of the large arteries from their original position immediately under the pharyngeal pouch region to their definitive position in the upper part of the thorax. The ventral extremity of the thymus, it will be recalled, is from the start in close relation with the bases of the carotid and aortic arteries, and as the latter become displaced to successively lower levels, this portion of the thymus is carried down with them. The elongation of the neck takes place, however, at a more rapid rate than that of the thymus, and thus produces on the latter a tension tending to carry it downwards. This, however, is prevented by the fact that the dorsal extremity of the thymus is, during the same period, relatively fixed in position by its attachment to the skin and pharynx. The result of such conditions would be to produce a strong tension in the intermediate connecting portion, which in consequence would become drawn out in the form of a thin cord, similar to that shown in the present stage (Fig. 21, Cv.C.). This view is supported by the fact that the diameter of the cord is actually, and not merely relatively, much less than in preceding stages.

As already mentioned, the dorsal extremity of the thymus is relatively fixed in position. This condition is readily explained when it is recalled that this portion is attached to both the ectoderm and the pharynx and also bears the voluminous carotid gland, the mere bulk of which alone would hinder any ready displacement, even through such a plastic medium as the surrounding mesenchyme.

An additional factor, first pointed out by Kastschenko, is found in the behavior of the hypoglossal nerve. The latter underlies the fundus præcervicalis. As this structure in harmony with the attached thymus becomes displaced in the ventral direction, it comes in contact with the nerve, which is also carried downwards with it until it forms a strong angular flexure, over which the outer part of the fundus curves like a hook over a cord. The elastic reaction of the nerve would naturally form a strong hindrance to any ready ventral movement of the head of

the thymus. That a decided tension of the kind indicated is actually produced is evidenced by the later behavior of the nerve—a subject which I shall consider more fully when considering the modifications of the fundus præcervicalis.

In a cat of 10.7 mm. the thymus has approximately the same characteristics as in the pig just considered. It shows, however, no clear lumen in any part.

In a pig of 20 mm. (No. 542, Harvard collection, Figs. 23-25) the thymus (Thy.) is considerably longer than hitherto and its ventral extremity is slightly lobed. Its lumen has entirely disappeared, owing to the thickening of its walls. The whole organ is thus composed of small-celled epithelioid tissue, which in every respect bears a close resemblance to ordinary lymphoid tissue. The dorsal plate is closely wedged in between the carotid gland and the fundus præcervicalis (Fig. 23). The thymus on the left side has completely separated from the pharynx, while that on the right is still connected with it by an extremely thin cord (Fig. 28).

The separation from the pharynx is probably connected with the inward flexure of the sinus piriformis and the consequent decrease in the lateral diameter of the pharynx. The dorsal extremity of the thymus and the attached carotid gland, however, retain their original position, with the result that the connecting cord is drawn out to an exceedingly thin strand, which subsequently constricts.

In the cat of 15 mm. (Fig. 63) the thymus shows no special features. It closely resembles the same structure in the pig just considered, but is located at a relatively lower level. In the pig its dorsal extremity is opposite the sinus piriformis, while in the cat it lies some distance below it.

In the 24 mm. pig (No. 64, Harvard collection, Figs. 29-31) the thymus on each side is completely separated from the pharynx. Its terminal thoracic portion has grown considerably below the level of the thyroid. It is more swollen than hitherto and its distal portion is subdivided into a considerable number of convolutions (Fig. 31, Thy.).

The intermediate cervical connective persists as an exceedingly thin solid cord (Cv.C.).

The dorsal plate is so intimately fused with the carotid gland and fundus præcervicalis (F.Pc.V.) as to be distinguishable from them only with difficulty.

The cat of 23.1 mm. (No. 466, Harvard collection) shows the thymus entirely free from the carotid gland, that on the left side being separated from the latter by a considerable interval. At its thoracic portion the organ is subdivided into numerous lobules.

In the 32 mm. pig (No. 74, Harvard collection) only the dorsal end of the thymus was specially examined. It still forms a flattened plate associated with the carotid gland and the lobules of the fundus præcervicalis. It is connected by the cervical connective with the now large and much lobed thoracic thymus.

In the 32 mm. cat (No. 500, Harvard collection, Fig. 68) the thymus is entirely unconnected with the carotid gland. The dorsal extremity of the cervical cord (Cv.C.) is placed immediately outside of the ventral edge of the lateral wing of the thyroid. The cord is somewhat convoluted. It is continuous at its ventral extremity with the thoracic thymus, which is much enlarged and subdivided into numerous lobules. The latter are solid and are composed of small-celled epithelial tissue. I could observe no indications of the formation of true lymphoid tissue in it.

In a rabbit of 20 days the thoracic thymus is very large and on each side it is subdivided into numerous lobules similar to those seen in the cat last described. It is connected by the cervical cord with the carotid gland, which is located close to the dorsal edge of the lateral wing of the thyroid.

(c″) The Origin and Structure of the Carotid Gland.

The carotid gland first appears in a 9 mm. pig (M^5 of my series, Fig. 36) as a mass of intertwined solid vesicles (C.Gl.), representing a series of folds of the anterior wall of the third pharyngeal pouch. The gland is therefore a purely epithelial structure of endodermal origin. The carotid artery (Car.) lies immediately in front of it and shows a small branch extending back toward the gland.

In the 10 mm. pig (Figs. 7-8, C.Gl.) the carotid gland is somewhat larger. As in the preceding stage, it is continuous with the peripheral half of the anterior wall of the pouch and even projects a slight distance beyond its lateral margin (Fig. 8). It here meets the ectoderm of the anterior wall of the third pharyngeal groove. Dorsally it projects a short distance above the upper margin of the pouch and partly curves backwards over it. The carotid artery (Car.) gives off a small branch, which, on reaching the gland, divides into numerous capillaries which form a rich network interpenetrating it in all directions. Ven-

trally they unite into a common vessel which opens into the inferior jugular vein.

In the 12 mm. and 13 mm. pigs the carotid gland forms a more regularly circumscribed, voluminous mass (Figs. 9-10, C.Gl.). It retains the same topographic relation to the third pouch as before, but has increased considerably in size (Fig. 13). Its follicular structure is clearly shown, and reminds one of that of the liver. Like the latter, it consists of a reticulum of numerous, closely intertwined follicles interpenetrated by a rich system of capillaries, the latter derived from the carotid artery (Fig. 53).

The gland and the associated solid wall of the pouch (= dorsal plate of the thymus) are intimately connected with each other (Figs. 38-40). In many specimens, owing to unsuitable staining, the two parts cannot be clearly distinguished from each other. In those appropriately double stained with hæmatoxylin and Bordeaux red or with alum-cochineal and orange G the definitive reticular structure of the gland is clearly shown.

In the 14 mm. pig (Figs. 14-15) the carotid gland shows no specially noteworthy features. On the dorsal side it projects considerably above the upper edge of the thymus and there comes in contact with the inner part of the fundus præcervicalis (F.Pc.).

In the 17 mm. pig (Figs. 19-20) the carotid gland appears to differ only in size from that just described. The same remark applies also to an 18 mm. animal (Figs. 45-46).

In the 20 mm. pig (Figs. 23-24) the carotid gland forms a moderately large ovoid organ lying to the outside of the sinus piriformis (S.Pi.). It is distinctly follicular in structure, but its individual follicles show no lumen.

In cats of 10.7 and 15 mm. the carotid gland is similar in essential respects to that in the pig last described. It appears to be less compact than the latter, the interspaces between the follicles being relatively larger (Fig. 63, C.Gl.).

In the pig of 24 mm. (Figs. 29-31) the carotid gland (C.Gl.) shows no peculiar characteristics.

In the cat of 23 mm. (Fig. 66) the carotid gland shows no special features. It resembles essentially that in a 15 mm. example.

In the pig of 32 mm. (Figs. 34-35, C.Gl.) the carotid gland has the same characteristics as hitherto, but is closely invested by the lobules of the proliferated fundus præcervicalis.

The cat of 31 mm. (Fig. 68, C.Gl.) shows the carotid gland as an ovoid body, located near the antero-dorsal angle of the lateral wing of the thyroid. It shows its follicular structure very clearly. It has lost its connection with the cervical cord of the thymus, the latter terminating opposite the ventral border of the thyroid.

In a 20-day rabbit (No. 172, Harvard series) the carotid gland shows its typical form and structure. It lies outside of the antero-dorsal angle of the lateral wing of the thyroid and is connected by the cervical cord with the thoracic thymus.

In the 21-day rabbit the gland occupies a depression in the outer surface of the lateral wing of the thyroid. It is now entirely unconnected with the cervical cord, the latter lying at a much lower level.

(c‴) The Sinus Præcervicalis and its Relation to the Thymus.

It will be recalled that in a 6.2 mm. cat (Figs. 59-60) the sinus præcervicalis (S.Pc.) forms an approximately funnel-shaped depression. The inner posterior portion corresponding to the stem of the funnel forms a deep pit, which extends diagonally inwards and backwards and terminates in a sharp edge, which at its ventral extremity is in contact with the lateral process of the fourth pouch. The outer relatively wide vestibule forms an approximately triangular depression, surrounded on all sides by the overhanging prominences of the adjacent parts—anteriorly by the hyoid arch, posteriorly by the anterior cervical region and ventrally by the pericardial prominence. Dorsally it becomes shallow and there blends with the side of the head without any perceptible break. At its ventro-anterior angle it is continued into the pericardio-cervical groove (Fig. 60). The inner wall of the sinus is formed by two low prominences representing the third and fourth pharyngeal arches.

In the 9.7 mm. cat the sinus præcervicalis (Fig. 61, S.Pc.) is deeper and narrower than in the stage just described—a difference due to the continued outgrowth and approximation of the adjacent hyoid and anterior cervical regions. That part of the third arch which immediately adjoins the hyoid region is rotated outwards with the latter and thus comes to face obliquely backwards. In this way the outer opening of the deeper part comes to lie on a level with the third pharyngeal groove (Ph.G.3). We shall henceforth designate this deeper part of the sinus the fundus præcervicalis (F.Pc.), a term applied to it by Kastschenko.

The opening of the fundus is triangular, narrow above, wider below (see right side of figure). At its dorsal apex the third pharyngeal arch

and anterior cervical prominence converge. The fourth pharyngeal arch, which is located at the inner extremity of the fundus, is thus partly hidden in lateral view.

The fundus has much the same features as hitherto. Its inner extremity, while still connected at one point with the fourth pouch (Fig. 62, Ph. P. 4), is prolonged above the latter and forms a slight dilatation situated a short distance back of the dorsal edge of the third pouch (Fig. 62, V.Pc.). This free, dilated portion is evidently to be compared with the vesicula præcervicalis (= vesicula thymicus of Kastschenko), which will be more fully considered in the descriptions of the pig.

The 10 mm. pig (Figs. 5-8) shows the sinus in a condition somewhat intermediate between the two last described. On the right side the fundus and the fourth pharyngeal pouch are still connected with each other, but on the opposite side they are entirely separate and are removed from each other by a considerable interval, which is largely occupied by the aortic arch proper (Ao.). The large size of the latter suggests that it may have been an active agent in effecting the separation of the pouch from the fundus. Thus, on the side where the two structures are still connected, the ventral side of the artery is closely pressed against the connecting part and is evidently exerting a pressure upon it which would tend to effect its separation. As we shall see, this soon takes place.

The inner extremity of the fundus is formed by a narrow, obliquely vertical groove—the fourth pharyngeal groove (Fig. 8, Ph. G.4). Where the fourth pouch retains its connection, it is confined to the ventro-internal angle of the fundus. From this point the remainder of the groove ascends diagonally forwards and at its dorsal extremity meets the corresponding part of the third groove (Fig. 7, Ph.G.3). There is thus included between the two a triangular convexity which represents the fourth pharyngeal arch. The third groove in its entire extent is connected with the underlying pouch. The latter is not joined to the bottom of the groove, but to its anterior wall, the lateral margin of the pouch reaching some distance beyond the deep part of the groove (Figs. 7-8).

On the side where it is no longer joined to the fourth pouch the blind, inner end of the fundus is turned obliquely backwards and comes into close relation with the inferior ganglion of the vagus. This part we shall hereafter designate the vesicula præcervicalis. In my estima-

tion, this is a more appropriate name for it than the term vesicula thymica, applied by Kastschenko.

In a 12 mm. pig, in consequence of the passive behavior of the sinus and the continued outgrowth of the surrounding parts, the sinus is still deeper and its margins are so near each other that, with the exception of its most external part, the entire sinus may be considered as included in the fundus (Fig. 13). The external opening of the latter is now relatively small. On its dorsal side the adjacent borders of the third pharyngeal arch and anterior cervical region have fused, leaving only a faint groove to mark the earlier extension of the sinus in that direction. On its ventral side the part of the head underlying the sinus has grown out and has united with the ventral extremity of the third arch, at the same time obliterating the groove earlier connecting the sinus with the pericardio-cervical fissure.

The outer limit of the fundus is approximately formed by the middle of the third pharyngeal arch. From this point it extends inwards and slightly backwards as a deep pocket, the blind inner extremity of which —the vesicula præcervicalis—terminates close to the inferior ganglion of the vagus. This part is formed by the third and fourth pharyngeal grooves and the intermediate fourth arch. In consequence of the diminished depth of the fourth groove, the fourth arch does not form as prominent a convexity as in the preceding stage.

In the 14 mm. pig (Figs. 14-16 and 18) all that remains of the sinus præcervicalis has become, by virture of its passive deepening and constriction, included in the fundus præcervicalis (F.Pc.), which now forms a deep, blind pocket opening to the exterior by a much reduced opening placed immediately under the posterior rim of the hyoid arch. The outer half of the fundus forms a relatively narrow duct—the ductus præcervicalis of Kastschenko—leading to the external opening (D.Pc.). The inner half is relatively wider and at its mesial end is continued into the vesicula (V.Pc.). In this part the earlier prominence of the fourth arch has flattened out and thus the third and fourth grooves cease to be longer distinguishable. In this way the inner end of the fundus assumes the form of a bulb.

In the next stage, *i.e.*, a 17 mm. pig, the narrow ductus forms a solid cord, which has just severed its connection with the external ectoderm (Figs. 20-21). The inner portion of the fundus now forms a relatively broad, flattened band, which is slightly concave on its posterior side (Fig. 21, F.Pc.). By its anterior wall it is closely connected with the

carotid gland and the epithelial plate now forming the dorsal end of the thymus, but representing originally the peripheral body of the third pouch (D.Pl.). With the exception of its vesicula, the fundus is without a distinct lumen. The vesicula originates at its ventro-internal angle, then bends backwards and terminates, as before, in the anterior part of the ganglion of the vagus.

In the 20 mm. pig the ductus has shrunken to a mere remnant (Fig. 28, f. pc.). The remainder of the fundus præcervicalis, excepting the vesicula (v. pc.), forms a flattened band, which is closely wedged in between the lateral surface of the carotid gland (c. gl.) and the hypoglossal nerve (xii), over which its free end curves after the manner of a hook. At the lower posterior side of the carotid gland it expands to form the vesicula, which retains the same relation to the ganglion of the vagus as hitherto. The dorsal extremity of the thymus is wedged in between this part of the fundus and the carotid gland (Fig. 45).

It will be noticed that the fundus now has an ascending course. Beginning at its vesicular extremity, it extends diagonally upwards and outwards over the lateral surface of the carotid gland to the upper side of the hypoglossal nerve, over which it curves like a hook. This condition, as I shall attempt to show presently, is to be correlated with the changes in position of the nerve mentioned.

The condition of the fundus præcervicalis is essentially similar in a cat of 10.7 mm. The left ductus, however, is considerably longer than that on the opposite side.

In a cat of 15 mm. the ductus has disappeared. The rest of the fundus (Fig. 63, F.Pc.) is coiled over the top and back of the carotid gland. It shows a distinct vesicle, located on the posterior surface of the gland.

The pig of 24 mm. shows the fundus as a much coiled, mostly solid, band. A slight lumen persists in the vesicula præcervicalis, which is now located on the postero-inferior surface of the carotid gland, some distance in front of the ganglion of the vagus. From this part the fundus curves upwards over the outer surface of the gland as an exceedingly thin, flattened ribbon, which at its dorsal extremity expands slightly into the hook-shaped process, which, as before, is curved outwards over the hypoglossal nerve (Fig. 31, F.Pc. and F.Pc.V.).

In a pig of 25 mm. the condition of the fundus is very similar to that just described. The part of it adjoining the vesicula is somewhat broader and is sub-divided into a number of small lobules.

In the 32 mm. pig (Figs. 34-35) the fundus shows a remarkable increase in size and now forms a prominent, irregularly lobed mass appendaged to the carotid gland (F. Pc.). That portion (F. Pc. V.) adjoining the vesicula has subdivided into several lobules, from which the original vesicula itself is not clearly distinguishable. From this part the thin band curves dorsally around the outer side of the carotid gland, and at its upper extremity is continued into the hook-shaped process, which has undergone a remarkable proliferation into a relatively immense, much convoluted mass (F. Pc.). The hypoglossal nerve (XII) partly divides it on the left side (Fig. 34) into two unequal lobes—a large outer and a smaller internal. On the right side (Fig. 35) the division is complete, the outer being separated from the inner by a thin plate of connective tissue. The outer, free portion represents the so-called thymus superficialis of Kastchenko. (Fig. 35; Th.S.).

This division of fundus is evidently—as indeed Kastchenko first pointed out—a result of the pressure produced by the hypoglossal nerve. On the left side (Fig. 34), where the two divisions of the præcervical mass are united, this nerve lies in the constriction between them immediately under the connecting cord. Where, as on the right side (Fig. 35), the division is complete, the nerve lies entirely above the præcervical mass. These relations naturally suggest that the displacement of the nerve itself has been the active cause in producing the present condition of the structure. This view is further supported by the relations between the two structures as observed in earlier stages. In pigs of 10, 12 and 14 mm, the nerve, after descending behind the sinus præcervicalis, curves forward some distance below its ventral margin (Fig. 40). In the 17 mm. pig it lies immediately under the fundus close to where the latter meets the carotid gland (Figs. 45-46). It has thus assumed, relative to the fundus, a more dorsal position—a change associated with the ventral displacement of the thymus owing to the elongation of the neck. Later, as these alterations in position continue, the nerve produces an upward pressure on the fundus, and thus causes it to assume an ascending course with its peripheral free extremity hanging loosely, like a hook, over the nerve. This is the condition observed in a 25 mm. pig (Fig. 31). This portion of the fundus then undergoes a rapid proliferation, perhaps an indirect result of the mechanical irritation produced by the nerve, and thus attains the

form characteristic of the present stage, when the præcervical mass is being finally constricted into two separate parts.

As this is the latest stage in the series of pig embryos which I have examined, I can state nothing as to the future history or fate of the præcervical body in this animal. It seems probable from its large size that it would be present at birth. Kastschenko observed it in an 80 mm. pig. Prenant claims that it is present at birth in the sheep.

In cats of 23.1 mm. and 31 mm. I was unable to find any certain traces of a fundus præcervicalis. This fact indicates that in this animal the later behavior of the organ must be less complicated than in the pig. It is probable that it rapidly disappears.[1]

In two late stages of the rabbit I could find only extremely uncertain traces of the fundus. In a twenty days' fœtus a slight process is present at the dorsal apex of the left carotid gland. In a twenty-one days' example this has apparently disappeared, but some distance above the gland and entirely disconnected from it is a minute lymphoid body. This may possibly represent the transformed process seen in the twenty days' individual. However, this point cannot be settled until additional material is examined.

Review and Comparisons.

The third pharyngeal pouch when typically developed closely resembles the second. Like the latter, it has a prominent ventral diverticulum.

The pouch becomes transformed into the thymus. The greater part of the latter, *i. e.,* its thoracic portion and cervical cord, are formed by the downgrowth of the ventral diverticulum.

The carotid gland is a derivative of the dorsal portion of the pouch. It arises as a series of follicular outgrowths from the anterior wall of the latter.

The pouch does not separate entirely from the ectoderm, but remains attached to that of the sinus præcervicalis. Separation from the superficial ectoderm takes place by the deepening and subsequent constriction of the sinus, which accompanies the pouch in its passive withdrawal from the surface of the body.

The connection of the pouch with the pharynx is at first formed by a wide opening. Later this is reduced to a solid cord, which subsequently constricts, thus leaving the pouch as an entirely independent body.

[1]Verdun asserts that it had entirely disappeared in an embryo of 16 mm.

The dorsal body of the pouch after the separation of the attached fundus præcervicalis from the skin forms the relatively inconspicuous dorsal extremity of the thymus. It loses all trace of a lumen and thus forms a solid epithelial plate wedged in between the carotid gland and fundus præcervicalis.

The fully formed thymus is differentiated into three parts—a ventral, thoracic thymus, an intermediate cervical cord and a dorsal plate to which the carotid gland is attached. In the cat the connection of the thymus with the carotid gland is interrupted in the later stages of development. In the rabbit the two structures become disconnected by the twenty-first day of development.

The carotid gland is typically an ovoidal body located in the neck close to the outer side of the lateral wing of the thyroid. Structurally it is a reticulum of solid follicles, interpenetrated by a system of capillaries derived from the carotid artery.

The sinus præcervicalis, as a result of its passive deepening by the outgrowth of surrounding parts, is transformed into a deep recess, the fundus præcervicalis. The latter is finally cut off from the ectoderm, and, by retaining its connection with the dorsal plate of the thymus, comes to lie at a considerable distance below the surface. Its inner extremity forms for some time a vesicle, which enters into close relation with the inferior ganglion of the vagus.

In the cat the fundus apparently is early atrophied. In the pig, however, it undergoes a strong proliferation, giving rise to a prominent, irregularly convoluted mass closely associated with the carotid gland. The peripheral lobe is separated from the remainder by the constriction effected by the hypoglossal nerve. This portion represents the so-called thymus superficialis of Kastschenko.

In late stages of the rabbit all remains of the fundus præcervicalis have largely, if not entirely, disappeared. Only very doubtful traces of it remain.

The formation of the thymus as described in this paper is in harmony with all the more recent observations. These prove that the organ is of purely endodermal origin and that all but an insignificant portion arises from the ventral diverticulum of the third pouch.

With regard to the final lymphatic transformation of the thymus, I can say little, owing to the fact that I did not have at my disposal a sufficient number of older stages to enable me to form any decided opinion as to the process by which the change took place. In the rabbit

in which I examined a large series of relatively late fœtal stages the follicles as late as the twenty-first day maintained the same histological character, that is, they were composed of small-celled epithelial tissue. The latter, however, bears a strong resemblance to ordinary lymphoid tissue, and its persistence at this late period in this animal suggests that the fundamental tissue of the definitive thymus may be really epithelial and not lymphoid tissue. Such a view has recently been supported by Stöhr. On page 9 of his article "Ueber die Thymus" (Sitzungs-Berichte der physikalisch-medicinischen Gesellschaft zu Würzburg) he writes, *"Die Thymus ist ein epitheliales Organ von Anfang bis zu Ende, so gut wie etwa eine Speicheldrüse."* My own observations do not cover sufficiently late stages to enable me to give any strong support to this view.

Regarding the origin and structure of the carotid gland there has been considerable diversity of opinion. Steida first described the organ and postulated its origin from the endoderm. This view was later supported by Fischelis. Kastschenko, on the other hand, makes no distinction between the carotid gland and the associated dorsal extremity of the thymus, both of which are included in his nodulus thymicus. The latter he regards as simply the much swollen dorsal end of the thymus. He apparently overlooks the vesicular structure of the gland—an oversight which is not surprising when one bears in mind that this structure is only shown in sections suitably double-stained.

Steida, while correct in his derivation of the gland from the endoderm, errs when he states that it later separates from the thymus *anlage* and comes into contact with the carotid artery. Kastschenko maintains that the nodulus thymicus, with which he considers the carotid gland of Steida to correspond, never separates from the thymus. He shows that the body which Steida took for the gland in later stages is of an entirely different character. It forms *ein verlängerter ellipsoider Knoten,* which surrounds the internal carotid at the bifurcation of the common artery. This he maintains is merely a local thickening of the adventitia of the artery.

My observations show that the contention of Kastschenko is correct. The carotid gland does not separate from the thymus, at least not in any stages examined by the two investigators mentioned. I find the same peculiar thickening of the adventitia of the internal carotid artery as described by Kastschenko in both the pig and cat. It is particularly large and prominent in pigs of 17-24 mm. and cats of 23-31 mm. In

both it is located at a considerably higher level than the true carotid gland.

Piersol in his study of the rabbit does not, like Kastschenko, distinguish between the carotid gland and the dorsal extremity of the thymus. It, however, is probably present, as it is clearly distinguishable in the later stages of the same animal. Its presence in the earlier stages has been shown by Verdun.

According to Prenant, the merit of having determined that the carotid gland is a proliferation from the epithelium of the third pouch belongs to de Meuron. Prenant describes and figures correctly the histological structure of the organ. His work is based upon the sheep, but his results are in all respects in harmony with what I have observed in the pig.

In Verdun's work, "Dérivés branchiaux chez les vertébrés supérieurs," the term *"la glandule branchiale III"* is applied to this organ. The term "carotid gland" he applies to the conjunctival proliferation surrounding the carotid artery at its bifurcation. There has been much confusion in the use of this term. As already mentioned, Steida applied it to both structures, though in the first part of his description, *i. e.,* of the earlier stages, he applies it to the endodermal derivative. I have, therefore, retained it for the latter. The conjunctival swelling itself is no gland and consequently does not deserve to be called one.

The exact share taken by the ectoderm in the formation of the thymus has been a puzzling problem. His early advanced the view that the entire thymus was an ectodermal structure, but soon abandoned it. Fischelis would apparently consider it as half endodermal, half ectodermal. Kastschenko derives the bulk of the organ from the endoderm, but considers that its dorso-peripheral portion, which he designates by the term, thymus superficialis, is of ectodermal origin.

Since the last investigator the part taken by the ectoderm in the formation of the thymus has been largely ignored. The prevailing opinion regards the thymus as of purely endodermal origin. My own observations, however, corroborate the statements of Kastschenko so far as his facts are concerned, but, unlike the latter, I do not consider the so-called thymus superficialis as of sufficient constancy or importance to warrant the application to it of this rather pretentious term or to be considered as an actual constituent of the thymus.

Kastschenko describes correctly the origin of his thymus superficialis by the constriction of the fundus præcervicalis.[2] His observations were

[2]This is "*Le fond du troisième sillon ectodermique*" of Verdun.

made upon pigs, and the large size which the outer free lobe of the fundus attains in these creatures probably led him to consider it as an important part of the dorsal extremity of the thymus. Its similarity in histological structure to the thoracic thymus was another fact upon which he based his view as to its importance.

To me these facts do not warrant the ascription of the ectodermal structure under consideration to the thymus. First, as regards the prominence of the outer lobe of the fundus, it is evident from my observations on the cat that this condition is not general among mammals. Even in the pig it does not seem to be absolutely constant, since Kastschenko himself speaks of an animal of 30 mm., in which he could find no trace of a thymus superficialis. In the sheep, according to Prenant's account, it is evidently similar to that in the pig. It might be inferred from these facts that a prominent fundus præcervicalis is limited in late fœtal life to the ungulates,[3] but is probably more or less early atrophied in other forms.

With regard to the histological structure of the so-called thymus superficialis, it will suffice to state that its similarity in this regard to the thymus is no greater than that which any branching epithelial mass shows. In specimens which I examined the lobuli of the fundus præcervicalis bore as strong a resemblance to those of the salivary glands as to the same parts in the thymus. The resemblance is therefore unimportant.

I would therefore conclude that the fundus præcervicalis is to be looked upon as an associate of the thymus, but not as an integral part of it.

Prenant evidently considers the vesicula thymica of Kastschenko as including all the derivatives of the fundus præcervicalis. He regards it apparently as of endodermal origin and hence as a part of the thymus. He says, "La tête du thymus se developpe aux dépens de la 3d poche entodermique et d'un diverticule de cette poche; celui-ci, qui est sans doute identique à la vesicule thymique Kastschenko, s'enforce dans le ganglion du vague." This statement is erroneous. The vesicula thymica of Kastschenko is not a diverticulum of the third pouch, but represents the inner blind recess of the fundus præcervicalis, which I prefer to call the vesicula præcervicalis.

Verdum correctly considers his *"le fond du troisième sillon ectodermique"* as corresponding to the "vesicule thymique" of Kastschenko.

[3]Verdun, however, states that it disappears entirely in an 18 mm. calf.

He, however, does not trace its transformations in the pig, merely stating that he had found it and its outer connective in a 19 mm. embryo.

D. THE FOURTH PHARYNGEAL AND ITS TRANSFORMATION INTO THE LATERAL THYROID AND GLANDULE THYROIDIENNE.

In a 6.2 mm. cat we noticed the division of the fourth pouch into two segments by a lateral constriction (Figs. 58-59). The more dorsal of these constitutes the body of the pouch; it projects strongly backwards and on its outer side gives off a slender process, which connects with the ectoderm of the inner extremity of the sinus præcervicalis (Fig. 60). The remaining segment forms a ventral diverticulum (V.D.4), which at this period extends for a short distance downwards, forwards and inwards.

The 9.7 mm. cat shows nearly similar conditions. The ventral diverticulum (Fig. 61, V.D.4) has lengthened slightly and begins to assume a more tubular aspect. The dorsal extremity forms a more distinct posterior process. The lateral process still persists, and, as before, connects with the ectoderm of the fundus præcervicalis.

In a 10 mm. pig (Student collection, Harvard) the fourth pharyngeal pouch of one side has entirely separated from the ectoderm, while on the opposite side the slender connecting process still persists (Figs. 7-8). The dorsal process (Gl.T.) projects strongly backwards. The ventral diverticulum forms a relatively short, rounded protuberance. Its ventral extremity lies immediately under the aortic arch. It bears the same relation to the latter that the corresponding part of the preceding pouch does to the carotid arch.

In a second 10 mm. pig (No. 401, Harvard series) the fourth pouch of each side has severed its connection with the ectoderm (Figs. 4-6). The ventral diverticulum (V.D.4) forms a compressed, antero-ventrally projecting sac. The lateral process has disappeared. The dorsal process (Gl.T.) retains the same characteristics as hitherto.

A 12 mm. pig is apparently exceptional in that the fourth pouch of one side retains its connection with the fundus præcervicalis (Fig. 10). On the opposite it has essentially the same features as in the preceding stage.

In two pigs of 13 and 14 mm., respectively, the fourth pouch has been transferred to a considerably lower level by the downward flexure of the sinus piriformis. The ventral diverticulum (Figs. 14 and 20, La.T.) shows increased length and forms a tubular process, whose axis

is more nearly vertical than in the preceding stages. Its distal extremity is somewhat bulb-like in form (Fig. 39, la. t.), but its basal portion has become constricted to a narrow duct, opening into the sinus piriformis (Fig. 40). The dorsal portion is much reduced; it is represented only by the dorsal process, which forms a spheroidal body attached by a narrow stalk to the duct (Figs. 14, 16, Gl.T.). It contains only a slight lumen. Otherwise it forms a solid mass, whose walls are apparently thrown into series of tight folds. These produce an appearance simulating that of the carotid gland—an organ produced from the homologous part of the preceding pouch.

At this period the distal extremity of the ventral diverticulum is without any connection with the median thyroid. The latter at this time is rather small and lies in the mesial plane above and between the ventral extremities of the thymus downgrowths.

In both the 17 and 18 mm. pigs the ventral diverticulum has still further elongated, largely as a result of the lengthening of its duct, which now appears as a slender, solid cord (Figs. 19, 21). A lumen is present only in the terminal vesicular part. The dorsal process (Gl.T.) presents the same appearance as before; its lumen, however, has disappeared and its structure more clearly resembles that of the carotid gland (Fig. 45, c.gl.). We shall henceforth designate it the "glandule thyroidienne"—a term applied to it by Prenant.

The median thyroid now occupies a position considerably posterior to that occupied by it in the preceding stage. It has grown considerably and has assumed a horseshoe shape, owing to the outgrowth of its lateral wings, which at their outer extremities almost touch the vesicles of the ventral diverticulum.

In a cat of 10.7 mm. the ventral diverticulum has separated from the pharynx and forms a pear-shaped vesicle—the lateral thyroid vesicle—lying free in the mesenchyme by the side of the trachea. Its lumen is reduced to a mere slit—a result of the internal proliferation of its walls. It bears the same relation to the thyroid as in the pig of the stage last described.

I was unable to distinguish in this individual any clear evidence of the presence of a "glandule thyroidienne."

In a 20 mm. pig the lateral thyroid vesicle shows only fragments of a lumen. Otherwise it is a solid structure and is composed of several layers of small cells of epithelial nature, but closely resembling lymphoid tissue. They have essentially the same character as the elements forming the lobules of the thymus.

The median thyroid has moved backwards to a position immediately in front of the trachea (Figs. 23, 25). Its lateral wings have grown back over the outer side of the lateral thyroids, the latter thus being partly embedded on their inner sides.

An exceedingly fine duct still connects the lateral thyroid with the pharynx.

The dorsal process (Gl.T.) forms a small spheroid attached to the remains of the duct. It is clearly composed—like the carotid gland—of a close network of solid follicles, the interstices of which are traversed by a system of capillaries (Fig. 54).

A cat of 15 mm. (Fig. 65) shows each lateral thyroid embedded in a depression on the inner side of the corresponding lateral wing of the median thyroid. Its minute structure is easily distinguishable from that of the latter organ by its solid lymphoid character.

A "glandule thyroidienne" does not appear to be present.

In a pig of 24 mm. the lateral thyroid is also largely surrounded by and embedded in the lateral wing of the thyroid. Only its more dorsal portion projects above the latter (Fig. 29, La.T.).

The "glandule thyroidienne" is present, at least on the right side. I found no clear trace of it on the opposite side.

In a 25 mm. pig conditions are similar to those just described, but both glands are present. That on the left, however, is much reduced, being only about a fifth the size of that on the right. I may add that the same difference in size between the glandules of the two sides was noticed in an 18 mm. pig.

In a 23.1 mm. cat the lateral thyroid bears the same relation to the lateral wings of the thyroid as in the pig last described. I could, however, find no readily distinguishable traces of the "glandule thyroidienne."

In a 31 mm. cat such lateral thyroid is deeply embedded in a concavity on the inner surface of the corresponding wing of the thyroid. No part of it projects beyond the periphery of the latter at any point.

Two minute bodies (Fig. 68) were observed, one on each side, close to the lateral border of the œsophagus. They apparently correspond in position with the glandules, but, as I could not readily determine their minute structure in the specimen examined, I think it improbable that they represent these. They are probably independent structures, lymphatic in origin.

In a 21-day rabbit the lateral thyroid forms a solid, ovoidal mass deeply embedded in a flask-shaped depression on the inner side of the

lateral wing of the thyroid. As in earlier stages, it is readily distinguishable from the latter by its different histological structure.

Review and Comparisons.

The fourth pharyngeal pouch resembles the third in producing two distinct structures, the lateral thyroid and the "glandule thyroidienne."

The lateral thyroid is formed by the elongation of the ventral diverticulum. This at first is perfectly continuous with the side of the pharynx, but the connecting part early becomes constricted, assumes the form of a solid cord and subsequently separates from the pharynx. The remaining ventral portion forms a piriform vesicle, which soon becomes solid and later by backward growth of the median thyroid becomes embedded in the lateral wings of the latter.

The dorsal body of the pouch early loses its connection with the ectoderm and undergoes partial atrophy. A considerable portion, however, is transformed into the *"glandule thyroidienne"* of Prenant. In the cat I have not been able to trace the history of this structure, but Verdun, who examined a large series in this type, asserts that along with the lateral thyroid it becomes embedded in the lateral lobe of the median thyroid. In the pig it persists for a considerable period, but never forms any connection with the median thyroid.

The results of my study of the fourth pouch and its derivatives are, as a whole, corroborative of previous investigations. The main facts in its development had been ably presented by Kastschenko, although he overlooked the "glandule thyroidienne" which was described by Prenant. The latter gives a full account of the microscopic structure of the organ and distinctly asserts its homology with the carotid gland of the preceding pouch.

Verdun derives from the fourth pouch another structure which he terms "thymus IV" on account of its supposed homology with the thymus of the preceding pouch. This, he states, arises as a "diverticule externe et ventral." In all the examples examined by me I have noticed nothing to suggest this structure. Verdun describes it most fully in the case of the cat, but states that it is only exceptionally, and then only slightly, developed in the rabbit. In the camel and ox he finds it doubtfully represented by certain lobules associated with the *"glandule thyroidienne."* In the other forms—man, mole, opussum, dog, pig, sheep—he gives no very convincing evidence of its presence. In view of these facts, *i. e.,* its exceptional presence in one form and its doubtful

presence in certain others, it seems to be that this thymus IV cannot in the mammals have the significance Verdun attributes to it. At least, to my mind, the actual facts do not bear it out, whatever its theoretical support may be.

The lateral thyroid Verdun regards as an autonomous structure, representing the post-branchial bodies of lower vertebrates. To me it appears that this is done for the most part on purely theoretical grounds. So far as actual facts are concerned, the lateral thyroid in the mammals closely follows the thymus in its behavior, and I can see no clear and convincing reason for regarding it as other than the ventral diverticulum of the fourth pouch and therefore homodynamous with the thymus of the preceding pouch. I know of no decisive evidence against the view advocated by Verdun, but the facts adduced by him are not sufficient to establish his point. I therefore follow the usage of most writers in regarding the lateral thyroid as a part of the fourth pouch.

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EXPLANATION OF FIGURES.

Fig. 1.—Lateral view of the pharynx in a 6.5 mm. pig, M^2, for parts consult Fig. 58. × 60, reduced ⅓.

Fig. 2.—Dorsal view of the pharynx in the same embryo. D. A. 1, dorsal apex of first pharyngeal pouch; HYP., hypophysis; Ph. P. 1-4, pharyngeal pouches; S. P., Seessel's pocket; S. T. P., sulcus tympanicus posterior; S. T. T. sulcus tubo-tympanicus; S. T. Ty., sulcus tensoris tympani; V. D. 1-3, ventral diverticula of the pharyngeal pouches; P.P. 4, posterior process of the fourth pouch. × 50, reduced ⅓.

Fig. 3.—Ventral view of pharynx and larger blood-vessels in the same embryo. HYP., hypophysis; Ph. P. 1-4, pharyngeal pouches; V. D. 1-4, ventral

diverticula; M., mouth; Tr., trachea; Ao. 2-5, aortic arches; D. Ao., dorsal aorta; Pul., pulmonary artery; T. Ao., truncus arteriosus; Tyr., thyroid; Ch. Ty., chorda tympani. × 50, reduced ⅓.

Fig. 4.—Lateral view of the pharynx in a 10 mm. pig, No. 401, Harvard medical collection. D. A. 1-3, dorsal apices of first three pouches; Gl. T., dorsal process of the fourth pouch, the primordium of the *glandule thyroidienne;* S. M. F., submeckelian fold; S. T. T., sulcus tubo-tympanicus; S. T. Ty., sulcus tensoris tympani; Ton. F., dorso-lateral region of the second pouch, later transformed into the tonsillar recess; V. D. 1-4, ventral diverticula; V. F., vestibular fold. × 60, reduced ³/₅.

Fig. 5.—Dorsal view of the pharyngeal region in the same specimen. Symbols as before. × 60, reduced ³/₅.

Fig. 6.—Ventral view of the same region in the same embryo. Symbols as before. × 60, reduced ³/₅.

Fig. 7.—Ventral view of the region of the third and fourth pouches in a 10 mm. pig, students' collection, Harvard medical collection. F. Pc., fundus præcervicalis; Ph. G. 3, third pharyngeal groove; 10, vagus; other symbols as in Fig. 8. × 80, reduced ½. Figure inverted.

Fig. 8.—Dorsal view of the same region shown in Fig. 7. Ao., aorta; Car., carotid; C. Gl., carotid gland; D. A. 3, dorsal apex of third pouch; Gl. T., dorsal process of fourth pouch, later the *glandule thyroidienne;* Ph. G. 4, fourth pharyngeal groove, forming the inner edge of the fundus præcervicalis; S. Pc., sinus præcervicalis; V. D. 2-3, ventral diverticula of second and third pouches. × 80, reduced ½.

Fig. 9.—Lateral view of the pharynx in a 12 mm. pig, No. 518, Harvard medical collection. C. Gl., carotid gland; remaining symbols as in Figs. 4-6. × 60, reduced ³/₅.

Fig. 10.—Dorsal view of the pharyngeal region in the same specimen. D. Pr., dorsal prominence of the tonsillar fold; F. Pc., fundus præcervicalis; V. Pc., vesicula præcervicalis; other symbols as in preceding figures. × 60, reduced ³/₅.

Fig. 11.—Ventral view of same parts as in Fig. 10. Symbols as in preceding figures. × 60, reduced ³/₅.

Fig. 12.—Region of the second pharyngeal pouch in a 12 mm. pig, No. 518, Harvard medical collection, viewed from below. cv., concavity on the lower surface of tonsillar fold (ton. f.); o., ridge connecting second and third pouches; v. d. 1-2, ventral diverticula of first and second pouches. × 30.

Fig. 13.—Region of sinus præcervicalis in a 12 mm. pig, students' collection, Harvard medical collection, ventral view. G. Nod., ganglion nodosum. Remaining symbols as before. × 80, reduced ½.

Fig. 14.—Lateral view of the pharynx in a 14 mm. pig, No. 65, Harvard medical collection. A-L. F., alveolo-lingual ridge; C. Gl., carotid gland; C. V., concavity on ventro-lateral wall of tonsillar fold; D. A. 1-2, dorsal apex of

first and second pouches; F. Pc., fundus præcervicalis; Fl. P., filiform process of second pouch; Gl. T., glandule thyroidienne; La. T., vesicle of lateral thyroid; P. T. R., posterior tympanal margin; S. M. F., submeckelian fold; S. T. T., sulcus tubo-tympanicus; S. T. Ty., sulcus tensoris tympani; Thy., thymus; Ton. F., tonsillar fold (=sinus tonsillaris); Tyr., median thyroid; V. D. 2, ventral diverticulum of second pouch; V. F., vestibular fold; y., interval between vestibular and submeckelian fold. × 60, reduced $^3/_5$.

Fig. 15.—Dorsal view of pharyngeal region in the same embryo, ectoderm shown only on one side. D. Pr., dorsal prominence of tonsillar fold; F. Pc., fundus præcervicalis; V. Pc., vesicula præcervicalis; other symbols as before. × 60, reduced $^3/_5$.

Fig. 16.—Ventral view of the parts shown in Fig. 15. × 60, reduced $^3/_5$.

Fig. 17.—The region of the second pharyngeal pouch, ventral view, in a 14 mm. pig, No. 65, Harvard collection. a-l. f., alveolo-lingual ridge; fl. p., filiform process of second pouch; s. pi., sinus piriformis; s t p., sulcus tympanicus posterior. Other symbols as in Fig. 12. × 30.

Fig. 18.—The region of the sinus præcervicalis in a 14 mm. pig, same specimen, ventral view. D. Pc., ductus præcervicalis; Fl. P., ventral end of filiform process of second pouch; F. Pc., fundus præcervicalis; G. Nod., ganglion nodosum; Ph. P. 3, third pharyngeal pouch; V. Pc., vesicula præcervicalis. × 80, reduced $^2/_3$.

Fig. 19.—Lateral view of pharynx in a 17 mm. pig, No. 51, Harvard medical collection. A-L. F., alveolo-lingual fold; C. V., concavity on ventro-lateral wall of tonsillar fold; Cv. C., cervical cord of the thymus; D. A. 1-2, dorsal apex of first and second pouches; D. Pl., dorsal plate of thymus (the carotid gland is closely associated with this part, but in this specimen it was not sufficiently differentiated by the stain to enable its outline to be accurately traced); Fl. P., filiform appendix of second pouch; F. Pc., fundus præcervicalis; La. T., lateral thyroid vesicle, the *glandule thyroidienne* projects backwards from its dorsal end; S. M. F., submeckelian fold; S. Pi., sinus piriformis; S. T. T., sulcus tubo-tympanicus; Ton. F., tonsillar fold; Thy., thymus; Tyr., thyroid; V. F., vestibular fold; y., space between vestibular and submeckelian folds. × 60, reduced $^3/_5$.

Fig. 20.—Dorsal view of same parts shown in Fig. 19. S. T. Ty., sulcus tensoris tympani; S. T. P., sulcus tympanicus posterior; D. Pr., dorsal prominence of tonsillar fold; C. Gl., carotid gland. × 60, reduced $^3/_5$.

Fig. 21.—Ventral view of same parts shown in Figs. 18-19. E. Au., external auditory tube; Gl. T., *glandule thyroidienne*. Other symbols as in Fig. 19. × 60, reduced $^3/_5$.

Fig. 22.—Region of the second pharyngeal pouch in a 17 mm. pig, No. 51, seen from below. Symbols as in Figs. 12 and 17. × 30.

Fig. 23.—Lateral view of pharynx in a 20 mm. pig, No. 542, Harvard medical collection. D. A. 1, dorsal apex (recessus anterior) of tympanic

pouch; Mn. F., manubrial fossa; S. Pi., sinus piriformis; z., indentation between tympanic pouch and tonsillar fold. × 60, reduced $^3/_5$.

Fig. 24.—Dorsal view of pharynx in same specimen. × 60, reduced $^3/_5$.

Fig. 25.—Ventral view in same specimen. × 60, reduced $^3/_5$.

Fig. 26.—A portion of the pharynx, including tympanic pouch and tonsillar fold in a 20 mm. pig, viewed from the posterior side. pm. f., post-manubrial ridge; ps. f., post-salpingeal fold. Other symbols as before. × 30, reduced ⅓.

Fig. 27.—The same structure as in Fig. 26, viewed from anterior side. Symbols as in preceding figure. × 30, reduced ⅓.

Fig. 28.—Thymus and associated parts in the same animal, front view, 12, hypoglossal nerve; other symbols as before. × 30.

Fig. 29.—Lateral view of pharynx in a 24 mm. pig, Harvard medical collection. × 60, reduced $^3/_5$.

Fig. 30.—Dorsal view of the same pharynx as in Fig. 29. × 60, reduced $^3/_5$.

Fig. 31.—Left thymus of same animal with carotid gland and præcervical appendix. Cv. C., cervical cord; F. Pc., hook-shaped portion of fundus præcervicalis; F. Pc. V., ventral segment of the fundus—this is joined to F. Pc. by a narrow connective extending over the outer surface of the carotid gland, but hidden from view in figure by the oblique position of the latter. × 80, reduced ½.

Fig. 32.—Lateral view of pharynx in a 32 mm. pig, Harvard medical collection. G. Ep., glosso-epiglottic fold; Mk. F., Meckelian fossa; Mn. F., manubrial fossa; other symbols as before. × 60, reduced $^3/_5$.

Fig. 33.—Dorsal view of same structure as in Fig. 32. The naso-pharynx is represented as cut across, thereby showing its interior. × 30, reduced ½.

Fig. 34.—Left carotid gland and associated præcervical mass and hypoglossal nerve in 32 mm. pig, anterior view. For symbols, see Fig. 31. × 80, reduced ½.

Fig. 35.—Right carotid gland and associated parts in the same animal, posterior view. The carotid gland is represented as sectioned in the plane of the paper. The præcervical mass has divided into two parts, internal, F. Pc., and external, Th. S. The latter is the thymus superficialis of Kastschenko. × 80, reduced ½.

Fig. 36.—Part of a sagittal section of the head of a 9 mm. pig, showing origin of carotid gland. C. Gl., carotid gland; Per., pericardial cavity. Other symbols as in preceding figures. × 50, reduced ⅓.

Fig. 37.—Part of a transverse section of a 13 mm. pig (M^1) showing the final separation of the first pouch from the skin. Coch., cochlea; Ch. Ty., chorda tympani; D. A. 1, dorsal apex with the part by which the pouch is last connected with the skin; Impr., impressio cochlearis; Ph. G. 1, the first pharyngeal groove, its undulating course causes it to be sectioned twice in the section; V. D. 1, ventral diverticulum of first pouch. × 50, reduced ½.

Fig. 38.—Part of a transverse section of the region of the third pouch in a 13 mm. pig (M^1). d. pl., dorsal lamina of the thymus. Other symbols as in preceding figures. × 50, reduced ½.

Fig. 39.—Similar section slightly posterior to last. ph. g. 2, second pharyngeal groove. × 50, reduced ½.

Fig. 40.—Section posterior to last, passing through fundus præcervicalis, f. pc.; or 3, ectodermal organ of third pouch; pul., pulmonary artery. × 50, reduced ½.

Fig. 41.—Part of a transverse section through the head of an 18 mm. pig, M^2. The section passes close to the oral extremity of the tympanic pouch. al. f., alveolo-lingual fold; G. Gas., gasserian ganglion; s. p. c., superior petrosal nerve; 5^3, inferior maxillary division of trigeminal. × 50, reduced ½.

Fig. 42.—Part of a similar section, a few sections behind the preceding. × 50, reduced ½.

Fig. 43.—Similar section, posterior to preceding. d. l. s., dorso-lateral wall of tympanic pouch; G. Gn., geniculate ganglion; p. g. 1, first pharyngeal groove. × 50, reduced ½.

Fig. 44.—Similar section in region of the dorsal apex of the tympanic pouch. G. Au., auditory ganglion; hy., hyoid; thr., thyroid cartilage; 7, main trunk of facial, showing its two divisions, the outer being the basal portion of the chorda tympani. × 50, reduced ½.

Fig. 45.—Section near hind margin of tympanic pouch. The latter lies in the upper right-hand corner. dc. t., duct of lateral thyroid; f. pc., fundus præcervicalis—the dorsal plate of the thymus lies between this and the carotid gland, c. gl. × 50, reduced ½.

Fig. 46.—Section slightly posterior to preceding. gl. t., glandule thyroidienne; ps. f., post-salpingeal fold; v. pc., vesicula præcervicalis. × 50, reduced ½.

Fig. 47.—Part of a transverse section of the head of a 25 mm. pig, M^4. The section passes near the front end of the tympanic pouch. v. f., vestibular groove. × 50, reduced ½.

Fig. 48.—Similar section near anterior edge of submeckelian fold in same animal. Mk. f., Meckelian fossa; s-m. f., submeckelian fold; vls., ventro-lateral wall of tympanic pouch. × 50, reduced ½

Fig. 49.—Section through middle part of the submeckelian fold in same animal. e. au., external auditory meatus. × 50, reduced ½.

Fig. 50.—Section slightly posterior to the point where tympanic pouch and pharynx are connected, pig, 25 mm. The post-salpingeal fold projects from the sides of the pharynx immediately internal to the tympanic pouch. mn., manubrium of the malleus. × 50, reduced ½.

Fig. 51.—Section through the posterior segment of the tympanic pouch. p. m. f., post-manubrial ridge; s. t. ty., sulcus tensoris tympani; t. s., tensor muscle; v. m. r., ventro-mesial border. × 50, reduced ½.

Fig. 52.—Part of a transverse section of the head of a 36 mm. pig, showing relation of the external auditory meatus. E. Au., to the tympanic pouch. prom., promontory of the tympanic pouch; the projection below the manubrium is the post-manubrial ridge. × 50, reduced ⅔.

Fig. 53.—Transverse section through carotid gland and adjacent part of third pouch. Pig, 13 mm., M¹. × 300 *circa*, reduced ⅓.

Fig. 54.—Cross section of a *glandule thyroidienne* in a 20 mm. pig, Harvard medical collection. × 300 *circa*, reduced ½.

Fig. 55.—Ventral view of the pharyngeal region of cat of 4.6 mm., No. 398, Harvard medical collection, showing associated blood-vessels. st., stomatodeum; v. v., vitelline veins; x., opening of enteron into yolk sac. × 50, reduced ⅓.

Fig. 56.—Lateral view of the same region. × 50, reduced ⅓.

Fig. 57.—Lateral view of the pharyngeal region in a cat, No. 413, Harvard medical collection, showing pharynx and associated aortic arches. M. Gr., median oral groove; Ph. P. 1-3, first to third pharyngeal pouches. × 80, reduced ½.

Fig. 58.—Lateral view of the pharynx in a 6.2 mm. cat, No. 380, Harvard medical collection. Ton. F., antero-lateral border of the second pouch, in later stages the tonsillar sinus. × 60, reduced ½.

Fig. 59.—Dorsal view of the pharynx in the same cat, showing also the related ectodermal parts. S. Pc., sinus præcervicalis; F. Pc., fundus præcervicalis. × 60, reduced ½.

Fig. 60.—Ventral view of the pharyngeal region in the same cat. × 60, reduced ½.

Fig. 61.—Ventral view of the pharyngeal region in a 9.7 mm. cat, No. 446, Harvard medical collection. On the right the plane of section is higher than on the left side. SM. F., submeckelian fold, barely visible at this stage; on the right the interior of the sinus præcervicalis is shown; Tub., tuberculum impar; V. F., vestibular fold. × 60, reduced ½.

Fig. 62.—Region of the sinus præcervicalis in the same cat. F. Pc., fundus præcervicalis; Ph. P. 4, fourth pharyngeal pouch, only its outer tip showing on the left side; V. D. 2-3, ventral diverticula of second and third pouches, their inferior parts cut off; V. Pc., vesicula præcervicalis. × 80, reduced ½.

Fig. 63.—Lateral view of the pharynx in a 15 mm. cat, No. 436, Harvard medical collection. Mn. f., manubrial fossa; P. S. F., post-salpingeal ridge; S. Pi., sinus piriformis; V. M. R., ventro-mesial border. × 60, reduced ⅗.

Fig. 64.—Dorso-posterior view of pharynx in the same animal. The figure shows the initial separation of the tympanic pouch and tonsillar fold. p. s. f., postsalpingeal ridge; s. t. p., sulcus tympanicus posterior; ton. f., tonsillar fold; v. m. r., ventro-mesial border; z., incision between tympanic pouch and tonsillar fold. × 30, reduced ⅓.

Fig. 65.—Median thyroid, lateral thyroid, la. t., carotid gland, c. gl., and præcervical body, f. pc., in a 15 mm. cat. × 30.

Fig. 66.—Lateral view of pharynx in a 23 mm. cat, No. 466, Harvard medical collection. I. Tn., incissura tensoris; Mn. F., manubrial fossa; Pl. B., postero-lateral border of the tympanic pouch; P. M. F., post-manubrial ridge; S. M. F., submeckelian fold; Ton. F., tonsillar fold. × 60, reduced 3/5.

Fig. 67.—Dorsal view of the pharynx in a 23 mm. cat. P. R., recessus posterior; S. R., recessus superior. × 60, reduced 3/5.

Fig. 68.—Lateral view of pharynx and mouth in a 32 mm. cat, Harvard medical collection; a doubtful body of lymphoid nature. × 60, reduced 3/5.

Fig. 69.—Dorsal view of pharynx in the same cat. × 60, reduced 3/5.

Fig. 70.—A part of the pharynx, including tympanic pouch and tonsillar fold in a 14 days rabbit, viewed from the posterior side. Symbols as in Fig. 26. × 30.

Fig. 71.—Part of the pharynx in the region of the tympanic pouch and tonsillar fold, rabbit, 16½ days. × 30.

Fig. 72.—Part of the pharynx in an 18 days rabbit, Harvard medical collection. i. tn., incissura tensoris; p. pl., palatine constriction; p. r., recessus posterior; ton. f., tonsillar fold. × 30.

Fig. 73.—The posterior portion of the pharynx of a rabbit of 21 days, Harvard medical collection, viewed from the front. The nasopharynx is represented as sectioned close to the base of the Eustachian tubes and the oral pharynx immediately in front of the tonsils. E. Au., external auditory meatus; Epi., epiglottis; G. Ep., glossi-epiglottic fold; I. Tn., incissura tensoris; Mk. F., Meckelian fossa; Mn. F., manubrial fossa; S. Pi., sinus piriformis; Ton., F., tonsillar fold; V. Ton., inferior tonsillar recess. × 30, reduced ½.

ABBREVIATIONS.

A-L. F., alveolar-lingual fold.
Ao. 2-5, 2d to 5th aortic arches.
Car., carotid artery.
C. Gl., carotid gland.
Ch. Ty., chorda tympani.
Coch., cochlea.
CV., concavity on ventro-lateral surface of tonsillar fold.
Cv. C., cervical cord of the thymus.
D. A. 1-3, dorsal apex of first to third pouches.
D. Ao., dorsal aorta.
dct., duct of the lateral thyroid.
d. l. s., dorso-lateral wall of the tympanic pouch.
D. Pc., ductus præcervicalis.
D. Pl., dorsal plate of the thymus.

D. Pr., dorsal prominence of tonsillar fold.
E. Au., external auditory tube.
F. Pc., fundus præcervicalis.
Fl. P., filiform appendix of 2d pouch.
F. Pc. V., ventral portion of fundus præcervicalis.
G. Au., auditory ganglion.
G. Ep., glosso-epiglottic fold.
G. Gas., Gasserian ganglion.
G. Gn., geniculate ganglion.
Gl. T., glandule thyroidienne, dorsal process of 4th pouch.
G. Nod., ganglion nodosum.
Hy., hyoid.
Hyp., hypophysis.
Impr., impressio cochlearis.
I. Tn., incissura tensoris.
La. T., lateral thyroid.
M., mouth.
M. Gr., median oral groove.
Mck., Meckel's cartilage.
Mk. F., Meckelian fossa.
Mn. F., manubrial fossa.
Ph. G. 1-4, pharyngeal grooves.
Ph. P. 1-4, pharyngeal pouches.
Pl. B., postero-lateral border of the tympanic pouch.
P-M. F., post-manubrial fold.
P. Pl., palatine constriction.
P. R., recessus posterior of the tympanic pouch.
Prom., promontory of the tympanic pouch.
Ps. F., post-salpingeal fold.
P. T. R., posterior tympanic margin.
Pul., pulmonary artery.
S-M. F., submeckelian fold.
S. P., Seessel's pocket.
S. Pc., sinus præcervicalis.
S. Pi., sinus piriformis.
S. R., recessus superior of the tympanic pouch.
St., stomatodeum.
S. T. P., sulcus tympanicus posterior.
S. T. T., sulcus tubo-tympanicus.
S. T. Ty., sulcus tensoris tympani.
T. Ao., truncus arteriosus.
Thr., thyroid cartilage.
Th. S., thymus superficialis.
Thy., thymus.
Ton. F., tonsillar fold of the 2d pouch.
Tr., trachea.
Tub., tuberculum impar.

Tyr., median thyroid.
V. D. 1-4, ventral diverticula of the pharyngeal pouches.
V. F., vestibular fold of mouth.
V. L. S., ventro-lateral wall of the tympanic pouch.
V. M. R., ventro-mesial border of the tympanic pouch.
V. Pc., vesicula præcervicalis.
v. v., vitelline veins.
x., opening of enteron into yolk-sac.
y., interval between vestibular and submeckelian folds.
z., indentation separating tympanic pouch and tonsillar fold.

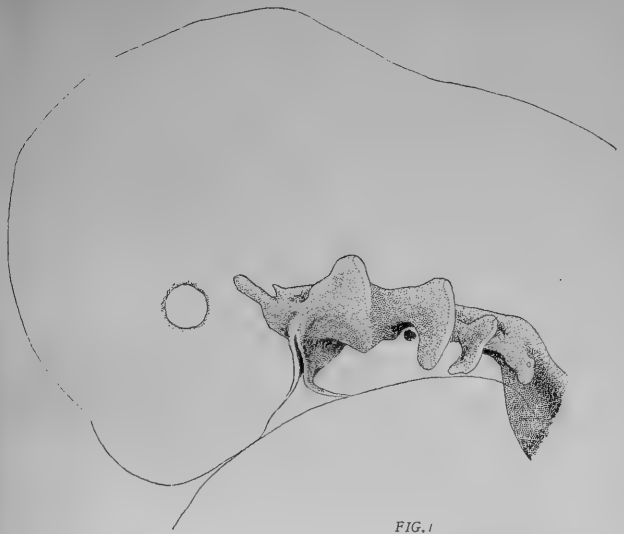


FIG. 1

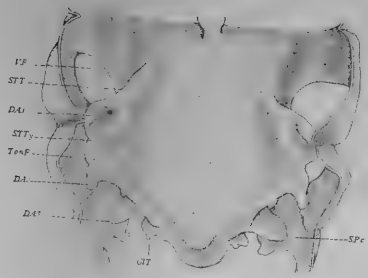


FIG. 5

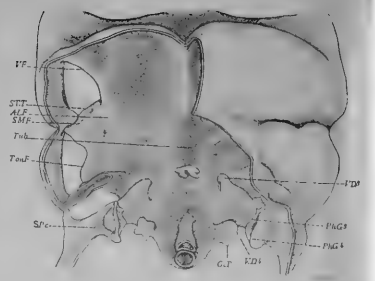


FIG. 6

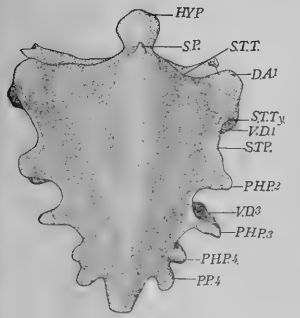


FIG. 2

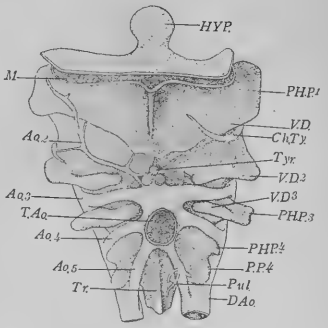


FIG 3

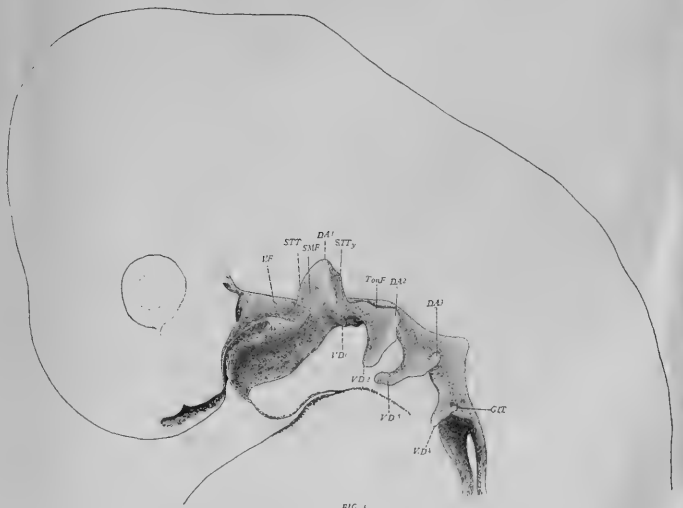


FIG. 4

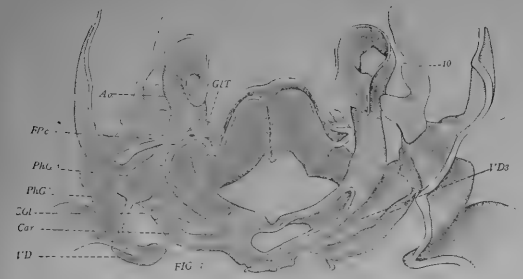


FIG.

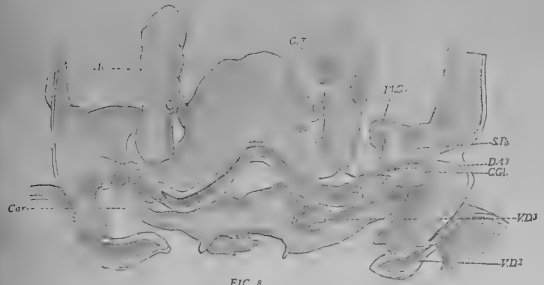


FIG 8

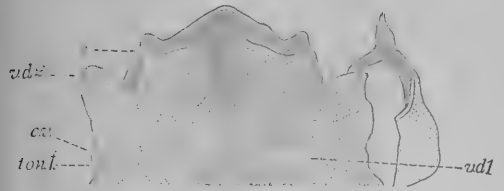


FIG. 12

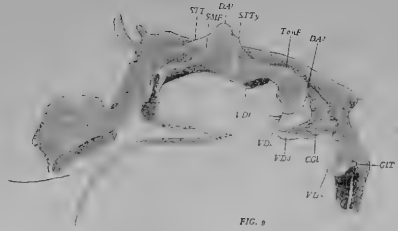


FIG. 9

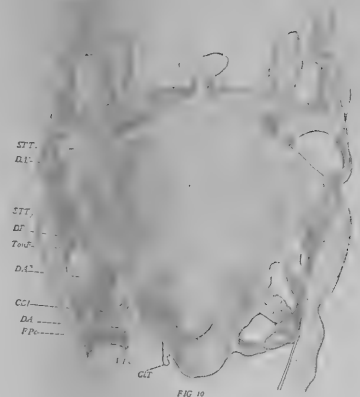


FIG 10

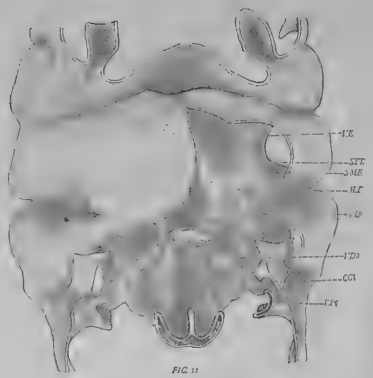


FIG 11

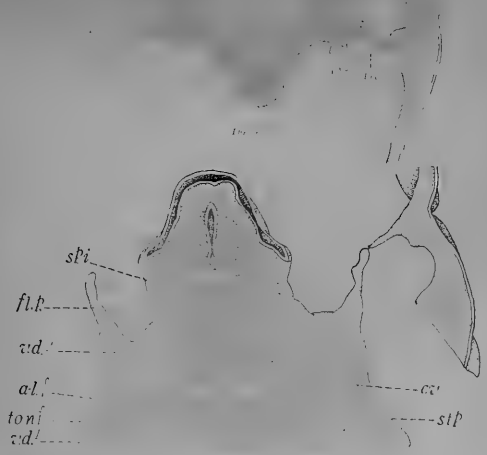


FIG. 17

HENRY FOX

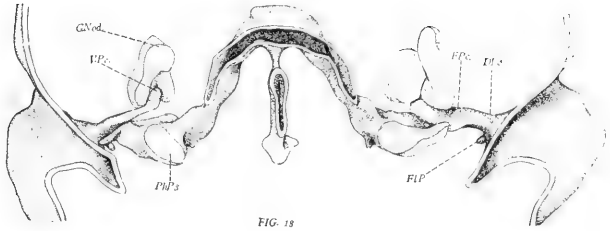


FIG. 18

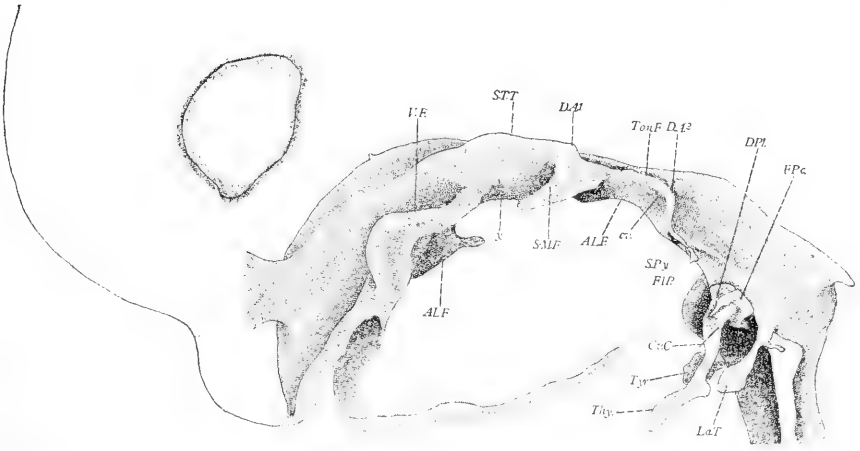


FIG. 19

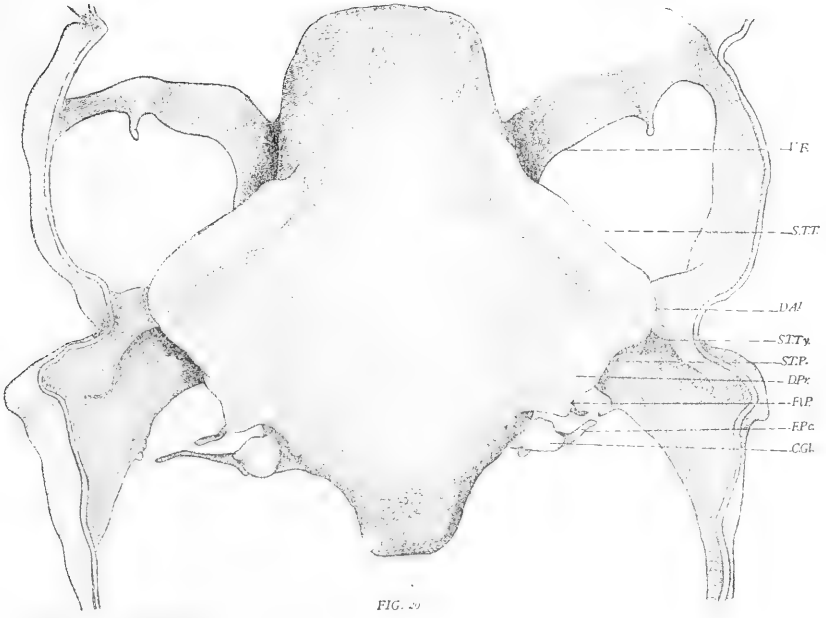


FIG. 20

FIG. 21

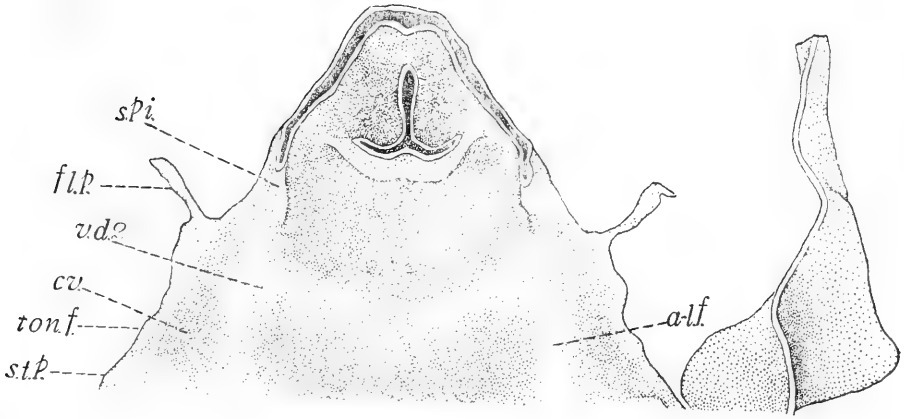


FIG. 22

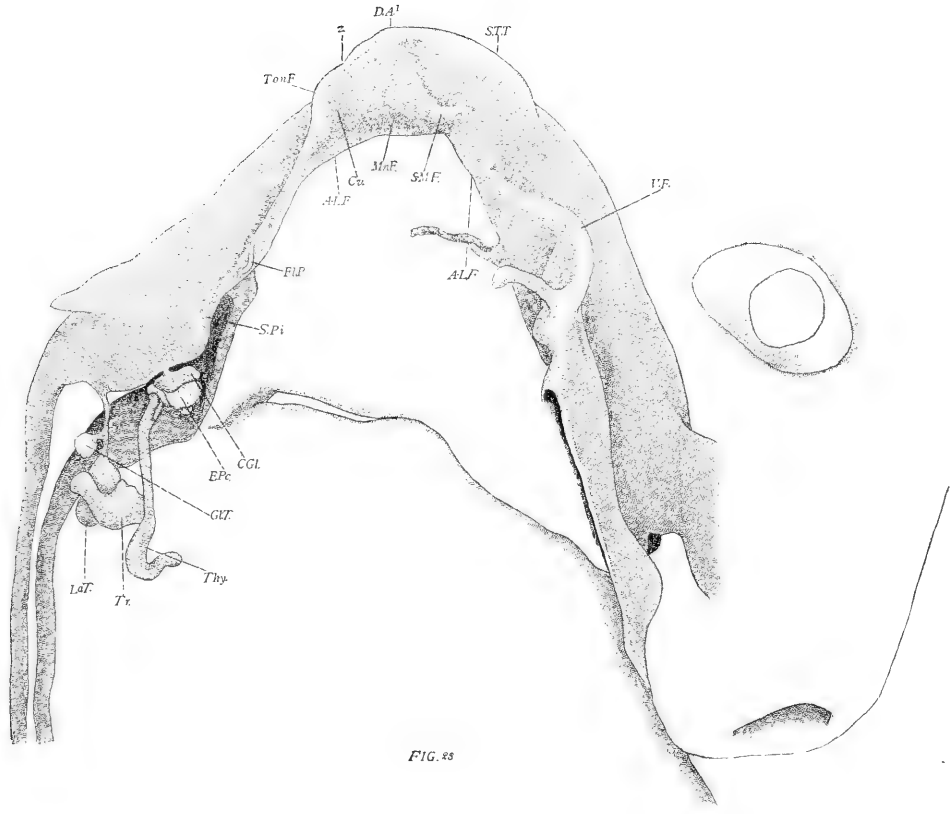


FIG. 28

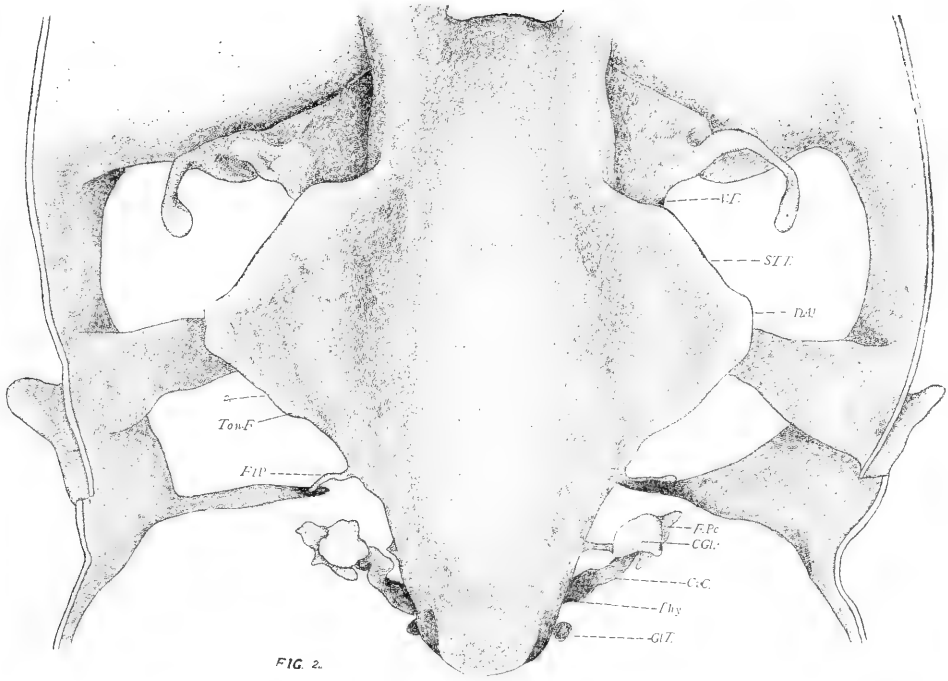

V.T.
SI.T.
DAV.
Tou.F.
FlP.
F.Pc.
CGl.
C.C.
Thy.
GlT.

FIG. 2.

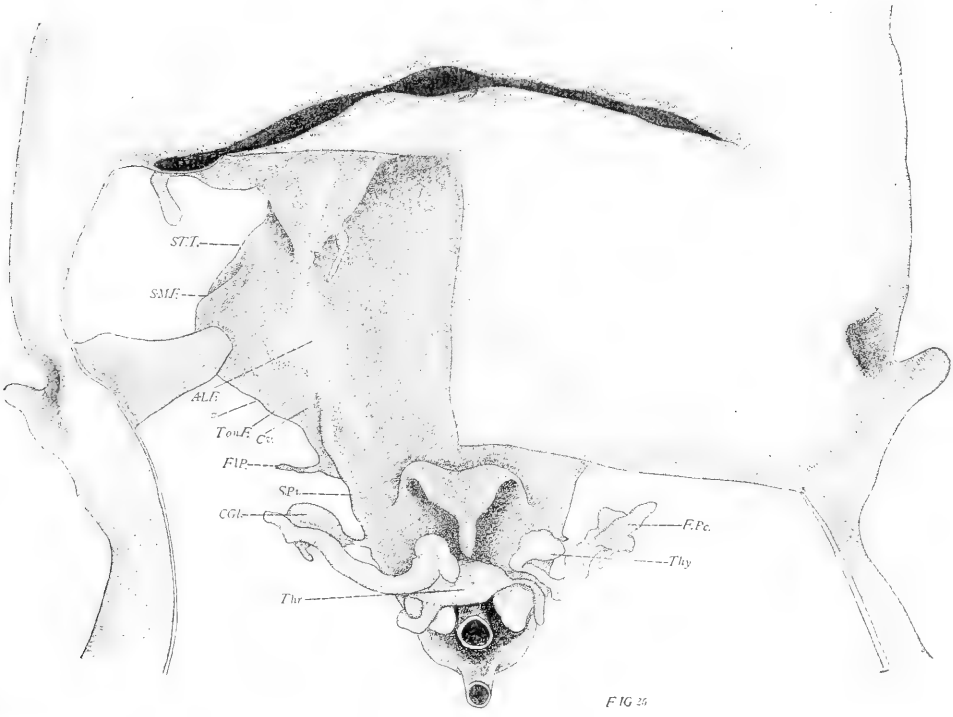

ST.T.
SMF.
ALF.
Tou.F.
Cc.
FlP.
SPt.
CGl.
F.Pc.
Thy.
Thr.

FIG 25

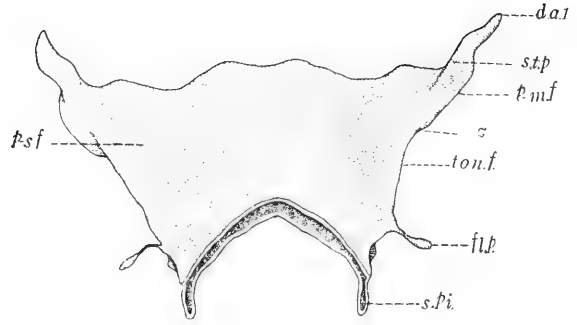


FIG. 26

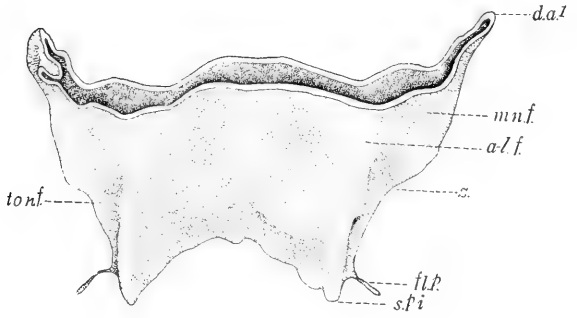


FIG. 27

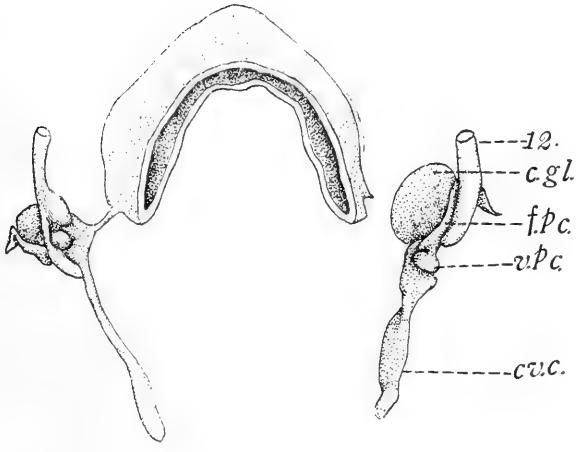


FIG. 28

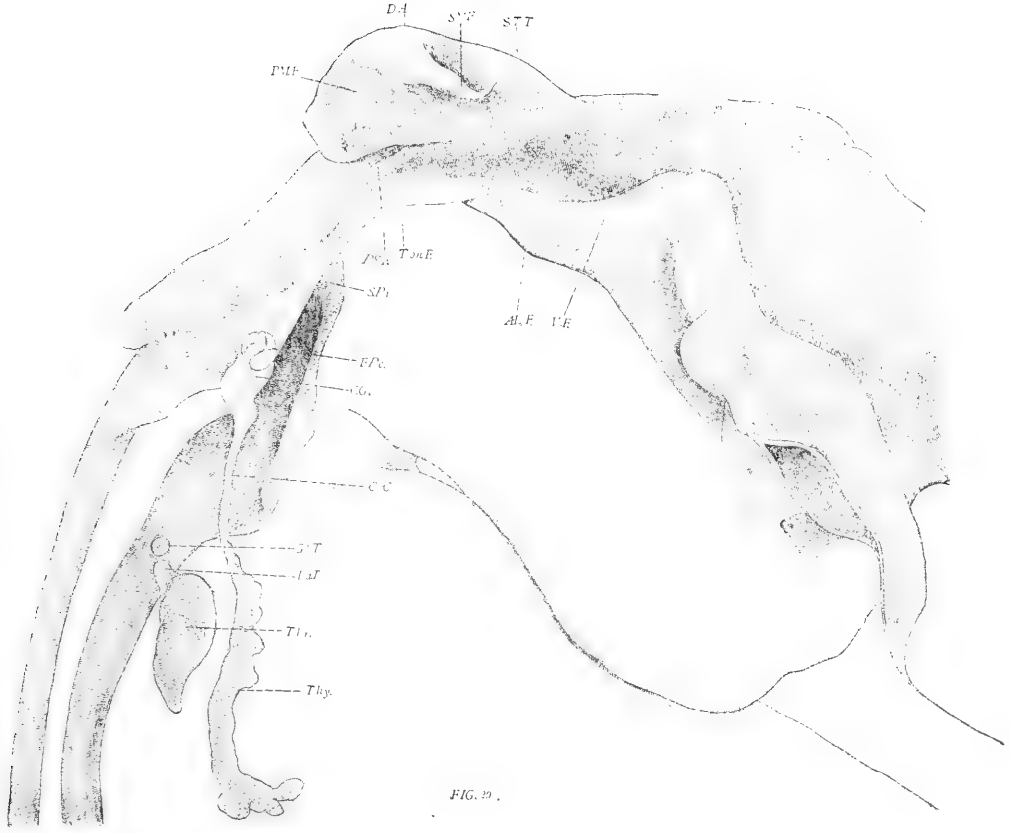
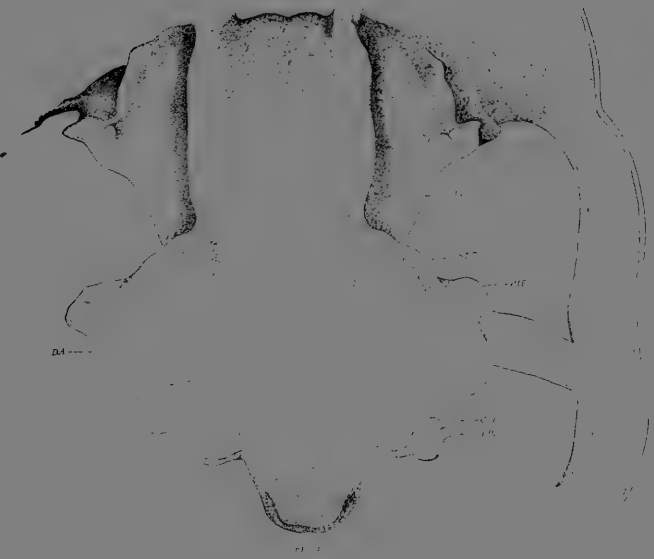
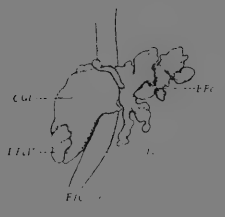


FIG. 19.





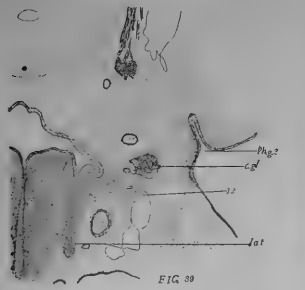


FIG. 39

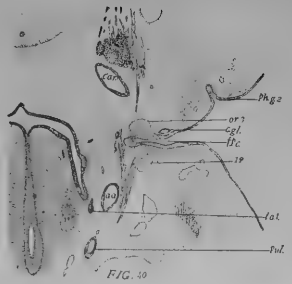


FIG. 40

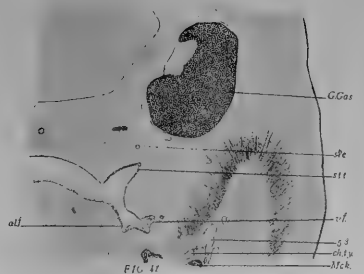


FIG. 41

FIG. 42

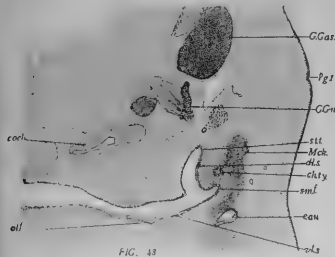


FIG. 43

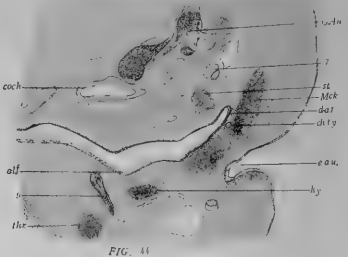


FIG. 44

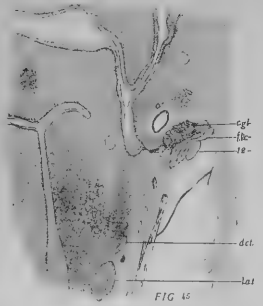


FIG. 45

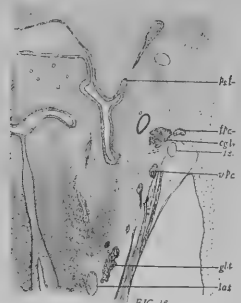


FIG. 46

FIG. 51

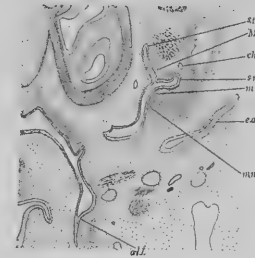


FIG. 50

FIG. 49

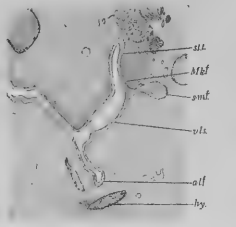


FIG. 48

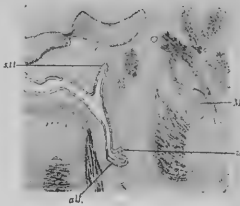


FIG. 47

FIG. 54

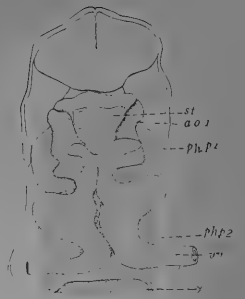


Fig 55

FIG. 58 1

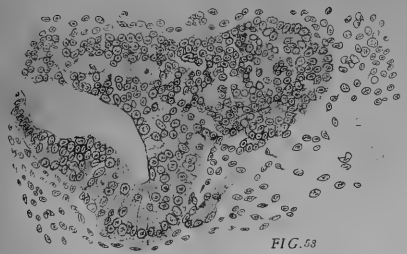


FIG. 53

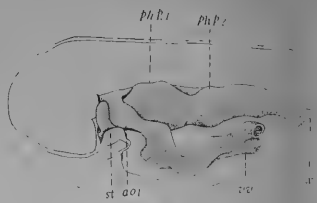


Fig 56

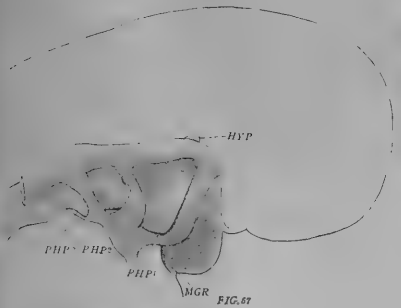


FIG. 57

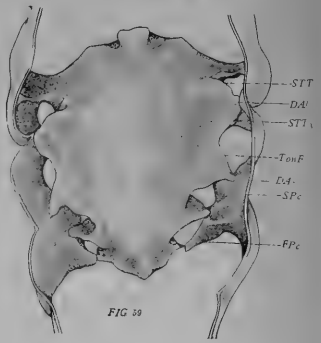


FIG 59

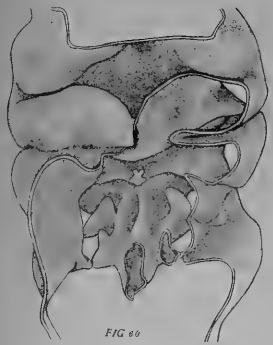


FIG 60

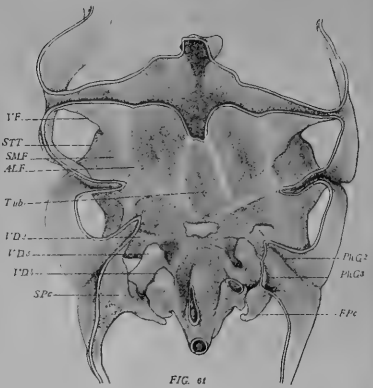


FIG. 61

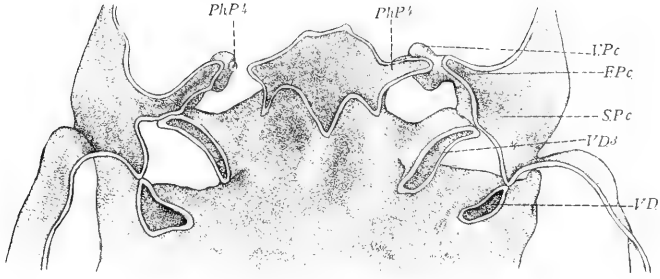

PhP 4
PhP 5
VPc
FPc
SPc
VD 3
VD

FIG. 62

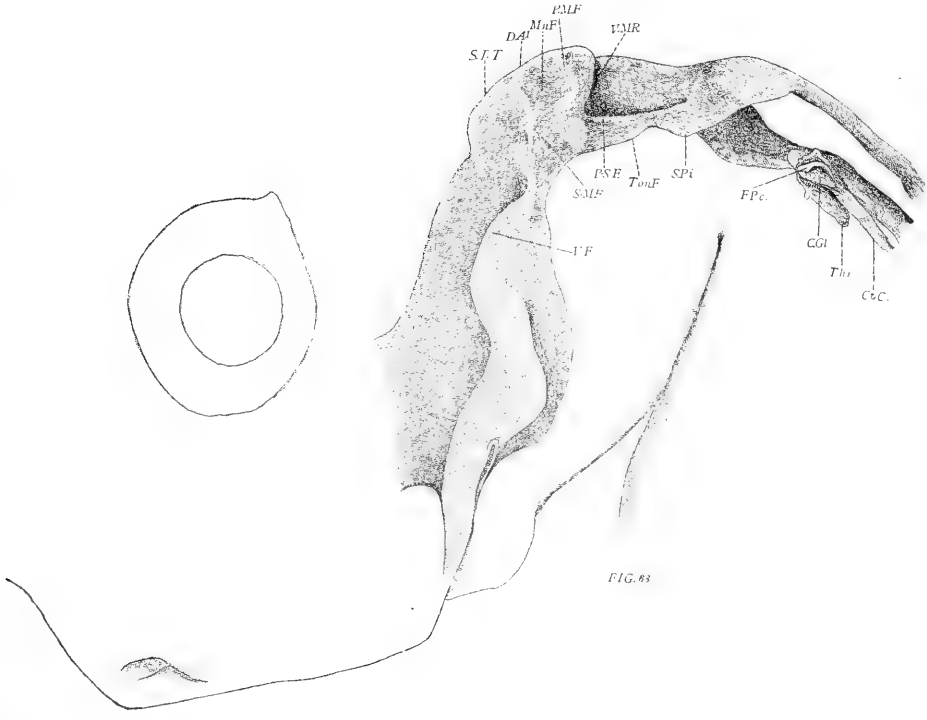

PMF
MuF
DAP
VMR
S.T.T
PSE
SMF
TonF
SPi
FPc.
VF
CGl
Thy
CbC.

FIG. 63

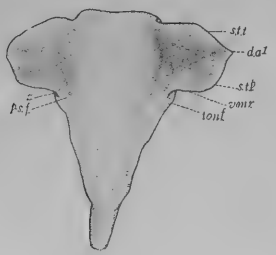


FIG 64

FIG. 65

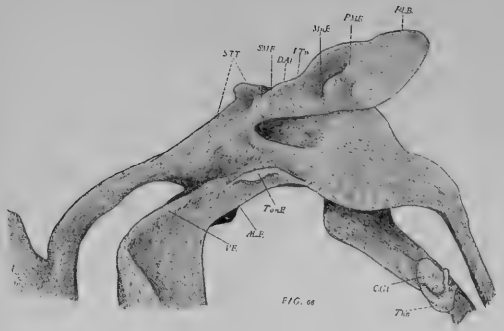


FIG. 66

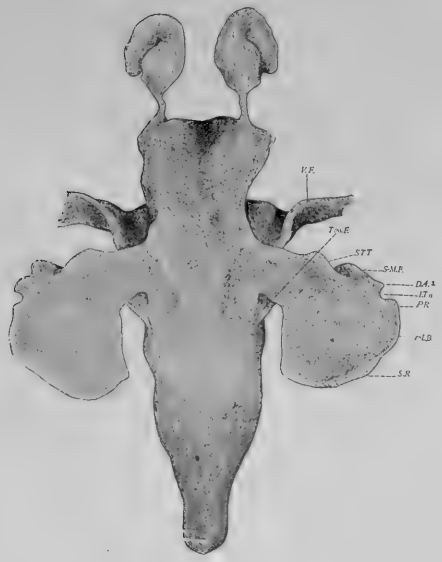


FIG. 67

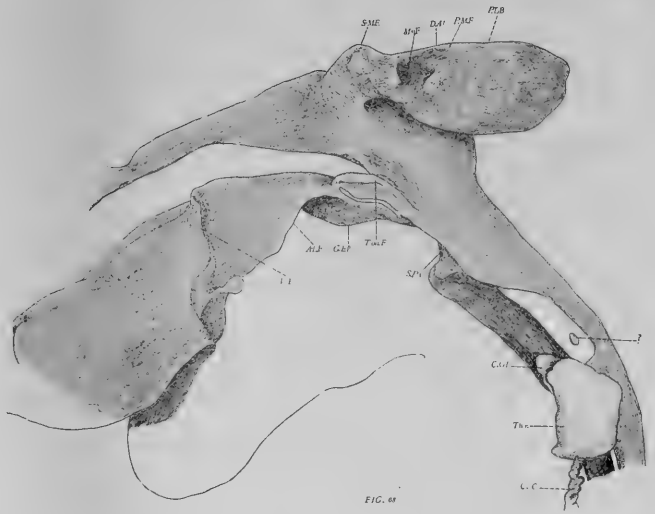


FIG. 68

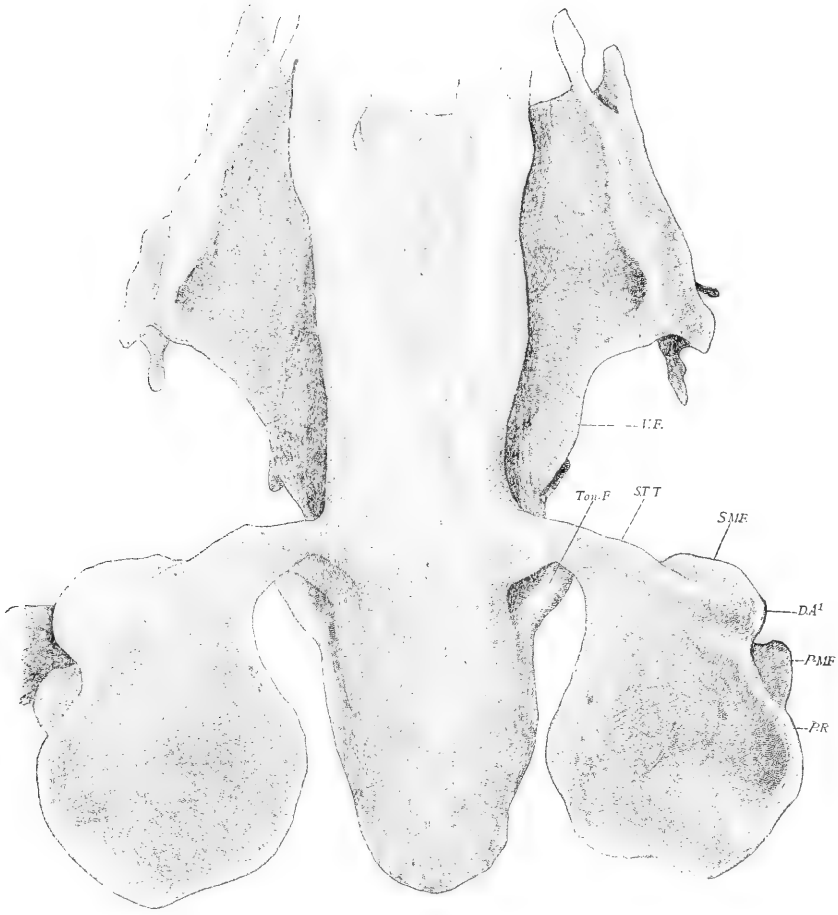


FIG. 69

FIG. 70

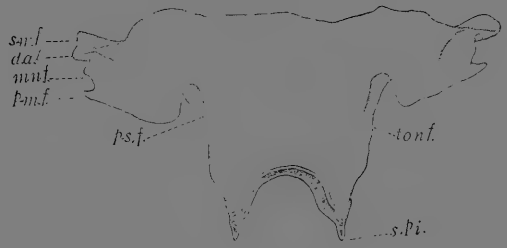


FIG. 71

FIG. 72.

THE LATER DEVELOPMENT OF THE NOTOCHORD IN MAMMALS.

BY

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The fate of the notochord in mammals has received, in recent years, very scant attention. This is well exemplified both by the briefness of the discussions of the subject in recent text-books and also in reference works, and by the contradictory statements found in different, or even in a single book.

The following shades of opinion are found in volumes which have appeared very recently:

"The notochord here" (in mammals) "persists longer intervertebrally than intravertebrally, but it disappears entirely by the time the adult condition is reached." (Wiedersheim's Comparative Anatomy, 6th German edition, 1906, p. 62, and 3d English edition, 1907, p. 60.)

"They (the intervertebral discs) are developed, like the bodies around the notochord, persisting parts of this structure forming a central core to each disc." (Piersol's Anatomy, 1907, p. 132.)

"The notochordal remains lying between each pair of vertebrae with the perichordal tissue grow and remain throughout life as the *nuclei pulposi* of the intervertebral discs." (Bonnet, Entwicklungsgeschichte, 1907, p. 381.)

"The notochord is essentially an embryonic structure in mammals, although it does not completely disappear, for traces of it are to be found throughout life in the middle of the intervertebral discs. When fully developed it is a cylindrical rod composed of clear epithelium-like cells, enclosed within a special sheath of homogeneous substance. These cells, although they may become considerably enlarged and vacuolated, undergo no marked histogenetic change and take no part in the formation of any tissue of the adult. . . . Within the (intervertebral) disc the notochord is enlarged and afterwards converted in each, along with

the surrounding tissue, into the *nucleus pulposus.*" (Bryce, in Quain's Anatomy, Vol. I, Embryology, 1908, p. 49 and 252.)

"The notochord not only remains intervertebrally, but grows continuously at that point, showing therewith the tendency (Neigung) after the loss of its sheath, to fuse with the surrounding connective tissue. (Leboucq, 1880.) . . . The nucleus pulposus or gelatinosus of the intervertebral ligament (intervertebral disc) consists in every case in the adult mammal, of such common growth of the notochord and of the tissue lying next to it. G. Jäger is indeed right when he compares, as mentioned above, the intervertebral longitudinal ligament (Längsband) of birds with the pulpy nucleus of the disc of mammals." (Schauinsland, in Hertwig's Handbuch d. vergl. u. exper. Entwickelungslehre der Wirbeltiere, Bd. 3, Teil 2, 1906, p. 517.) The statement referred to is as follows: "Only inconspicuous remnants of it remain finally in the interior of the intervertebral ligament; they lie there enclosed in a longitudinal band which, as the *'ligamentum suspensorium,'* binds together the successive vertebræ (G. Jäger, 1858)."

"Finally the notochord disappears from the vertebral regions, although a canal, representing its former position, traverses each body for a considerable time, and in the intervertebral regions it persists as relatively large flat discs, forming the pulpy nuclei of the fibro-cartilages." (McMurrich, The Development of the Human Body, 1907, p. 170.)

"La corde dorsale, par exemple, constitue à elle seule tout le squelette axial chez les Chordés primitifs, tandis qu'elle disparait entièrement dans les formes superieures." (L. Vialleton, Un Problème de l'Evolution, 1908, p. 87.)

The cause of this unflattering state of our knowledge is that the theory concerning the fate of the notochord of mammals, which was widely accepted years ago, was not well founded and does not explain the known facts. In the three decades between 1850 and 1880 the subject aroused considerable interest. Two theories were in the field: one proposed in 1852 by Luschka, and advocated by Kölliker, H. Müller and Löwe; the other originated by Virchow, and defended by Luschka after 1856, Robin, Dursy, and Leboucq.

The nucleus pulposus in man was carefully described, in 1852, in the first edition of "Die Halbgelenke," by Luschka, who found that it arises from the intervertebral expansion of the notochord.

Virchow later contended that the nucleus pulposus of the new-born

child is formed by the liquefaction of the central portion of the connective tissue of the intervertebral disc. He also described a tumor found upon the inner surface of the base of the skull, and, believing it to be a growth of cartilage, named it *Ecchondrosis physalifora.*

Luschka, in 1856, adopting in part Virchow's theory of the origin of the nucleus pulposus, found that its characteristic tissue, which consists of whitish clusters of vacuolated cells in a transparent gelatinous matrix, arises primarily by the liquefaction of the intervertebral notochord expansion, but that it is augmented by the liquefaction of the surrounding fibro-cartilage. He also accepted Virchow's theory of the nature of *Ecchondrosis physalifora.*

Two years later, 1858, Luschka published the second edition of his "Halbgelenke," in which he described the nucleus pulposus at various ages. He found further evidence of the close relationship of notochordal tissue and cartilage. The sharp boundary line between the notochord and the intervertebral disc which occurs in the new-born child, owing to the formation of papillæ of fibro-cartilage which project into the notochordal tissue, disappears during childhood. Liquefaction finally leads to the obliteration of the boundary between the two tissues. In old age the nucleus pulposus becomes of dirty green or gray color. It loses its gelatinous and elastic character while cheesy masses, the products of fatty degeneration, as well as calcareous masses, appear in it. A large number of cartilage cells with thick, strongly laminated walls are found in it. Some of these are immense mother cells with innumerable daughter cells. Fat vacuoles are visible in many cells.

In the same year Heinrich Müller noted that portions of the notochord persist for a long time after birth in the base of the skull, in the odontoid process of the axis and in the coccyx. He tried to demonstrate that *Ecchondrosis physalifora* is produced by excessive growth of notochordal tissue.

Kölliker says in the fifth edition of his "Histology:"—"In 1858 I pointed out that the intervertebral ligament of a child of one year contains ordinarily a pear-shaped cavity which is filled with the continuously growing mass of the notochord; and that this mass, which consists of a soft matrix and many cells with characteristic vacuoles arranged in clusters or in a network of strands, forms in the adult a large part of the nucleus pulposus in which, in certain cases, the characteristic fœtal notochordal cells can be recognized. . . . This soft mass" (of fibro-cartilage, which Kölliker regards as the peripheral

part of the nucleus pulposus) "which often bears the irregular processes, first described by Luschka, surrounds the notochordal remnants (Reste) so that the two structures interlock with one another and a sharply marked cavity, such as occurs in the child, does not exist." The original article is in the Verh. phys. med. Gesellsch., Würzburg, 1859, IX, pp. 193-242.

This clear and precise statement by so acknowledged a leader as Kölliker did not suffice to settle the question, for in the following year Robin, describing carefully a large series of stages in the development of the notochord of mammals, maintained that the notochord undergoes mucoid degeneration and that its intervertebral expansion is gradually invaded by papillæ of fibro-cartilage which, meeting at its center and expanding gradually, finally replace the degenerated notochordal tissue.

Kölliker's theory of the origin of the nucleus pulposus was again attacked in 1869. Dursy found that the nucleus pulposus is formed primarily by the liquefaction of the connective tissue of the intervertebral disc and that the notochord takes no part in the formation of the definitive nucleus pulposus. This view is like Luschka's second theory, except that he found that the notochord is liquefied first and later fuses with the liquefied connective tissue.

Ten years later Löwe entered the field in defense of Kölliker's theory. He agreed essentially with Kölliker, but found that the entire nucleus pulposus of the adult rat is formed by the notochord. This difference is merely one of definition, for, as was noted above, Kölliker considered that the looser fibro-cartilage of the disc should be regarded as the peripheral portion of the nucleus pulposus, which, by this definition, is composed of the notochordal tissue and the loose fibro-cartilage of the disc.

Heiberg, 1878, says: "dann muss man zu dem Schluss kommen dass die Chorda dorsalis beim Menschen keinen Antheil an der Bildung der Pulpa des Intervertebralligamentes nimmt."

In 1880 Leboucq published the last considerable article upon the question of the fate of the mammalian notochord. He found that in the human and in other mammalian embryos, the notochordal tissue is practically destroyed long before birth. In the vertebra the notochord degenerates and is absorbed, but the intervertebral notochordal expansion is first invaded by connective tissue and is ultimately replaced by it.

This piece of work, coming after a long controversy, was widely accepted in spite of the fact that it contradicted practically all previous

writers, for it indicated that the notochord disappears much earlier than had been believed by others.

Fric, however, in his "Handbuch der Gelenke" (1904), accepts Kölliker's work and, figuring the nucleus pulposus, describes its peculiar tissue as the remnant (Rest) of the notochord.

Turning now to Müller's contention that Virchow's tumor, *Ecchondrosis physalifora,* actually arises from the notochord, not from cartilage, we find Virchow's view universally accepted until 1894, when H. Steiner, working under Ribbert, published a careful study of a case of the tumor and found that Müller was right in believing it to be an abnormal growth of the notochord.

Ribbert, a year later, proved that the tumor can be produced experimentally in the rabbit, by puncturing the intervertebral ligament so as to allow a portion of the nucleus pulposus to escape. This tissue, lying in the connective tissue and muscle near the ligament, grows for some time and forms a characteristic *Ecchondrosis physalifora.* This knowledge led Ribbert in his "Geschwülstlehre," 1904, to propose and use the name chordoma, instead of Virchow's name for the tumor. Fischer and Steiner, working in Ribbert's laboratory, described a case of malign chordoma in 1906.

The generally accepted interpretation of the formation of the vertebræ in the Amniota is the theory of Remak of the resegmentation of the vertebræ. Among recent exponents of Remak's attractive generalization are Schultze, Schauinsland, Weiss, and Bardeen. According to this theory the vertebræ are formed by the division of the sclerotomes and by the subsequent fusion of the sclerotome halves adjacent to each intersegmental plane to form an intersegmental vertebra. The fissure of von Ebner, or the intervertebral fissure, a mid-segmental transverse diverticulum of the myocœle which in mammals, however, arises independently of the myocœle and after its disappearance, divides the sclerotome into half segments. The anterior half of each sclerotome is formed of looser tissue than the posterior half. The latter is apparently a mesenchymal condensation and has been called "the primitive vertebra" by Remak, the "scleromere" by Bardeen. Its central portion is the "hypochordal rod" of Froriep, the "horizontal plate" of Weiss, and the "primitive disc" of Bardeen. Its lateral portions are the "vertebral arches" of Froriep, and the "costal and neural processes" of Bardeen. Weiss divides the lateral portion of the primitive vertebra into a "vertical plate" which extends backward from the outer

end of the "horizontal plate" to the intersegmental artery, and the "vertebral arch" which extends outward from that artery between the myotomes. Weiss finds that the transverse portion of the primitive vertebra forms the *annulus fibrosus* of the intervertebral disc; Schultze and Bardeen, that it forms part of that structure and also the anterior portion of the vertebra. Schultze asserts that the rib belongs to the posterior half of the segment, and Bardeen that from this point of origin it moves into an intersegmental position. Weiss maintains that the vertical plate and the arch fuse with the vertebra, Bardeen that only the arch does so.

In this paper I have undertaken to trace the development of the notochord, in the pig, from the time of the appearance of its segmental waves. It was also found necessary to review the formation of the vertebræ in order to determine the exact relation between the notochordal waves and other metameric structures.

The development of the notochord in man, the rabbit, cat, dog and opossum has also been studied, but in less detail. The shape of the intervetebral notochordal expansions has been found to be sufficiently characteristic in each species to justify a brief description of the form of the notochordal enlargements.

The study has been made possible by the extensive series of mammalian embryos in the Harvard Embryological Collection, and the series referred to by number belong to this collection.

I am greatly indebted to Prof. Charles S. Minot for many helpful suggestions for the prosecution of the work.

The Formation of the Notochordal Sheaths and of the Precartilaginous Vertebrae of the Pig.

The notochord of a very young pig embryo (5.5 mm., H. E. C. Nos. 915, 916, 917) is a dorso-ventrally flattened rod with major and minor axes approximately 25 and 50 micra long. Each cross section contains about eight wedge-shaped cells whose exposed walls form a thin notochordal sheath. As was shown by Dr. Minot in 1907, the notochord and the floor of the spinal cord of young mammalian embryos are thrown into a series of segmental undulations. In the pig the crests or dorsal curves of the notochord are nearly intersegmental, for they occur very slightly in front of the transverse plane of the intersegmental vessels, the troughs being nearly mid-segmental.

In the head the notochord is nearly midway between the medulla and the pharynx, but posteriorly it gradually approaches the cord until, in about the 25th segment, the two are in contact. In front of this point, the mesenchyma of the sclerotomes extends from the myotomes to the notochord as a dense mass which is interrupted at the level of the notochord by scarcely perceptible light transverse zones which connect each pair of intersegmental vessels, and by a narrow longitudinal median zone of similarly light tissue.

In order to determine accurately the density of the nuclei I have counted the nuclei in an area 24 microns square in sections 10 microns thick, or in 5,760 cubic microns. In one or two cases the series are cut at a different thickness, and it was necessary to calculate the number of nuclei in this volume from the data for another volume. The percentage of error in this calculation is less than that of the counting. In every case the number given is the mean between at least two counts in different places. At the level of the notochord there are 36 nuclei in 5,760 cubic microns in the transverse light zones, 48 in the longitudinal zone and 62 in the denser regions. Below the notochord the mesenchyma is of nearly uniform density and has 54 nuclei in 5,760 cubic microns.

Higher up, beside the spinal cord, the structures of the anterior half of the segment, the spinal ganglion and the roots of the spinal nerves, are surrounded by loose mesenchyma; and the dense tissue, like that below the spinal cord, is confined to the posterior half of the segment. The cavities of the myotomes have closed. The fissure of von Ebner, which in the Sauropsida divides the sclerotome into anterior and posterior halves, has not appeared and consequently the sclerotome is not divided into anterior and posterior portions.

Behind the point where the spinal cord and notochord first come in contact, there is a region in which the notochord is not in contact with the sclerotomes, but lies in a small cavity. Farther back the notochord is in contact with the spinal cord, the post-anal gut, and the somites.

Slight condensations of mesenchyma become visible in embryos of 6 mm. They occur in the middle of the segments and lie just under and perhaps a trifle behind the troughs of the notochordal waves. They are produced by the extension of the intersegmental zones of loose tissue, forward and backward toward the centers of the sclerotomes, and are the intervertebral discs of Froriep or the primitive discs of Bardeen. Their position is mid-segmental in the pig as in the cow

(Froriep), not in the posterior half of the sclerotome as in man (Bardeen).

These structures are more clearly defined in still later embryos, 7.8 mm. (Fig. 1), and it is evident that the differentiation of the axial structures is brought about as much by the spreading apart of the mesenchymal cells as by their aggregation or condensation. There are in 5,760 cubic microns about 100 nuclei in the disc and 29 in the light transverse zones. The enumeration of nuclei in the dense regions is too difficult to yield reliable results, and the approximate number only can be given. Below the level of the notochord the tissue of the disc is much less dense than at the level of the notochord. The dense tissue of the discs does not extend much above the notochord, but the discs are now united by a median cord of dense tissue, the perichordal septum, which surrounds the notochord and forms a dense band below it. The rounded intersegmental zones of looser tissue are deeply constricted between the notochord above and perichordal septum below, but the two lateral portions of each seem always to be connected at least by a slender cord of loose tissue which passes under the crest of the corresponding notochordal undulation.

The notochordal sheath appears first in embryos of 7 mm. and is apparently fully formed in embryos of 7.8 mm. It is an anhistic membrane about 1 to 1.5 microns thick and it is faintly striated concentrically. The formation of this sheath, or of the inner sheath which appears later, does not affect the proper walls of the notochordal cells which can still be seen inside the sheath.

The loosening up of the axial mesenchyma reaches its maximum in embryos of 9 mm., for there are 20 nuclei in 5,760 cubic microns in the light zones and 63 in the discs (Fig. 2). In embryos of 10 mm. the mesenchyma is denser, and the loose tissue of the vertebræ has 50 nuclei in the same volume. The mesenchymal tissue above the notochord has increased largely, for in the 5.5 mm. embryo the notochord was separated from the spinal cord by a small plate of mesenchyma scarcely thicker than the notochord; it is now separated by more than thrice its diameter. The perichordal septum surrounds the notochord and the vertebral anlages. The septum, nevertheless, is incomplete, for, as stated above, a small isthmus under the notochordal crest connects the lateral masses of the vertebral anlage.

The multiplication of the cells of the discs and of the perichordal septum has been sufficiently rapid, up to this age, to maintain approxi-

mately the same density of tissue in them despite the rapid increase in volume of this part of the embryo, but the cells of the vertebræ do not keep pace with the general growth and are consequently drawn apart.

The notochord is larger and about 15 cells occur at the periphery and 3 or 4 at the center of each transverse plane.

The fissure of von Ebner is present in the trunk. It scarcely reaches downward to the level of the notochord and it does not reach inward as far as the intersegmental arteries. Its position is such that, if it were extended downward and inward, it would divide the intervertebral disc. Bardeen finds that in man this fissure is mid-segmental and that the "primitive disc" lies in the posterior half of the sclerotome in early stages, but that the intervertebral disc is later formed upon the site of the fissure of von Ebner. In the pig, however, the fissure of von Ebner does not divide the sclerotome into anterior and posterior portions; on the contrary, the sclerotomes fuse with one another in the median line and longitudinally, as we saw in the 5.5 mm. embryo, and, in the axial rod thus formed, appear the loose transverse zones which will form later the bodies of the vertebræ.

The dense mesenchyma of the intervertebral disc extends outward to the spinal nerves and then divides into an anterior and a posterior process. The former, the interdiscal membrane of Bardeen, extends forward on the inner side of the spinal nerve to the preceding disc. The latter, representing the "costal and neural processes" of Bardeen, extends outward and backward, and downward and upward. The upper, or "neural" process, extends upward behind the spinal ganglion and upon the inner side of the posterior half of the myotome. The lower, or "costal" process, extends downward and outward between the divergent lower ends of the myotomes.

As Bardeen found in man, all the axial mesenchyma is as yet blastemal, and I believe that, although this tissue has greatly increased in volume, almost all visible differentiation has been effected by the separation of its cells from one another.

The apparent condensations give rise "to cartilage, perichondrium and ligaments" (Bardeen) and consequently the blastemal "sclerotome" of Bardeen, which is composed of the intervertebral discs with the costal and neural processes, cannot justly be regarded as a morphological skeletal unit. In short, definite skeletal differentiation, the formation of cartilage or precartilage, has not as yet begun in the "primitive vertebræ," but is foreshadowed in the definitive vertebræ by the

loosening up of the blastemal tissue which, at least in the spine of the pig, always precedes the condensation that forms precartilage.

An extraordinary multiplication of the cells of the vertebra, disc, and neural and costal processes has begun in pig embryos of 11 mm. A further differentiation of the discs and the vertebræ accompanies this new phase of growth. The tissue of the vertebræ has become precartilage, for the nuclei stain less intensely and, although the protoplasmic network remains, it becomes attenuated and stains less readily than elsewhere. The cells and cytoplasm of the discs, on the other hand, continue to take stains as before.

The edges of the discs are continuous with a similar but less dense tissue which completely surrounds the vertebræ and, in the median line, fuses with the upper and lower edges of the perichordal septum. The neural processes are possibly separated from the vertebral bodies for a time by this sheet of tissue, but long before chondrification begins the neural processes or arches are united to the vertebræ.

The notochordal cells have lost all definite arrangement and are more or less vacuolated. They are flattened antero-posteriorly and are closely packed together.

The number of cell divisions in the vertebræ apparently reaches a maximum in embryos of 12 mm. (Fig. 3), and there are 54 nuclei in 5,760 cubic microns. In addition to the exceptionally large number of mitoses, one sees many elongated and dumb-bell-shaped nuclei, as well as a few pairs of top-shaped nuclei united by their points at a large acute or an obtuse angle. The three nuclei in Fig. 13, as well as a number of similar nuclei, were found in a single section of one vertebra (Section 894, H. E. C. No. 5). This embryo is well preserved, and similar nuclei occur in two other 12 mm. embryos (Nos. 6 and 518), but seem to be absent from a fourth embryo (No. 7). I am inclined to believe that the rapid cell division which accompanies the transformation of blastemal tissue into precartilage is partly mitotic and partly amitotic. Rod- and dumb-bell-shaped nuclei occur in embryos of 10 and 14 mm., but they are rare and do not furnish acceptable evidence of amitosis.

The precartilage of embryos of 12 mm. has reached its maximum density. The nuclei are surrounded by small quantities of cytoplasm which forms a delicate network.

A considerable quantity of loose mesenchyma separates the vertebræ and intervertebral discs from the spinal cord. Anteriorly the base of the spinal cord has lost its segmental undulations, but posteriorly

they persist even in embryos of 14 mm. Only a small part of the neural and costal processes has been transformed into precartilage. At the level of the base of the spinal cord, the neural process of the scleromere is approximately triangular in frontal section. Two acute and equal angles are directed inward and outward and its obtuse angle is directed forward. The last lies close behind the spinal nerve and is continuous with the "interdorsal" and the "interdiscal ligaments" (of Bardeen) which lie respectively upon the outer and inner sides of the nerve. The outer angle projects between the myotomic muscles and is separated from the blastemal tissue of the anterior end of the interdorsal and interdiscal ligaments of the next segment by the ramus dorsalis of the spinal nerve. Above the ramus dorsalis there is a rounded blastemal mass which cannot be assigned to one or the other segment. The outer angle of the neural process remains blastemal for some time and seems finally to form the myoseptum. The inner angle is continuous below and anteriorly with the costal process and with the periphery of the intervertebral disc. The precartilage of the neural arch appears upon the posterior side of the inner angle of the blastemal neural process. It reaches only to the upper edge of the myotomes. The costal process is largely blastemal, but it contains the small elongated precartilage of the rib.

In embryos of 14 mm. (Fig. 4) the vertebræ are larger and are more definitely outlined. A sheet of elongated, closely-placed nuclei, formed by the extension of the interdiscal ligament and by its fusion with the perichordal septum, surrounds the vertebra and binds together the successive intervertebral discs. It represents the fibrous tissue of the perichondrium and of the dorsal and ventral common ligaments. A mass of dense blastemal tissue, which is perforated by the ramus dorsalis, extends from the neural arch to the rib.

The vacuolization of the notochord has continued and an inner sheath, which is much thicker than the outer sheath, has been formed. The inner sheath and the vacuoles of the notochord are composed of mucin or a mucin-like substance, for they are stained by mucicarmine. For convenience this substance is referred to hereafter in this paper as mucin, but I do not intend to convey the impression that its composition is even approximately known. The notochord is surrounded within its inner sheath by an apparently continuous wall which is formed by the exposed walls of its superficial cells.

The intervertebral disc begins a little later, in a pig of 14.2 mm., to differentiate into a looser central portion, with nuclei irregular both

in shape and arrangement, and an outer and larger region with nuclei which are elongated longitudinally and are united by strands of protoplasm into layers concentric with the center of the disc. The inner portion later (in 24 mm. embryos) forms the cartilage which serves, as has been shown by Schultze, Minot, and Weiss, to bind together the successive vertebræ in a continuous rod of cartilage, the chondrostyle. It should be noted in passing that the development of the cartilage of the intervertebral disc at this late period, as compared with the vertebral cartilage, is another indication that the apparent condensation, the scleromere, is not the first but the last portion of the vertebral column to be differentiated. It is undifferentiated rather than precociously differentiated tissue.

The vertebral precartilage is still further differentiated in embryos of 17 mm. Each nucleus is now surrounded by a small cell body in which are enclosed one, or more commonly two, vacuoles, each of which is nearly or quite as large as the nucleus. The cytoplasmic network has disappeared and the cells lie in a homogeneous matrix.

The perichordal septum has ceased to be recognizable as such, but its upper portion now remains as the fundament of the dorsal common vertebral ligament. It lies in a deep groove in the precartilage of the body of the vertebra. The ribs and vertebræ are sharply marked off by the perichondrium from surrounding tissues.

Chondrification of the vertebræ begins before embryos are 20 mm. long. (Fig. 5.) At this time the vertebral cells have much the same character as before, but the vacuoles are less conspicuous and the cytoplasm is more granular and stains more heavily. Each cell, however, is now separated from the matrix by a heavily stained capsule. A considerable space often separates the cell from its capsule; this, however, may be due to shrinkage.

The cartilage is now surrounded on all sides by a layer of small, closely-packed, rounded nuclei. This layer, together with the fibrous tissue surrounding the vertebra, forms the embryonic perichondrium. The central portion of the intervertebral disc, which includes from one-third to one-quarter of its diameter, is now precartilaginous. The outer portion of the disc is gradually becoming more fibrous. The interdorsal ligament is now well differentiated from the blastemal portion of the ligament and from the neural arch. Its upper edge and outer portion still remain blastemal. The same is true of the upper end and outer portion of the neural process. The upper blaste-

mal tissue will later differentiate into the upper portion of the interdorsal ligaments and of the neural arch which now extends but to the middle of the side of the spinal cord. The outer blastemal tissue of the neural process, as noted above, seems to form the myoseptum. A column of blastemal tissue from which will be formed the transverse process of the vertebra, the tubercle of the rib, the costo-transverse ligaments, etc., extends from the rib to the neural arch.

The notochord has also undergone fundamental alteration. The cell walls, which up to this time have remained intact, are now breaking down (or are being absorbed) and the mucin from the cell vacuoles escapes. The cells are united by strands of cytoplasm and the notochordal tissue now resembles mesenchyma. A part of the mucin remains in the cytoplasmic mesh, some of it, escaping, helps to thicken the inner sheath of the notochord, and a large quantity collects within the intervertebral portion of the notochord whose sheaths are compressed slightly by the intervertebral disc. The vertebral portion of the notochord, owing to the escape of the mucin from its vacuoles into the inner sheath, or into the intervertebral portion of the notochord, is much reduced in size and is much denser than before, but the corresponding portion of its sheaths is dilated. The notochord is thus dilated intervertebrally and contracted vertebrally, but the reverse is true of its sheaths, the outer sheath being of greater diameter, and the inner sheath both of greater diameter and also of greater thickness in the vertebra. The notochordal undulations are obliterated by these changes in the notochord and vertebræ.

A brief discussion and summary of the relation of the notochordal undulations and the ribs and vertebræ to the segments is desirable at this point.

Dr. Minot has shown that the segmental waves of the notochord of the pig are somewhat different from those of other mammals. The crests of the undulations are a very short distance in front of the intersegmental arteries, and are in the posterior fourth of the segment; the troughs are in the second fourth; the ascending or anterior slope in the third; and the posterior slope in the first fourth of the segment. The intervertebral disc, which is formed from the transverse portion of the primitive vertebra, is mid-segmental, and lies just behind the trough of each notochordal undulation. The edge of the blastemal intervertebral disc abuts upon the posterior edge of the spinal nerve and from this point the dense tissue of the primitive arch extends backward

and outward into the neural and costal processes which belong to the posterior part of the segment. These relations persist until the formation of precartilage begins, when the blastemal primitive vertebra breaks up into the intervertebral disc, the neural arches, ribs, myosepta and such diverse structures as cartilage, fibrocartilage, fibrous connective tissue, and perichondrium.

Finally, I am convinced that the delimitation of the "primitive vertebra" is not due to its becoming differentiated before the surrounding structures, but to the more rapid differentiation of the definitive vertebræ which leaves the more slowly developing blastemal tissue between the successive vertebræ as the "primitive vertebra." These considerations suggest that the scleromere is not a morphological unit or anlage; it is rather a residual mass of undifferentiated sclerotomic tissue which later forms such diverse morphological units as the annulus fibrosus and the fibro-cartilage of the intervertebral discs, the rib, the neural arch and the myoseptum. In short, the "primitive vertebra" is a lager rather than an anlage, a store of rudiments, not a rudiment. If this is true, the conception of the resegmentation of the primitive vertebræ is without foundation, for the "primitive vertebra" is not a vertebra at all. Moreover, the evidence presented by Bardeen in support of his belief that the intervertebral disc is formed by the union of the tissue from the anterior surface of the primitive disc and from the posterior surface of the anterior half of the sclerotome, is not conclusive. He says (p. 165): "During the period of differentiation of the scleromeres the myotomes undergo a rapid development. The median surface of each myotome gradually protrudes opposite the fissure of von Ebner. The dorsal and ventral processes of each scleromere are then slowly forced into the interval between the belly of the myotome to which it belongs and the one next posterior, and thus finally they come to occupy an intersegmental position." Again (p. 166), "During the development of the interdiscal membranes, the primitive discs become hollowed out on the posterior surface. A comparison of Fig. 2 with Fig. 3 demonstrates this." On page 167, "Each primitive disc has become further hollowed out at its posterior surface, owing in all probability to the conversion of its tissue into that of the area between the discs. The tissue of each segment immediately anterior to the primitive disc has become greatly thickened and the line between it and the disc indistinct." These facts are summarized on page 167, "The primitive discs become hollowed out posteriorly by a loosening up of their tissue

and strengthened anteriorly by a condensation of the tissue immediately bounding the fissure of von Ebner." The evidence for the most important point, whether or not the primitive disc is partitioned between the vertebra and the intervertebral disc, is very slight; and if the process described in the first and second quotations were to continue for some time, it would perfectly account for the fact stated in the third and fourth quotations. However, Weiss found in the white rat, and I find in the pig, that the primitive disc becomes the intervertebral disc. The fundamental mistake, I believe, in all work upon the primitive vertebræ, is the assumption that the primary sclerotomic condensations either are precartilage or are skeletal anlages. The fact is that they are neither the one nor the other. Precartilage, of the mammalian vertebræ at least, arises from such primary condensations only after a preliminary loosening up and subsequent condensation.

The Segmentation of the Notochord.

The notochord shows a most marked change in pig embryos of 24 mm. (Fig. 6). The advancing chondrification of the vertebræ is the apparent cause of a considerable expansion which, on the one hand, presses the notochord, together with the greater part of its semifluid inner sheath, from the vertebra toward the intervertebral discs; and on the other hand draws the disc away from the notochord so that a cavity is formed within the disc for the reception of the notochord. The outer sheath seems not to be broken and the inner sheath adheres to it so that, at no point, does the notochordal tissue come in contact with the cartilage of the intervertebral disc or even with the outer sheath. The intervertebral cavity is fusiform and the notochordal enlargement is irregularly diamond-shaped. The dense tissue from the vertebral portion of the notochord usually forms two slender cones whose broadened bases, opposing the bases of similar cones from the adjacent vertebræ, compress the intervertebral part of the notochordal tissue and flatten antero-posteriorly the masses of mucin within it. The two notochordal sheaths are very much compressed at the center of the vertebra, but less and less so the farther from its center. The greater part of the mucin which forms the inner sheath is forced into the intervertebral cavity; but a small part of it, and occasionally a few notochordal cells, are retained within the vertebræ. The notochordal tissue retains its syncytial character, and there begins at this time a more rapid increase of its mass, affecting alike nuclei, cytoplasm and mucin.

The chondrostyle is now complete anteriorly, for the tissue of the inner portion of the intervertebral disc is passing in this stage into true cartilage. The outer part of the disc is more and more fibrillar and is clearly destined to form the *annulus fibrosus*. The edge of the disc is still attached to the head of the rib, but the formation of the articulation is indicated by a small cavity which has now appeared between the two structures.

The cartilage of the vertebræ is more advanced. A large quantity of matrix intervenes between the cell-capsules, and many cells, owing to division, have two nuclei. The notochord forms approximately .2, the cartilage .3, and the fibrous tissue .5 of the diameter of the intervertebral disc.

Comparatively slight changes are seen in the notochord of an embryo of 39 mm. The syncytial network has been enlarged both by growth and by the formation of a relatively greater number of vacuoles of mucin, and, consequently, the nuclei are farther apart. The cytoplasm of the syncytium forms in places a regular continuous boundary, but at other points the vacuoles seem about to escape to the exterior. The small fragments of the notochord which have been enclosed within the vertebræ are degenerating. The first step in this process is apparently indicated by the separation of the cells from one another and by a change in the cytoplasm and nucleus which causes the former to take Orange G. more intensely and the latter to stain more deeply with hæmatoxylin. Somewhat later the nucleus becomes deeply and irregularly constricted and it is finally broken up into small pieces. The cytoplasm later is fragmented in the same manner.

Calcification of the centers of the vertebræ and of the notochordal sheaths within them begins in embryos of 32 mm. (Series 136) and has affected the greater part of the vertebral bodies in an embryo of 39 mm. Within the intervertebral disc, the outer notochordal sheath is no longer recognizable in the larger embryos, having been, in all probability, stretched to excessive thinness. The inner sheath has the same character and the same relative size as before.

Mitotic figures are very frequent in the cartilage just outside the region of calcification, and many characteristic cell-nests have been formed.

The cartilaginous portion of the intervertebral disc has increased in volume with advancing chondrification much more rapidly than its fibrous portion, and now forms about .41 of the disc, the notochord form-

ing about .25 and the fibrous tissue .33. The cartilage of the disc now has the structure which was earlier (17 mm. embryos) characteristic of the cartilage of the vertebræ; that is, each cell contains one or two vacuoles as large as or larger than the nucleus. A few cell capsules contain two nuclei. The fibrous tissue has begun to assume its characteristic arrangement in alternating layers whose fibers almost form right angles with one another and are inclined at an angle of 15° or 20° to the longitudinal axis of the spine.

A great change in the shape of the notochordal enlargement has occurred in an embryo of 75 mm. (Fig. 7). It is flattened antero-posteriorly and in vertical or horizontal section it is elliptical except for slight projections forward and backward into the open ends of its sheaths. The notochord now forms .41 of the diameter of the disc, the fibrous tissue .36, and the cartilage .23. The notochordal syncytium is larger but retains the same general character. It is bounded by a clearly defined cytoplasmic layer which has fewer vacuoles and more nuclei than the central portion of the notochordal tissue. The cells of the fibrocartilage of the disc are flattened as though by the radial pressure produced by the growth of the notochord, and the cells of the numerous cell-clusters are arranged in rows parallel to the adjacent portion of the notochordal sheath. Periosteal buds have filled the centers of the vertebræ and bone formation has begun. In a few places the calcified notochordal sheaths have been destroyed by the periosteal buds. This process finally destroys completely the vertebral portion of the notochord and hereafter the notochord is confined to the intervertebral discs.

The Formation of the Nucleus Pulposus of the Adult Pig.

The flattening of the notochordal enlargement continues until, in the cervical region of an embryo of 150 mm., it is thrice as broad as thick and forms one-half the diameter of the disc, the cartilage having shrunken to .15 and the fibrous tissue having remained of the same relative size (.36). The notochord in an embryo of 250 mm. forms .58, the cartilage only .08 and the fibrous tissue .34 of the disc's diameter. In short, the notochord is expanding at the expense of the fibro-cartilage, which, being attached to the cartilaginous faces of the vertebræ near their common axis, is stretched over their faces by the expanding notochordal tissue. Consequently the cartilage finally forms a thin capsule which surrounds the notochordal disc. The diameter of the mass

of notochordal tissue is about six times as great as its thickness. The peripheral portion of the notochordal syncytium is more continuous and regular, and is also denser. The notochordal tissue (Fig. 15) contains a few very large vacuoles at its center, but elsewhere is filled with a multitude of small vacuoles.

The vast increase in nuclei which accompanies the growth of the notochord is apparently due entirely to mitotic division, for in well-preserved material mitotic figures are abundant and there is no suggestion of amitotic division. In poorly preserved tissue mitosis cannot be recognized, and the irregularity of certain nuclei suggests amitosis, but this condition is probably due entirely to improper fixation.

In a larger embryo (250 mm.) the large central vacuoles of the notochord are apparently moving toward the periphery, and in a few places they have broken through the dense peripheral layer into the inner sheath. As they reach the surface these vacuoles often tear off portions of the dense peripheral layer which form rounded isolated masses. I find upon the lower edge of a single disc in this embryo, an interdigitation of processes of the cartilage and notochord such as Kölliker and Luschka describe in the adult man. The cartilage has constricted off a few small nodules of notochordal tissue which are assuming the structure characteristic of adult notochordal tissue. Large vacuoles which do not consist of mucin are forming in the cells which have become visible in the syncytium.

In the half-grown pig the notochord has encroached yet farther upon the remainder of the disc and forms about .74, and the fibrous tissue and fibro-cartilage .26 of the diameter of the disc. In shape the notochordal expansion is a very thin, lenticular disc. It is still surrounded by its inner sheath of mucin, which has become more dense, and after fixation in Zenker's solution it appears very finely and somewhat irregularly fibrillar. It now stains with hæmatoxylin more strongly than the fibro-cartilage. The formerly continuous peripheral sheet of dense syncytial tissue is now broken in many places by large masses of mucin, and in other regions it contains large vacuoles which seem about to escape into the inner sheath. The formation of mucin has continued until the center of the notochordal mass consists of a large quantity of mucin in which the slender syncytial network seems suspended. Between the very loose central mass of the notochord and the much broken dense peripheral layer, there is a zone which contains moderately small vacuoles in a syncytial mass. The mucin is gradually replacing a large

portion of the syncytial tissue and, beginning at the center, is gradually coming to surround the notochordal tissue instead of being surrounded by it. The mucin vacuoles at first are imbedded in the syncytium; the vacuoles, enlarging, touch and finally unite with one another, leaving a coarse network of syncytium; the strands gradually become attenuated and finally break, so that masses of notochordal tissue, which are very small near the center and large at the periphery of the nucleus pulposus, are isolated.

The cartilaginous portion of the intervertebral disc is represented by a very thin sheet of fibro-cartilage which lines the cavity in which the notochord lies. The portion of this sheet which lies upon the calcified cartilage of the epiphysis is more fibrillar than the portion which stretches around the notochord from vertebra to vertebra. The fibrous portion of the disc is very dense, and its inner portion, like the cartilaginous portion of the disc at an earlier stage, is being pressed radially outward by the notochord and forms a capsule around the notochord.

In the adult (Fig. 8) the notochordal enlargement is relatively thicker than in the half-grown pig. It is also relatively smaller, for it now forms but .4 of the diameter of the disc, the fibrous tissue forming the remaining .6. The expansion of the fibrous tissue is produced by the thickening of its various layers, not by the addition of new layers. The fibro-cartilage forms, as before, a thin lining of the notochordal cavity.

The mucin of the notochord retains the same character, but the tissue has undergone a most astonishing modification. The mucin now divides the notochordal tissue into a great number of relatively large masses which in turn are divided by smaller quantities of mucin into subsidiary masses. Each of the latter consists of a number of very peculiar cells or cell-like structures (Fig. 16) which are bound together by small quantities of syncytial cytoplasm. These cells each contain two, or more rarely one or three, large vacuoles which are surrounded by thin cytoplasmic walls and are separated by a small amount of cytoplasm in which lie, in the great majority of, if not in all cells, two small nuclei. All efforts to determine the nature of these vacuoles have failed. No stains affect them. They do not shrink in absolute alcohol but they do swell in water. Each cell of material which has been fixed in formalin and immersed in water for some time, owing to the swelling of the vacuoles, becomes elongated and constricted in the middle. Cells with but one vacuole resemble fat cells, but the vacuoles are not fat,

for they are not stained by osmic acid, Sharlach R, or Sudan III. The cytoplasm of these cells contains granules of glycogen.

It is a cause of regret that I have not been able to obtain notochordal tissue from immature pigs of various ages and from very old animals in order to follow carefully the process of formation of these cells and the ultimate modifications of the nucleus pulposus. It should be noted that although there are several points of similarity between notochordal tissue and cartilage in the pig and, as we shall find later, greater similarity in other animals, nevertheless, they are distinct tissues. The nucleus pulposus is formed entirely by the notochord.

Kölliker describes and figures clusters of cells from a child of one year which are essentially like the cell clusters of the adult pig; and Fric describes and pictures the same tissue from the nucleus pulposus of the human adult. Both men, however, consider that this notochordal tissue forms only the central part of the nucleus pulposus and that the weak fibro-cartilage of the disc is the peripheral portion of the nucleus pulposus. No transitions occur between the two tissues, and the inclusion of the fibro-cartilage in the nucleus pulposus is merely a matter of definition, not a question of fact; but unfortunately the description of the nucleus pulposus as formed of notochord and cartilage has led many to believe that it is produced by a fusion of the two tissues. The two tissues remain as distinct in the adult, despite their interlocking papillæ, as in the new-born child, in which they are separated by a sharp boundary. Both Kölliker and Fric call the notochordal tissue of the nucleus pulposus a "remnant" (Rest) of the notochord. This terminology is not allowable because it makes the remnant of a part greater than the whole; for the notochordal tissue of a single disc is much greater than the entire notochordal rod of the embryo.

The Notochord in Other Mammals.

It has not been possible to follow out the development of the notochord in other mammals as carefully as in the pig, nor is it necessary, for unless there appears in the literature of the subject or in the tissues of the adult some confusion or doubtful evidence, it is permissible to assume that similar structures in mammals have a similar developmental history.

The notochord of an opossum embryo of 7.5 mm. is a slender rod without segmental undulations. Anteriorly it is surrounded by an

anhistic sheath, and its tissue is syncytial and vacuolated. At the base of the tail, the notochord is cellular, vacuolated, and the somewhat thickened exposed cell-walls form its only sheath. In the tail, vacuoles are absent, and I am unable to find either cell-walls or sheath. A mesenchymal sheath surrounds the notochord in the tail and in the posterior part of the trunk, but there is no indication of a perichordal septum.

The dense sclerotomic tissue is interrupted, at the level of the notochord, by broad intersegmental zones of looser tissue. The myocœle has closed, and I do not find the fissure of von Ebner. The lighter zones are broad anteriorly, and in the neck and thorax they have become precartilage. The intervertebral discs lie in the third and fourth fifths of the segments, and are consequently a trifle farther back than in the pig. In an embryo of 8 mm., the centers of the discs of the anterior part of the spine have become precartilage.

The chondrostyle is well formed in an embryo of 11 mm. (Series 925), and is a cylindrical rod which encloses the notochord and bears the ribs and neural arches. Near the tip of the tail, the vertebræ are represented by broad zones of loose blastemal tissue which are separated by the denser tissue of the intervertebral discs. In the middle of the tail the notochordal undulations have appeared, and the crest of each undulation lies in an intervertebral disc, the trough in the precartilage of the vertebra. The center of each intervertebral disc in the sacral region is now precartilage, and the peripheral portion of each disc forms a slight thickening of the continuous perichondrium of the chondrostyle. The enlargement of the vertebræ, which is caused by their chondrification, is forcing the notochord in the lumbar region from the vertebræ into the intervertebral discs and is also both compressing the cells of the disc and carrying the lower and lateral parts of the disc away from the notochord. This process makes the vertebræ, which before chondrification are smaller than the intervertebral discs, larger than the intervening discs. In the trunk and neck, however, the chondrification of the cartilage of the discs has caused them to become of nearly as great diameter as the vertebræ. In this region, therefore, the discs are recognizable only by the notochordal enlargement, by a slight compression of the cartilage cells, and by the slight thickening of the perichondrium which represents the fibrous portion of the disc. The result of all these processes is that the spine of this embryo is represented anteriorly by the nearly cylindrical chondrostyle; in the

posterior part of the trunk by the cartilaginous vertebræ and the constricted precartilaginous or blastemal intervertebral discs; and posteriorly by the constricted blastemal vertebræ and the dense blastemal discs.

The notochordal crests correspond, at first, quite closely with the intervertebral discs; but later (assuming that the posterior portion of the notochord represents an earlier, and the anterior part a later phase of identical processes) the crests appear to be a little in front of the centers of the discs. As the notochord is driven from the vertebræ, it forces its sheath downward and outward so that its lower limit in the intervertebral disc is brought down as far as the troughs of the notochordal undulations (Fig. 10). The enlargement consequently becomes irregularly fusiform, its lower surface being flat. As more tissue is forced into the disc, the enlargement bulges downward sharply at a point near the middle of the disc and somewhat behind the crest of the notochordal wave. This process continues until, in an embryo of 12 mm., the notochordal enlargements are roughly diamond-shaped (Fig. 17). The lower angle is always less acute and prominent than the upper or primary angle, which represents the crest of the notochordal wave. The notochordal sheath is not broken by the expansion of the notochord. The inner notochordal sheath appears late and is relatively thin. The accumulation of mucin within the intervertebral enlargement of the notochord is quite large. The anterior end of the notochord terminates, at a point midway between the hypophysial fossa and the foramen magnum, in a rounded knob. The cranial portion of the notochord, with the exception of the knob just mentioned, lies upon the upper surface of the cartilage, under the perichondrium, and forms a distinct ridge. The head of each rib is continuous with the intervertebral disc, and the tubercle is continuous with the neural process of the vertebra behind the disc. The transverse process (or cervical rib) of each cervical vertebra is continuous with the neural arch above and with the body of the vertebra at the base of the arch. The head of the rib seems to be displaced forward in the trunk of the opossum.

The process of differentiation of the vertebral column of the opossum seems to be identical with that in the pig, but the scantiness of the material at hand does not permit a precise determination of the conditions in the opossum. I am quite sure, however, that in both animals there should be recognized four distinct processes of vertebral differ-

entiation: the blastemal stage, in which the mesenchymal tissue is loosening up; the precartilaginous, in which a rapid multiplication of cells occurs; the cartilaginous and the osseous stage.

In the adult opossum the nucleus pulposus forms a large part of the intervertebral disc. In the tail, it forms 63 per cent of the disc; the remainder being formed, as would be inferred from the great size of its cartilaginous portion in the embryo, almost entirely of fibro-cartilage. The notochordal tissue has much the same character as in the pig, but the cells have ordinarily but one nucleus and the vacuoles are smaller and of very variable number. The cell or tissue clusters are much larger than in the pig.

The notochord of an adult mouse forms about 62 per cent of the cervical intervertebral discs. Of the remainder, the portion below the nucleus pulposus is of about twice the diameter of the part above it. Fibro-cartilage forms about two-thirds of the former, and but one-third of the latter. The notochordal tissue forms practically a single mass which contains very little mucin, but is surrounded by a thick layer of it, the inner sheath. The cells have usually one nucleus and relatively small vacuoles.

The structure of the nucleus pulposus of the guinea-pig is quite different from that of the mouse. Its relatively small and nearly spherical cells form small strands or clusters that are suspended in a large mass of mucin. They commonly contain small vacuoles. The cartilaginous portion of the disc, as in the pig, is very small. In a few places the notochord interdigitates with the fibro-cartilage.

In the adult dog (of advanced but unknown age) the *annulus fibrosus* encloses a mass of soft friable tissue of yellowish color which appears, at first sight, to be homogeneous. A small rounded but irregular mass, however, forms the center of the disc. This is quite distinct, and can be lifted out whole, leaving a cavity of sharp and smooth contour. Sections of the soft center of the disc at first seem to be composed of a single tissue, but it is seen that the cell clusters at the center of the disc are of much more variable size than those of the peripheral part and also that they are of different composition. The peripheral portion of the center of the disc is clearly cartilage containing immense cell nests. Not having been able to make out fibrils in the matrix, I am inclined to believe that this is hyaline cartilage with a very soft matrix. Luschka figures and describes, in the human adult, papillæ of fibro-cartilage which project into the notochordal tissue and

which contain similar but much smaller nests of cells. The central mass consists of a firm and apparently fibrillar matrix in which are embedded, without any regularity, clusters of cells of various size and appearance. Certain clusters contain small non-vacuolated cells which are from 10 to 14 microns in diameter and stain intensely with Orange G. The nuclei have a diameter about one-third as large as that of the cells and each contains small masses of chromatin and a nucleolus. Many cells contain nuclei, and the cells are often arranged in pairs or fours like cartilage cells. These cells are probably non-vacuolated notochordal cells. Other cell clusters are larger and are enclosed in a definite rounded cavity. Many of the cells in these clusters are of the type just described, the others contain vacuoles of various sizes. The cells with large vacuoles are similar to the notochordal cells described by Luschka, Kölliker and Fric in man, and are somewhat like those of the pig's notochord. There can be little doubt that these are also notochordal cells. The boundary of the central mass or notochord can be recognized under the microscope by a slight difference in staining property and texture between the matrix of the cartilage and of the notochord. Not having studied the formation of the intervertebral disc of the dog, I am unable to assert more than the probability that its soft center is formed of notochordal and cartilaginous tissue, and that as age advances the two tissues become more and more alike.

The morphological and physiological meaning of the segmentation of the notochord is quite clear. The notochord and its membranous, cartilaginous or bony sheath have been assumed to be developed in inverse ratio to one another: the former being the predominant structure in less, and the latter in more specialized forms. This is, in a general way, true, but the notochord does not degenerate in mammals. On the contrary, while it loses its primary continuity and surrenders to the vertebræ a part of its primary function, nevertheless the notochord continues to perform a part of its primary function, but in a somewhat different way and in connection with the segmented spine. The notochord is primarily surrounded by a continuous sheath of connective tissue, in which later appear isolated metameric cartilaginous elements. In mammals the cartilaginous elements unite, as we have seen, at such an early stage in development that they may scarcely be said to exist as separate units. The chondrostyle is deeply constricted near the center of each segment by the fibrous tissue of the intervertebral disc. Without these constrictions the chondrostyle would be too rigid

to admit ready flexion, and with them the chondrostyle would not offer a sufficient resistance to axial stresses; hence the need of the nucleus pulposus which, being incompressible and also being closely invested by the fibro-cartilage and fibrous tissue of the disc, serves as a pad upon which the vertebræ turn. When the spine is unbent, the nucleus pulposus forms a rounded mass which is bound in on all sides by the fibrous tissue and fibro-cartilage of the disc, which, being attached to the heads of the vertebræ, forms a capsule whose layers are concentric with the nucleus pulposus. When the spine is bent forward, for example, the posterior portion of the annulus fibrosus is stretched straight, forcing the nucleus pulposus forward as a wedge-shaped mass between the inclined faces of the vertebræ, while the anterior part of the disc is pushed forward, its surfaces being drawn together, in a sharp curve or in one or more folds. Corresponding changes occur as the spine is flexed in other directions or is circumducted. The nucleus pulposus contributes largely to the strength of the spine and to its flexibility. The chondrostyle is partially replaced by bone, but its intervertebral portions persist.

The tissue of the notochord is at first cellular and epithelial. Later it becomes syncytial and resembles closely mucoid connective tissue. It finally becomes cellular a second time and then is very similar to cartilage. Notochordal tissue is perfectly distinct from all other tissues of mammals, and passes through a very characteristic cytomorphosis.

The Shape of the Notochordal Enlargements in Mammals.

A description of the shape of the notochordal enlargements is very unsatisfactory alike because of the difficulty of accurate description; because the shape of any particular dilation changes with growth; and because, although the shape of the enlargement in each species is remarkably characteristic, the great amount of variation which occurs renders it difficult to determine the normal type of expansion. In the opossum, as has been noted above, the crest of the notochordal undulation makes the upper contour of the expansion. From this boundary the enlargement grows downward to the level of the troughs (Figs. 10 and 17). Later a small ventral process appears somewhat behind the crest of the enlargement and, as this process enlarges, the expansion becomes somewhat diamond-shaped, but the upper angle always remains in ad-

vance of the lower. Thus, although the shape of the notochordal enlargements is constantly changing, it is characteristic of the opossum at each stage.

In the pig, the trough of the notochordal wave lies slightly in front of the center of the intervertebral discs, and, as in the opossum, the convex wall of the notochord gives the cue to subsequent changes of form. The upper or concave wall of the notochord moves upward and, at the same time, the chondrification of the vertebra forces, or at least seems to force, the notochordal crest or summit forward until it comes to lie at the posterior edge of the disc. The notochord now makes a sharp descent from the posterior to the anterior edge of the intervertebral disc, and as it gradually expands the upper point moves forward to the center of the disc and the lower moves backward until a symmetrical diamond-shaped expansion is formed.

The notochord of the rabbit is first enlarged vertebrally, as in the pig and opossum, but to a greater extent. These dilations appear in the anterior vertebræ of an embryo of 10.5 mm. which are just passing over into precartilage. The convex side (the lower) of the notochord is usually more expanded than the upper, and there is usually formed a sharp ventral expansion of its sheath. The vertebral enlargements are larger and more symmetrical in an embryo of 12 mm., in which the vertebræ are precartilaginous. They occur throughout the trunk and they have apparently obliterated the notochordal undulations. Chondrification forces the notochord from the vertebræ into the intervertebral expansions, and in an embryo of 14.5 mm. (Fig. 18) the vertebral expansions have disappeared. The centers of the intervertebral discs are now loosening up in preparation for the formation of precartilage. The notochord first expands upward in the disc and later downward also. In an embryo of 18.8 mm., the enlargements are quite rounded and somewhat later they become of greater diameter than length. The upper moiety is usually somewhat larger than the lower, and somewhat in front of it (Fig. 9). The notochord is vastly more vacuolated in the embryo of the rabbit, and the vacuoles are more evenly distributed than in the other mammals studied.

In the cat, as in the pig, opossum and rabbit, the first notochordal expansions are vertebral. These appear in an embryo of 10.7 mm. in the anterior vertebræ which consist of very loose mesenchymal tissue; and in an embryo of 12 mm. they are larger and more numerous, the vertebræ being precartilaginous. The vertebræ are cartilaginous in an

embryo of 15 mm., and the discs are precartilaginous. The intervertebral expansions (Fig. 19) are forming, but, unlike those of other mammals, the vertebral expansions persist at least until the cartilaginous vertebræ are calcified (in embryos of 39 mm.) (Fig. 11). The first indication of the intervertebral expansion is a slight angular point which appears upon the convex or upper side of the crest of the notochord at the middle or near the anterior edge of the disc. As this increases in size, a similar but smaller and usually more rounded ventral point appears somewhat behind the first. The two angles usually become nearly equal, but they retain for a long time their asymmetrical position, and the enlargements are usually more flattened antero-posteriorly than in other mammals. There is also greater variation of the shape of the enlargement than in other mammals.

It should be noted in passing that a large part of the upper edge of the annulus fibrosus of the eighth to the seventeenth discs of the cat, and of the eighth to the sixteenth in the rabbit is converted into a transverse intercostal ligament which binds together the heads of each pair of ribs. In older rabbit embryos these ligaments are less distinct than in younger embryos.

The notochord of a sheep embryo of 14.6 mm. is of uniform diameter, and the chondrification of the vertebræ has just begun. In an embryo of 16.1 mm. enlargements have appeared in the first few vertebræ, but at 17 mm. the enlargements are being compressed. The chondrification of the vertebræ is far advanced in the next older embryo in the collection, 26.1 mm. (Fig. 14). The centers of the intervertebral discs are precartilaginous and a somewhat top-shaped enlargement of the notochord has formed in each at the summit of the notochordal wave. The vertebral enlargement has been divided and the parts have been driven forward and backward toward, but not into the adjacent discs. The notochordal enlargements are thus intervertebral, but each is a deeply constricted cord, consisting of the top-shaped central or intervertebral lobe and a pair of somewhat irregular and larger lobes which lie at a considerably lower level in the ends of the adjacent vertebræ.

The human notochordal expansions are of yet another type. The notochord is situated considerably below the center of the vertebral column and vertebral expansions do not occur. In an embryo of 22 mm. chondrification of the vertebræ has advanced considerably and the notochord is sharply compressed in the center of each vertebra. It is correspondingly and symmetrically dilated intervertebrally. The centers

of the discs are composed of precartilage. In an embryo of 32 mm. (Figs. 12 and 20) the chondrostyle is practically complete. The otherwise fusiform intervertebral expansion of the notochord is compressed above as by the sharp edges of the vertebræ, and consequently bears dorsally a small angular process which projects into the broad but thin cartilage of the disc.

The shape of the notochordal enlargements, in the mammals which have been studied, is perfectly characteristic at each stage of their development until they are transformed into the *nuclei pulposi* of the intervertebral discs.

The Relation of the Notochord to Chordoma.

The course of the notochord in the skull of the human embryo, taken in connection with the results that have been reached in the preceding part of this paper, offers some suggestions as to the origin and nature of chordoma. It will be seen in Fig. 20 that the notochord makes a single large sigmoid curve in the base of the skull and that it lies near the surface of the cartilage at four points. It is near the upper surface, in the hypophysial fossa, a short distance behind the fossa, and near the foramen magnum and near the lower surface at a point midway between the hypophysial fossa and the foramen magnum. This is the normal course of the notochord in the skull of human embryos. Its curve is due to the fact that after the formation of the notochord, the mesenchyma, growing inward between the base of the brain and the pharynx, surrounds the anterior and posterior ends of the cranial portion of the notochord; but, since the notochord is attached to the epithelium of the vault of the pharynx longer than elsewhere (until embryos are 9 or 10 mm. long), it collects above the central portion of the notochord. As the parachordal cartilages unite, they surround the notochord and hold it in this position. These facts were discovered by Froriep (1882), who described the later history of the notochord in the skull, and Gaupp cites them in his article upon the skull in Hertwig's "Handbuch der Entwickelungslehre." The middle section bears a large but variable number of kinks, short branches, thickenings, and other irregularities. These I find often involve the pharyngeal epithelium, which is here thickened and often invaginated. This section of the notochord has been found by Froriep to degenerate first, but in one of the embryos in the H. E. C., No. 851, 22 mm., it forms small

masses of tissue imbedded in the retropharyngeal connective tissue which are very similar both to the adult notochordal tissue pictured by Kölliker and Fric and to the tissue of chordoma. The posterior part of the notochord is forced upward and backward and forms a large mass upon the upper surface of the skull-base a short distance in front of the tip of the tooth of the axis. The anterior part of the notochord is forced forward and, forming a large mass between the cartilage and the perichondrium of the hypophysial fossa, persists longer than elsewhere in the skull. We have seen that notochordal tissue, which is enclosed in a large mass of cartilage, is either forced from the cartilage or is enclosed in it and degenerates. If the tissue escapes from the cartilage it undergoes a typical cytomorphosis and forms adult notochordal tissue which is in all essentials like chordomal tissue. If this same process takes place in the skull we should expect to find notochordal tissue forced by the first chondrification of this region, that of the *dorsum sellæ,* either forward into the hypophysial fossa, or backward and upward upon the *dorsum sellæ.* The chondrification of the posterior end of the parachordal plate would, under the same conditions, force the notochord backward toward the apex of the odontoid process of the axis, or forward. In the latter case the notochordal tissue would be forced either out under the skull or forward to the junction of the sphenoidal and occipital cartilages or bones. Chordoma occurs at all these points, except between the pharyngeal epithelium and the skull, and only at these points. It occurs most frequently upon the *dorsum sellæ,* less frequently in the hypophysial fossa and at the spheno-occipital junction, and in the malignant case reported by Fischer and Steiner it was found upon the upper surface of the basi-occipital bone. It should be noted also that the tumors which occur at the spheno-occipital junction lie in the marrow spaces, as though the tissue of the tumor had been forced into the bone under great pressure, as would be the case if notochordal tissue were compressed by the growth of both bones.

It seems to me probable that at least the majority of chordomas are comparable to cranial *nuclei pulposi,* and that chordoma should not be regarded as an abnormal growth of notochordal tissue, but merely a normal growth in an abnormal position. I am confident that chordoma also occurs beneath as well as above the spheno-occipital junction, but no such cases have been reported.

Summary.

1. The primitive vertebra of Remak or the scleromere of Bardeen is not a morphological unit and, in the pig, it is not resegmented to form the posterior part of the intervertebral disc and the anterior part of the following vertebra. Its central part forms the annulus fibrosus and the intervertebral portion of the chondrostyle from which arises the fibro-cartilage of the intervertebral disc. Its lateral portions form a large variety of structures, among which may be mentioned the ribs, the neural arches (or parts of them), the costo-transverse articulations, ligaments, myosepta, and perichondrium. In short, the primitive vertebra is a mass of undifferentiated mesenchyma which is never segmented longitudinally.

2. The cartilage of the vertebra does not arise from a primary condensation of mesenchyma but from a secondary condensation which follows a loosening up of the relatively dense tissue of the scleromere. In the pig, mesenchymal tissue of nearly uniform density collects around the notochord of the trunk before the embryo is 7 mm. long. From this time until the embryo is 9 mm. long, the intersegmental or vertebral portions of this tissue become constantly looser while the midsegmental or intervertebral portions probably become slightly denser. A secondary condensation of the vertebral tissue takes place as the embryo grows from 9 to 12 mm., and at the same time there occurs a loosening up of the central part of the intervertebral disc preparatory to its secondary condensation. The secondary condensation of the tissue of the vertebræ and of the intervertebral discs produces precartilage. Chondrification begins when embryos are 14 to 17 mm. long.

3. The notochord expands slightly in each vertebra at the time of the formation of precartilage in all mammals studied except possibly man. This vertebral expansion is usually obliterated as the vertebra chondrifies, and the vertebral portion of the notochordal sheaths and small pieces of notochordal tissue occasionally or regularly retained in the vertebra are destroyed before the ossification of the vertebra. Most of the notochordal tissue is forced into the intervertebral disc and, growing, forms the nucleus pulposus.

4. Notochordal tissue undergoes a characteristic cytomorphosis. It is primarily cellular and epithelial; later it becomes a syncytial network with a mucin-like substance in its vacuoles; and finally it becomes cellular and closely resembles cartilage.

5. The form of the notochordal enlargements in each species studied, is characteristic of that species at each stage of its development.

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EXPLANATION OF FIGURES.

FIGS. 1 to 3 are photographs of the same magnification of similar frontal sections of pig embryos of 7.8, 9, and 12 mm. The notochord, the spinal nerves, the intersegmental vessels, the loose tissue of the vertebræ and the dense tissue of the "scleromere" should be noted.

FIG. 1. 7.8 mm. pig embryo, section 381, Harvard Embryological Collection, No. 430, × 306.

FIG. 2. 9 mm. pig embryo, section 595, H. E. C., No. 54, × 306.

FIG. 3. 12 mm. pig embryo, section 562, H. E. C., No. 6, × 306.

FIGS. 4 to 7 are photographs of median sagittal sections of vertebræ of pig embryos of 14, 20, 24, and 75 mm.

FIG. 4. Fourth dorsal vertebra, embryo of 14 mm. H. E. C., No. 66, section 134, × 133.

FIG. 5. First dorsal vertebra, embryo of 20 mm. H. E. C., No. 60, section 246, × 110.

FIG. 6. Fifth vertebra, embryo of 24 mm. H. E. C., No. 63, section 28, × 76.

FIG. 7. Eleventh dorsal vertebra, embryo of 75 mm. × 30.

FIG. 8. The nucleus pulposus and portions of the *annulus fibrosus* and of the epiphyses of an adult pig. × 10.

FIGS. 9 to 12 are photographs of median sagittal sections of vertebræ of embryos of the rabbit, opossum, cat and man.

FIG. 9. Twelfth dorsal vertebra of a rabbit embryo of 29 mm. H. E. C., No. 171, section 182, × 60.

FIG. 10. Fourteenth dorsal vertebra of an opossum embryo of 12 mm. H. E. C., No. 616, section 196, × 112.

FIG. 11. First dorsal vertebra of a cat embryo of 39 mm. H. E. C., No. 394, section 195, × 56.

FIG. 12. Eighth dorsal vertebra, human embryo of 32 mm. H. E. C., No. 292, section 176, × 56.

FIG. 13. Nuclei, which are possibly undergoing amitotic division, from a vertebra of a pig embryo of 12 mm. H. E. C., No. 5, section 894, × 1000.

FIG. 14. Third dorsal vertebra of a sheep embryo of 26.1 mm. H. E. C., No. 1112, section 235, × 36. The trilobate character of the intervertebral notochordal enlargement is shown.

FIG. 15. Notochordal syncytium with mucin-filled spaces from a pig embryo of 150 mm. × 800.

FIG. 16. Three vacuolated cells from the nucleus pulposus of an adult pig. × 452.

FIGS. 17 to 20 are reconstructions of a median section of the notochord and chondrostyle of embryos of the opossum, rabbit, cat and man.

FIG. 17. From an opossum embryo of 12 mm. H. E. C., No. 616, × 16.

FIG. 18. From a rabbit embryo of 14.5 mm. H. E. C., No. 162, × 13.

FIG. 19. From a cat embryo of 15 mm. H. E. C., No. 437, × 12.

FIG. 20. From a human embryo of 32 mm. H. E. C., No. 292, × 7.

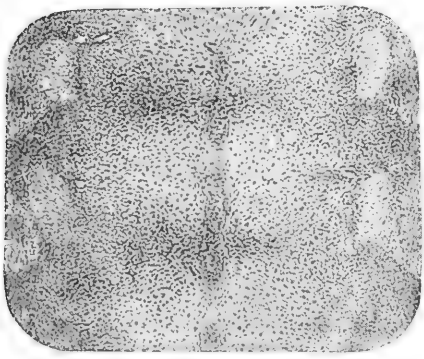

Fig. 1

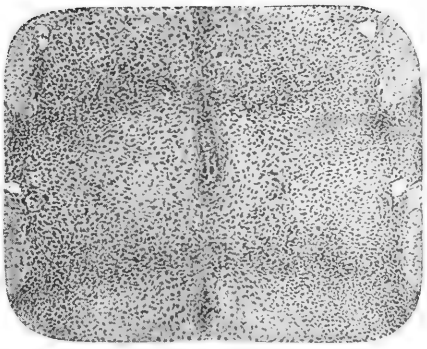

Fig. 2

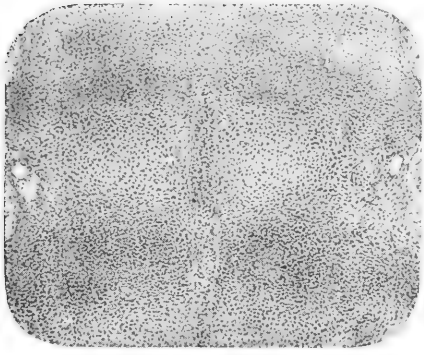

Fig. 3

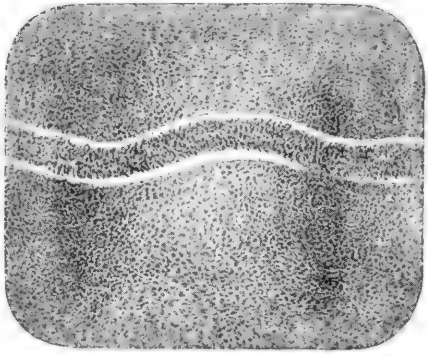

Fig. 4

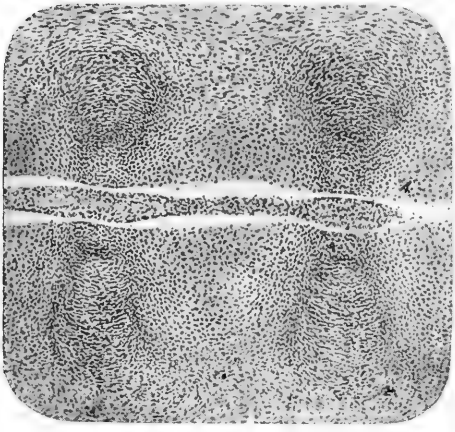

Fig. 5

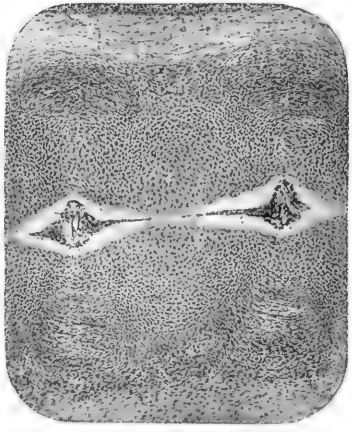

Fig. 6

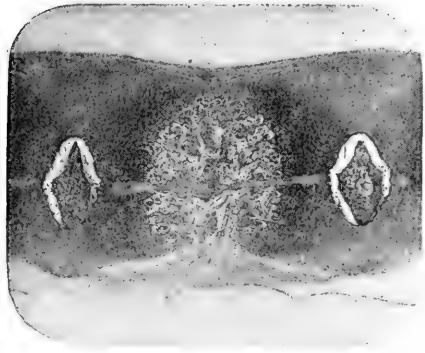

Fig. 7

Fig. 8

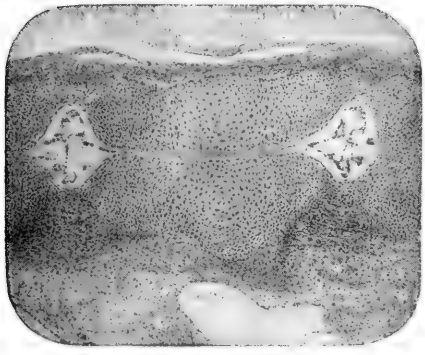

Fig. 9

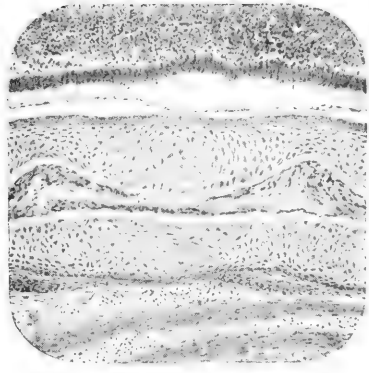

Fig. 10

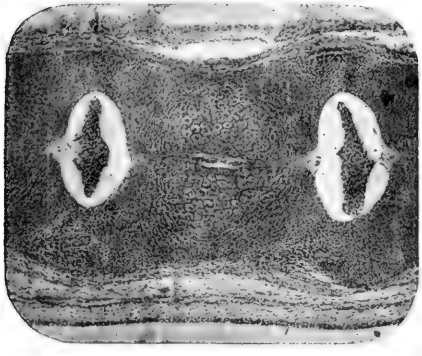

Fig. 11

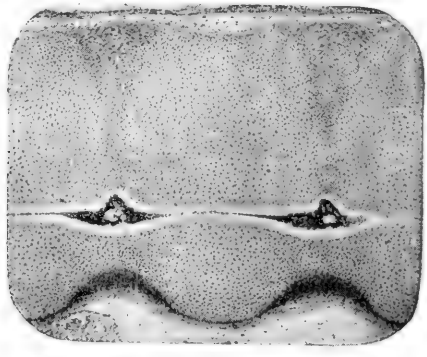

Fig. 12

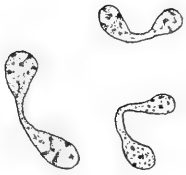

Fig. 13

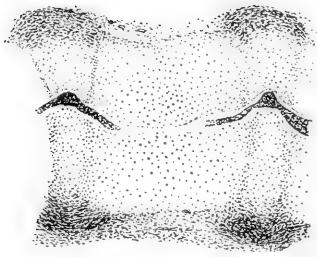

Fig. 14

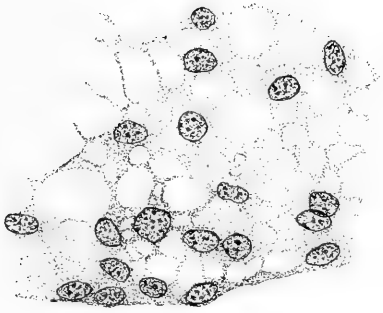

Fig. 15

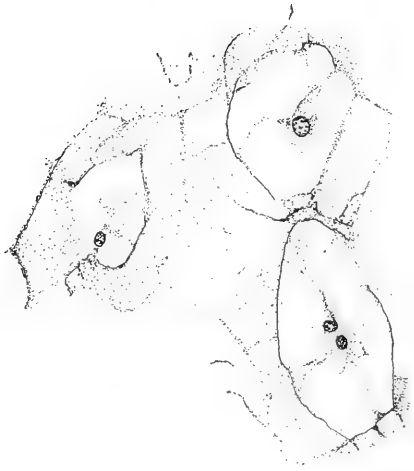

Fig. 16

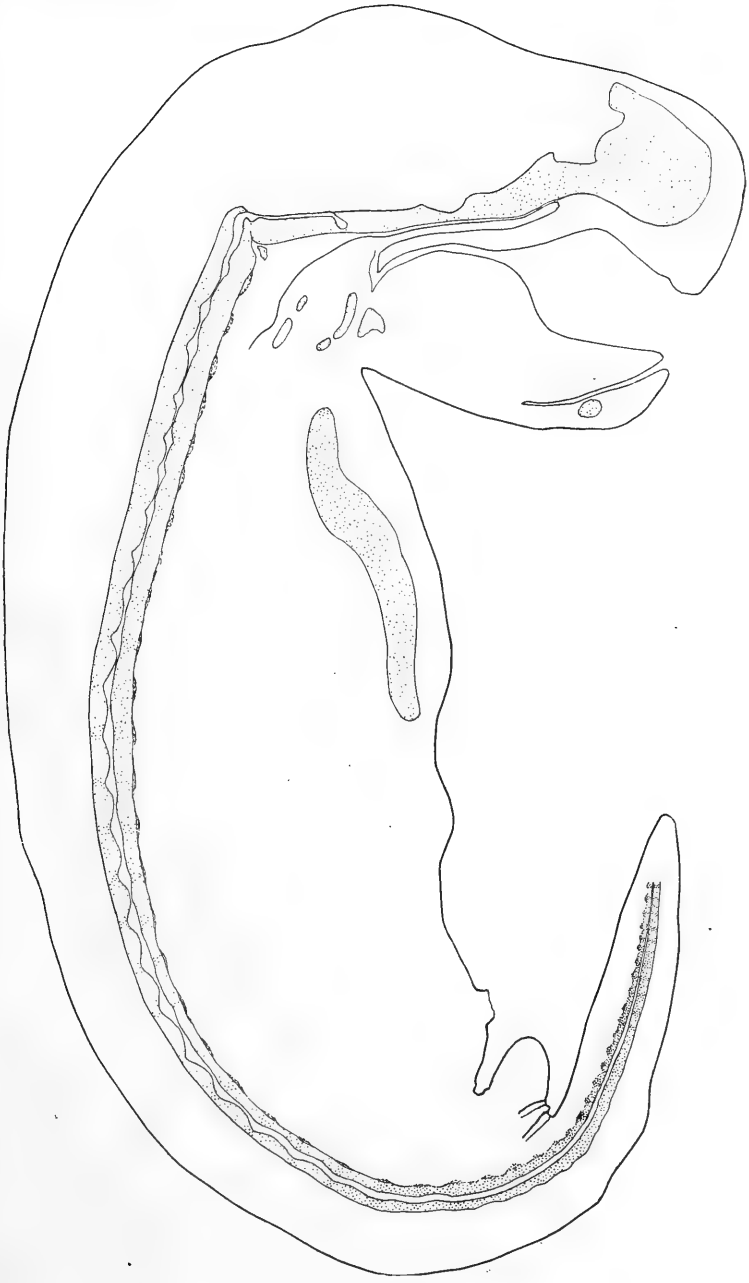

Fig. 17

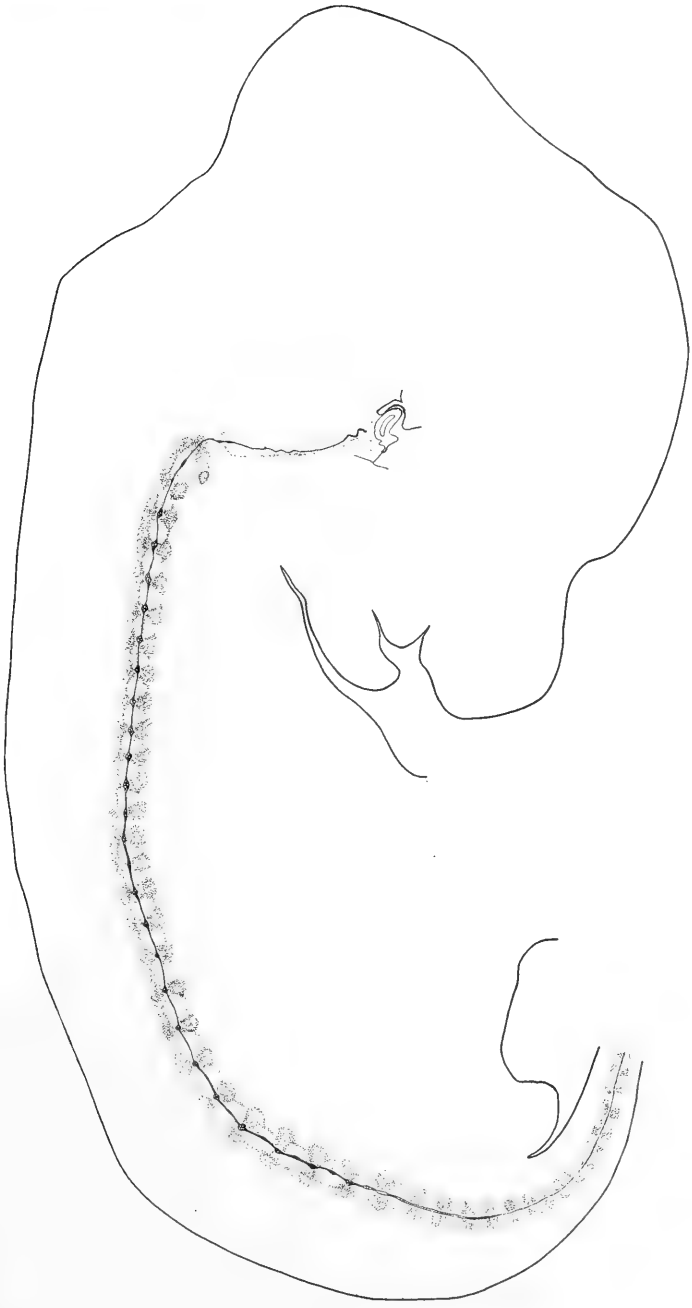

Fig. 18

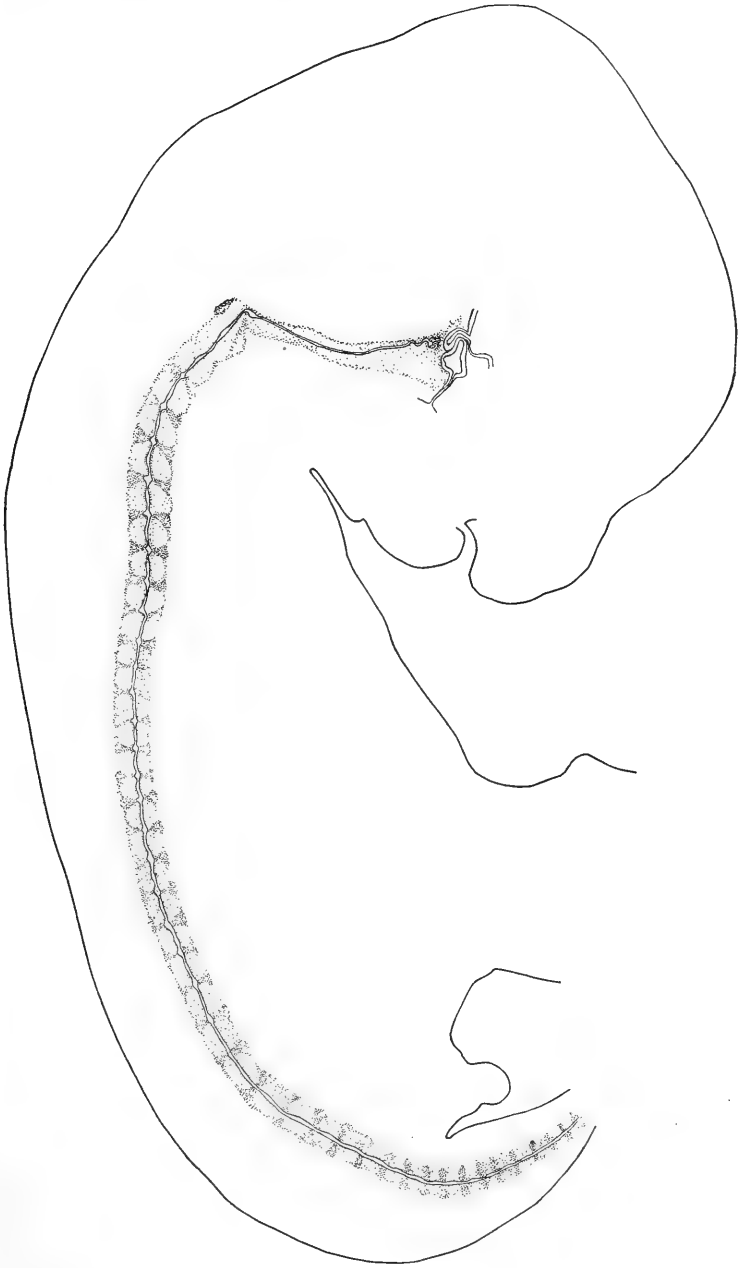

Fig. 19

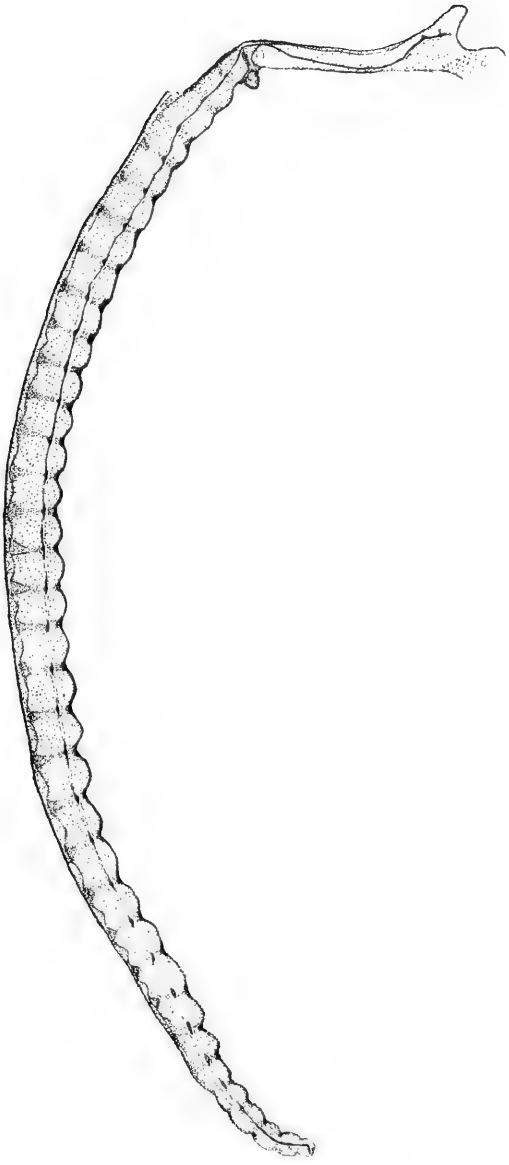

Fig. 20

THE PERIPHERAL NERVOUS SYSTEM IN THE HUMAN EMBRYO AT THE END OF THE FIRST MONTH (10 mm.).

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(With 3 Plates and 1 Text Figure.)

The period of development under consideration represents the completion of what we may call the primary stage in the growth of the nervous system. The primary neurones forming the peripheral nerves are by the end of the first month well laid down; all their chief peripheral branches and plexuses are indicated, and centrally the nerve roots can be traced to their distribution in the brain and spinal cord, where the nuclei of the motor roots can be outlined and the sensory roots can be recognized as definite bundles extending up and down in the wall of the neural tube. The higher neurone systems, however, are still in a most rudimentary state, and in sections through the brain and cord at this time we see only the primary apparatus differentiated. Such co-ordinating centers as the pons, olive and cerebellum are still undeveloped, and the forebrain is not much more than an undifferentiated thin-walled tube. It can thus be seen that the period with which we are dealing represents a definite stage in the growth of the nervous system, the stage of the primary brain, and a stage which is of particular importance for a proper conception of the embryology of this system.

A general view of the nervous system as it exists in embryos at the end of the first month is represented on Plate I. It can be seen that the reconstruction shown there corresponds in age almost exactly with the well known His reconstruction of his embryo KO of 10.2 mm. Nl. That investigator early recognized the significance of the stage of the primary brain. However, since His, '88, published his monograph and description of the embryo KO there have been introduced many improvements in the methods of work, and before all others should be mentioned the Born wax plate procedure. It is with such

aid and by means of the increased supply of available embryos that it was possible by Lewis, '02, to elicit further detail and obtain greater completeness in our conception of the formation of the brachial plexus and the development of the nerves of the arm, and Bardeen, '07, the nerves of the leg, and myself the nerves of the occipital region (Streeter, '04). With this in mind it seemed desirable to go over the same ground covered by His in his reconstruction of the embryo KO with the purpose of bringing out the same structures with more accurate detail and in more plastic form, and at the same time to incorporate the results of the work of the investigators just mentioned.

Some of the features brought out by this study with regard to the cranial nerves were reported at the Chicago meeting of the Association of American Anatomists (Streeter, '08). It is the purpose of the present paper to include the whole peripheral nervous system of the same embryo.

Material and Methods. The embryo on which this study is based constitutes No. 3 of Professor Huber's Collection, and was kindly loaned by him for this purpose. After fixation in alcohol the specimen measured 10 mm. greatest length. Its estimated age is 31 days. Unfortunately there was no clinical history obtainable. The embryo is cut in a series of 5 micra sagittal sections, and the tissues are in an excellent state of preservation. The description and drawings are based in part on wax plate models and in part on profile reconstructions made in the usual way by superimposing transparent papers.

Brain and Spinal Cord.

The general form of the brain and spinal cord and their relation to the body outlines is shown in Plate I. The spinal cord is largest in the cervical region, and from there slowly tapers down, being somewhat larger again in the lumbar region, and finally abruptly tapers off at the coccyx. In transverse section the cord possesses a trapezoid outline with rounded corners, the width of the ventral half being a little greater than that of the dorsal half. A large ventricle or central canal extends throughout its whole length. By the lanceolate border of this canal the cord is divided on each side of the median line into an alar and basal plate.

Toward the head the spinal cord enlarges and gradually merges into the rhombencephalon. In this transition the basal plates become thicker,

and the alar plates become wider, and at the same time flare apart. As the alar plates spread apart the narrow dorsal seam, that exists between the two in the spinal region, widens out into the broad roof of the fourth ventricle. The most striking feature of the rhombencephalon

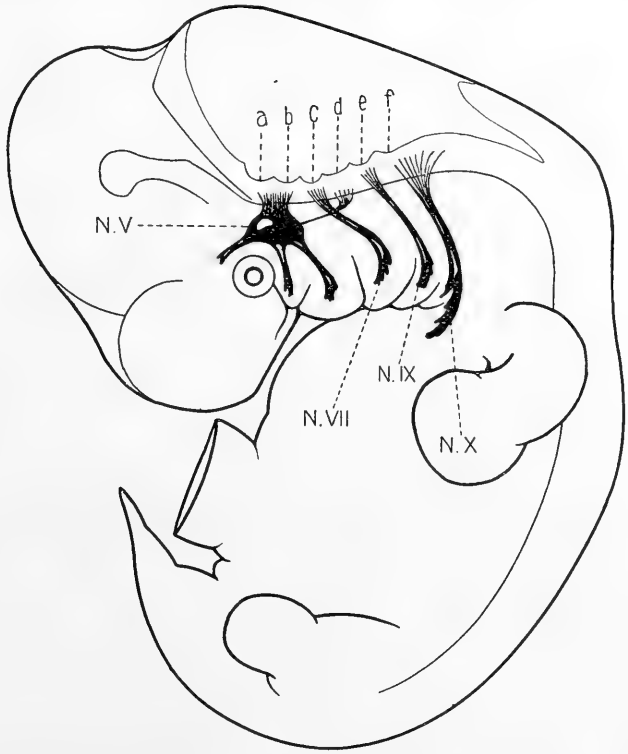

Fig. 1. Composite sagittal view of a 10 mm. human embryo (Huber collection No. 3), showing the rhombencephalon and the so-called rhombic grooves, which exist temporarily as transverse furrows in the floor of the ventricle. They are connected by the fifth, seventh, ninth and tenth nerves with the branchial arches. The fourth groove (d.) is an exception and has no corresponding visceral nerve. Arising from it can be seen the sixth nerve, extending forward to reach the anlage of the external rectus muscle.

in this embryo is its large size as compared with the rest of the brain. Its general form is shown in the drawing. It will be noticed that that part of the alar plate cephalad to the trigeminal nerve, which is to take part in the formation of the cerebellum, shows as yet little signs of differentiation.

The rhombic grooves present in the floor of the fourth ventricle were described in the paper previously mentioned (Streeter, '08), and their relation to the cranial nerves was also referred to. It will only be necessary here to refer to the accompanying Fig. 1., in which is shown a composite sagittal view of the embryo. The six rhombic grooves are indicated by the letters a. to f. Extending from the rhombic grooves to the branchial arches may be seen the trigeminal, facial, glossopharyngeal and vagus nerves. The correspondence of the arches, the nerves and the grooves strongly suggests the branchiomeric character of the whole group. Arising from groove d. is the n. abducens extending forward to the region median to the trigeminal. This is included in the drawing, though it is recognized that it may have no determinative connection with the fourth groove with which it stands in relation.

The outlines between the mesencephalon, thalamencephalon and prosencephalon are easily made out, and correspond closely with the His KO embryo (Tab. II, Fig. 3). It is to be noted, however, that in this case the olfactory bulb is not as well developed as indicated by the His drawing, the beginning olfactory pouch being represented by only a slight depression in the brain wall just lateral to the lamina terminalis.

The general structure of the neural tube at this stage is shown in a series of cross sections given in Figs. 20-26 in the monograph of His, '88, mentioned above. They show the division of the wall into three layers, the so-called ependymal, mantle and marginal zones; the first is made up of deeply staining primitive cylindrical cells, the second of clumps of budding neuroblasts, and the third is almost wholly fibrous. In the mantle zone are developed the nuclei of origin of the motor nerve roots, which can be outlined as shown in the reconstructions. The marginal zone consists of a reticulated framework through which the various fibre tracts make their way. At this time the only tracts that stand out prominently are the dorsal funiculi of the spinal cord, consisting of processes from the dorsal roots of the spinal nerves, and in the brain the corresponding tractus solitarius and spinal tract of the trigeminal nerve. In addition to these a portion of the marginal zone can be outlined which contains developing longitudinal fibres, and represents the so-called ventral ground bundle. In the cord it serves to connect the different levels of the mantle layer. It is continued through the hindbrain, and longitudinal fibres grow through it in that region, eventually resulting in the three main longitudinal tracts: the fasciculus longitudinalis medialis, the lemniscus and the tractus pyramidalis. This

ground bundle has been modelled out and forms the support to the reconstruction shown in Plate II.

Cerebral Nerves.

For purposes of description the nerves of the head will be grouped in accordance with their relation to the four functional systems of Gaskell, the significance of which has been emphasized in the recent writings of Johnston, C. J. Herrick, and others. According to Gaskell the functional systems are determined by the two chief activities of the organism; first, actions in relation to the external world (somatic), and second, internal activities having to do with the processes of nutrition, etc. (visceral). In each case there is the double activity on the part of the nervous system, sensory and motor, making in all four primary functional divisions. Now some of the cranial nerves consist of elements belonging exclusively to one functional division, for example, the n. abducens which consists entirely of somatic motor fibres, while others are complex nerves containing elements of more than one system, such as the n. glossopharyngeus which contains elements from three functional divisions, somatic sensory, visceral sensory and visceral motor. The nerves will therefore be grouped according to the predominance of their functional elements as follows:

Somatic Sensory.	*Somatic Motor*	*Visceral*
Olfactory	Oculomotor	Trigeminal
Optic	Trochlear	Facial
Acoustic	Abducens	Glossopharyngeal
	Hypoglossal	Vagus and Accessory

In general the basal plate of the neural tube is motor and the lateral plate is sensory; thus the somatic motor group arises entirely from the basal plate, while the visceral group arises in large part from the lateral plate and in lesser part from the basal plate. The somatic sensory group is specialized and these nerves have individual processes or lobes of the nervous system devoted to them, *i. e.,* the olfactory bulb, the eye bulb and stalk, and the tuberculum acusticum.

Nerves of Special Sense Organs.

These nerves belong to that large group of afferent nerves that connect the integument with the central nervous system, the somatic

sensory nerves. The general cutaneous nerves supplying the whole surface of the body compose the bulk of this group, and they are represented in the head by fibres belonging to the trigeminal, ninth and tenth nerves. In addition there are in the head region special somatic sensory nerves. The union of nerve and integument has resulted in these cases in the formation of special sense organs, that is the olfactory organ, the eye and the ear, composed partly of nerve elements and partly of integument. In this sense the olfactory nerves, the retinal ganglion cells and the acoustic nerve, though differing so widely in their adult morphology, may be considered as analogous in development and function.

Nn. olfactorii. At the end of the first month the ectodermal olfactory pit is definitely formed and is already in the process of differentiation, evidenced by the increase of body-protoplasm of its epithelial cells. A corresponding pouch is just beginning to form at the olfactory area at the base of the cerebral hemisphere, the anlage of the olfactory bulb. The fibres which later connect the two, nn. olfactorii, cannot yet be made out.

N. opticus. In case of the optic apparatus the chief contribution on the part of the integument is the lens; and the nerve contribution is the retina. The optic nerve corresponds to the olfactory stalk, and it is formed by the conversion of the optic stalk into a fibre tract connecting the retina with the brain. In the embryo studied the optic stalk consists of a thick-walled hollow tube whose cavity still freely communicates with the general brain cavity. The lower border is indented by the choroidal fissure which gives it a crescentic outline in cross section. The structure of this stalk is like that of the wall of the hemisphere, consisting of a thick ependymal layer covered in by a thin fibrous marginal zone. This marginal zone later thickens at the expense of the ependymal layer and is converted into a framework through which the nerve fibres from the retina make their way to the brain. At the end of the first month we cannot yet refer to this stalk properly as the optic nerve.

N. acusticus. This nerve is in a more advanced stage of development than the optic and olfactory nerves. The epithelial part of this apparatus, the ear vesicle, is already pinched off from the skin, as is shown in Plate I, and consists of a closed sac consisting of a double pouch having an upper vestibular portion and a lower cochlear portion; at the junction of the two on its median side is attached the ductus endolymphaticus.

The acoustic ganglion lies closely against the cephalic and median border of the ear vesicle. Two groups of fibres from the ganglion can

be made out entering into connection with the cells of the vesicle; the upper group corresponds to the nerves to the superior and lateral ampullæ and the utricle, and the lower group the nerves to the saccule and posterior ampulla. The ganglion is somewhat elongated and consists of an upper and lower portion. The upper portion is wholly vestibular, and the lower is partly vestibular and partly cochlear. The cochlear part, or ganglion spiral, is the thickened border of the lower division of the ganglion of which it is a derivative. The acoustic nerve emerges from the proximal end of the ganglion and enters the brain just lateral to the n. intermedius. The nerve at this time consists almost wholly of vestibular fibres. It is shortly after this that a well defined separate cochlear trunk can be made out connecting the ganglion spirale with the brain. What has been mistaken in younger embryos for a cochlear trunk are the fibres from the lower division of the vestibular ganglion. The acoustic fibres enter the brain wall near its border opposite the third and fourth rhombic grooves, and spread out in the marginal zone just dorsal to the spinal tract of the trigeminal nerve to form the anlage of the tuberculum acusticum.

Somatic Motor Group.

The hypoglossal and the three nerves to the extrinsic eye muscles (nn. oculomotorius, trochlearis and abducens) that compose this group are all shown in Plates I and II. As can be seen in Plate II, their nuclei of origin may be considered as a cephalic continuation of the ventral motor column of the spinal cord. This is particularly evident in case of the hypoglossal nerve, whose nucleus and emerging fibres form a continuous line with the ventral roots of the cervical nerves, and their close relation is shown by the tendency of the two to unite in the formation of a plexus. The eye nerves are in the same series with the hypoglossal, and always maintain a similar position near the median line and directly beneath the floor of the ventricle, though they are separated longitudinally at varying intervals. The character of the muclei of origin is the same in all four nerves.

There are no ganglia on these nerves such as are found in the spinal region, though occasionally a ganglion and also at times a dorsal root is associated with the more caudal roots of the hypoglossal. In such cases the ganglion is to be regarded as a precervical one, the exact counterpart of the spinal ganglia. This ganglion when present is the so-called Froriep ganglion.

The *n. oculomotorius* arises from a group of neuroblasts forming the ventral part of the mantle layer in the mesencephalon. These neuroblasts converge to form small rootlets which pass through the ground bundle and emerge on the ventral surface of the neural tube in the concavity of the cephalic bend. Here they unite into a common trunk, which at first passes directly ventralward and then making a slight angle bends lateralward and finally breaks up median and between the first and second divisions of the trigeminal nerve, in the cellular mass which is to form the eye muscles.

The *n. trochlearis* arises from a group of neuroblasts similar and lying just caudal to those of the oculomotor. The rootlets derived from them, instead of emerging directly ventralward, curve dorsalward to reach the roof of the isthmus, where they decussate and emerge as a solid trunk which passes down lateral to the neural tube and breaks up among the cells which are to form the superior oblique muscle.

The *n. abducens* arises from a group of neuroblasts forming the median part of the mantle layer directly beneath the fourth rhombic groove. See Fig. 1. The rootlets arising from these neuroblasts pass directly ventralward and after emerging they unite to form the main trunk, which bends forward immediately at an angle of nearly 90°, and passes forward into the region of the terminal rootlets of the oculomotor, as shown in Plate I. The relative positions of the abducens and the facial nerve will be referred to under the description of the latter nerve.

Visceral Group.

The facial, glossopharyngeal and vagus form a series of similar nerves which consist almost wholly of visceral fibres. As can be seen on Plates II and III, the visceral motor fibres arise from the nucleus ambiguus, which consists of a column of neuroblasts continuous with the lateral horn cells of the cord. The visceral sensory fibres arise from the peripheral ganglia and enter the alar plate of the neural tube and form a longitudinal strand which in the adult we know as the tractus solitarius. In addition to these visceral fibres there is a small number of somatic sensory fibres, supplying the integument of the adjoining region, which arise and have a course similar to the visceral sensory fibres. In aquatic vertebrates there are also the special somatic sensory fibres of the lateral line system, whose fibres join the rootlets of the facial, glossopharyngeal and vagus to reach the brain, and the ganglia from which these fibres are derived become incorporated in the geniculate, petrosal and nodosal

ganglia. We still have in the human embryo a trace of these organs in the form of a temporary thickening of the ectoderm directly over the ganglia of these three nerves.

The *n. facialis* is characterized by a large predominance of visceral motor fibres. They make up the bulk of the adult nerve, and in the higher vertebrates they have been made use of to supply the muscles of expression. These motor fibres arise from a group of neuroblasts situated beneath the third rhombic groove. Fibre bundles are assembled and pass directly lateral under the floor of this groove gradually converging to form a solid trunk which emerges from the neural tube just median to the acoustic ganglion. The trunk curves backward, as can be seen in Plate I, and breaks up among the cells of the hyoid arch, from which the facial musculature is to be derived. The sensory fibres of this nerve are derived from the geniculate ganglion. From the proximal end of the ganglion the fibres are assembled to form the so-called n. intermedius which enters the alar plate of the neural tube and forms the beginning of the tractus solitarius as shown in Plate III. From the peripheral end of the ganglion the fibres pass down to form the chorda tympani, and finally leave the main trunk of the nerve to enter the mandibular arch, eventually joining the third division of the trigeminal nerve. The great superficial petrosal is another peripheral derivative of this ganglion which makes its appearance a little later. Though the facial and acoustic nerves are closely united in position, and connecting fibres are usually present between the two in the adult, it must still be remembered that this is only due to the fact they lie close together. Further than that they have nothing in common, being nerves which belong to entirely different embryological and functional classes. The term facial-acoustic complex should only be used in the sense of position.

In a paper already referred to (Streeter, '08,) it was pointed out that the facial (motor root) and abducens nerves occupy positions in the embryo which are relatively reversed in the adult. The facial at first lies directly under the third rhombic groove, while the abducens is more caudal and is under the fourth rhombic groove. As development progresses the nuclei of these two nerves shift their relative positions, the abducens migrating forward. This migration results in the bending of the motor root of the facial out of its original course and produces the genu facialis which is characteristic of the adult.

The *n. glossopharyngeus* forms a more typical visceral nerve than either the facial or vagus. It possesses a ganglion of the root and

ganglion of the trunk, the latter being temporarily connected with the placode over the third arch. As can be seen from the relative size of the ganglia the nerve consists mostly of sensory fibres, connected peripherally with the structures developing from the second (r. tympanicus) and third (r. lingualis) arches. The tympanic branch is not well defined until we come to embryos between twelve and fourteen mm. long. Centrally the rootlets enter the brain wall and, joining with the fibres from the facial, extend caudally (Plate III) as the tractus solitarius. The motor rootlets of this nerve arise from a group of neuroblasts in the nucleus ambiguus series, situated beneath the floor of the fifth rhombic groove. The motor bundles extend directly lateral beneath this groove and pass under the spinal tract of the trigeminal and then emerge from the brain wall and join the main trunk of the nerve.

The *n. vagus* like the facial represents a branchial nerve the motor fibres of which have in man undergone special development, for the purpose of supplying a group of muscles derived from its branchial arch or arches. The large motor trunk of the facial nerve, as we have seen, is distributed to the muscle cells of the hyoid arch and, as these cells group themselves into the muscles of expression and spread forward over the face, the facial branches are drawn along with them. In a similar way the more caudal rootlets of the vagus become predominantly motor and form a distinct bundle which we know as the spinal accessory nerve, and this bundle is distributed to a group of muscle cells originally belonging to the more caudal branchial arches, and in man are destined to form muscles for the arm girdle, the mm. sternocleidomastoideus and trapezius. As these muscles spread out into their eventual position the nerve is drawn down across the neck with them. Coincident with the increased importance of this musculature as we ascend the vertebrate scale we meet with increased development of the spinal accessory, and it obtains additional rootlets of origin by spreading down into the region of the spinal cord. As can be seen in Plate I, the spinal accessory may reach as far down as the fourth cervical segment. The nucleus of origin of the spinal accessory and other motor rootlets of the vagus constitutes the nucleus ambiguus of the medulla oblongata and the lateral horn of the spinal cord, the two being directly continuous. This is best shown in Plate II.

The neuroblasts of the basal plate of the neural tube form two columns, a larger median one and a smaller lateral one; the median column furnishes somatic motor fibres to the ventral spinal roots and hypoglossal,

and at intervals further forward the motor nerves of the eye; the lateral column furnishes visceral motor fibres to the dorsal spinal roots and to the vagus (spinal accessory), glossopharyngeal, facial and trigeminal nerves. In the 10 mm. embryo these neuroblast columns are longitudinally continuous from the spinal cord into the vagus region, and there is present a continuous series of median (ventral) and lateral rootlets. As other structures develop the columns become interrupted and particularly the lateral column; thus in the nucleus ambiguus of the adult we have a broken series of discrete nuclei.

The motor neuroblasts of the vagus point dorso-lateralward and form rootlets which emerge just ventral to the entrance of the sensory roots. After emergence they turn forward and form a common trunk which in the spinal region lies between the dorsal roots and the side of the spinal cord. The more caudal rootlets are devoid of sensory fibres; but as we go forward we meet with ganglionated rootlets. In the vagus as in the glossopharyngeal there are the ganglia of the roots and the ganglion of the trunk (ganglion nodosum). The ganglia of the roots represent a series diminishing in the caudal direction, as shown in Plate I. In the adult the more caudal ganglia usually disappear except for traces of scattered ganglion cells found occasionally on the rootlets of the spinal accessory division. These more caudal vagus ganglia are not to be mistaken for the Froriep ganglion, which represents a persistent precervical ganglion. In the one case we have a series diminishing from the head toward the tail, and in the other it is in the opposite direction. Owing to the tendency to regression on the part of more caudal of the vagus root ganglia the vagus complex, as was shown in a former paper (Streeter, '04), becomes differentiated into a fore part or vagus division which is predominantly sensory, and a back part or accessory division which is almost wholly motor. In the 10 mm. embryo there is no division between the two parts.

On entering the wall of the neural tube the sensory fibres immediately unite in a longitudinal tract continuous with similar fibres from the facial and glossopharyngeal thus completing the formation of the tractus solitarius. In Plate III is shown a cross section of the neural tube in the vagus region, and on it is indicated the position of the tractus solitarius. The marginal or reticular zone of the alar plate in this region is mostly made up of the longitudinal fibres of this fasciculus, and directly ventral lies the similar group of fibres belonging to the trigeminal nerve. The relation of the two is best shown in Plate II.

Peripherally the fibres from the ganglia of the roots together with the remaining motor fibres that are not included in the accessory bundle are collected into a common trunk and pass down caudally to be lost in the ganglion nodosum. After they emerge at the distal end of this ganglion they bend medialward and lose themselves on the wall of the oesophagus.

The *n. trigeminus* possesses the largest ganglion of the whole embryo. From this ganglion the three large peripheral divisions extend ventralward. The ophthalmic division passes forward and subdivides into the frontal and nasociliary nerves, the latter forming a long slender well defined branch passing just dorsal to the eye stalk. The maxillary and mandibular divisions pass downward and break up in their terminal branches among the cells of the maxillary process and mandibular arch respectively. Centrally the ganglion is connected with the brain by a thick short trunk which enters the wall at the pontal bend and opposite the first and second rhombic grooves. Within the wall the fibres immediately form a flattened longitudinal tract, as shown in Plate II, part of which extends caudally as the spinal tract, and part extends forward and upward to enter the cerebellar ridge. These fibres must be considered as containing both somatic and visceral elements, between which no difference could be made out embryologically.

In its motor elements the trigeminal nerve departs somewhat from the type represented in the other three nerves of this visceral group. In the others the nucleus of origin is in the basal plate, and the nerve rootlets exhibit a characteristic curved course to reach the point of emergence; while in the trigeminal the nucleus is more lateral and lies directly against the entering sensory fibres, so that the fibres of the motor root pass directly ventralward to fuse with the mandibular division.

It is possible that the motor nucleus of the trigeminal is to be considered as an hypertrophied example of one of the dorsal motor nuclei found in the adult ninth and tenth nerves, both median and lateral to the tractus solitarius[1] and which have not yet been recognized in the embryo. In that case we must conclude that either the nucleus ambiguus and ventral motor root are not present in this nerve, or that they are represented by the mesencephalic motor root. In analyzing these nerves

[1]For a description of the motor nuclei connected with the tractus solitarius see E. L. Mellus, '02.

it is to be remembered that in man the typical visceral cranial nerve has three central terminations:

1. Sensory root (tractus solitarius).
2. Curved ventral motor root (nucleus ambiguus).
3. Straight dorsal motor root (nucleus vagi dorsalis).

These three elements may be represented in the different nerves in different proportions. The ninth nerve approaches the mean and all elements are fairly represented. In the vagus the curved ventral motor roots are increased in proportion in the caudal portions and form the spinal accessory. In the facial the sensory root (n. intermedius) is diminutive, while the curved ventral root becomes the main trunk of the nerve. In the trigeminal it is the straight dorsal motor root that forms the principal motor supply, while the curved ventral motor root is either not present or is represented by its mesencephalic root.

Spinal Nerves.

At the end of the first month each segmental nerve of the trunk possesses a sharply outlined spinal ganglion, whose constituent cells are in the early stages of differentiation. On examination it can be seen that many of these cells consist of a prominent nucleus surrounded by a thin rim of ill defined body protoplasm. In other cells the body protoplasm has increased in the form of a process at one or both ends. Cells of this kind are clustered so that their processes unite to form fibrous strands. These strands in turn fuse into larger bundles and lead toward the two poles of the ganglion. At the proximal pole they become grouped into the dorsal roots, which enter the spinal cord in an uninterrupted longitudinal series. In the cord they unite and extend up and down in the marginal zone in the form of a flattened band of fibres which later constitutes one of the dorsal funiculi of the cord.

The fibres from the distal pole of the ganglion unite in a common bundle which is almost immediately joined by the fibres of the ventral root, the two together forming the main trunk of the nerve. The ventral roots consist of a continuous series of rootlets emerging from the ventrolateral border of the neural tube, and derived from the neuroblasts of the mantel layer of its basal plate. These neuroblasts form a longitudinal column which, as shown in Plate II, is continuous with and of the same character as the nucleus of the hypoglossal nerve.

At the same time that the dorsal and ventral roots unite to form the main trunk they give off lateral fibres to form the dorsal branch, the so-called posterior primary division, which turns back dorsalward and covers in the distal part of the ganglion, and breaks up among the cells which are to form the long muscles of the back.

The remainder of the nerve trunk is continued forward as the ventral branch or anterior primary division. From its median side there is given off the ramus communicans, which extends medianward to the region of the aorta and ends in the sympathetic ganglion cord. The rami communicantes and the sympathetic cord are not shown in Plate I. The main trunk terminates in two branches, the anterior and lateral terminal branches, which correspond to the anterior and lateral cutaneous branches of the adult, and which in the thoracic and abdominal regions end among the cells giving rise to the musculature of the front and lateral body wall.

Throughout the spinal region there is a tendency for the nerve trunks to unite at the level of the lateral terminal branches and form intersegmental loops. This loop—or plexus—formation may involve either the lateral or the anterior terminal branches, or both. We thus have produced the cervical, brachial and lumbosacral plexuses.

In the cervical region the anterior and lateral terminal branches form two separate plexuses; the former produces the deep cervical plexus and the latter the superficial cervical plexus. The superficial cervical plexus consists of the union of the lateral terminal branches into loops from which are given off the cutaneous branches to the auricular, cervical and occipital regions. The deep plexus results in the formation of the ansa hypoglossi and the phrenic nerve. The former is produced by the fusion of the second and third cervical nerves into the descendens cervicis, which unites in a loop with the hypoglossal, together with which the first cervical has been incorporated above. From this loop are given off the short branches which end among the cells that are to form the hyoid musculature. The main trunk of the hypoglossal bends sharply medianward to end in the tongue anlage. The deep cervical plexus was studied in an older embryo (14 mm.—Mall embryo No. 144) and described in a former paper (Streeter, '04). The ansa hypoglossi is shown in Fig. 11 and is essentially the same as in the present case, differing only in that the communication between the first cervical and the hypoglossal could not be traced. In Plate II of that paper the r. descendens is labelled wrong; the leader should extend to a point above

where it is joined by the descendens cervicis, which can be seen as a slender nerve made up of branches from the second and third cervical nerves.

The phrenic nerve is formed by anterior terminal branches from the fourth and fifth cervical nerves. A contribution on the part of the sixth could not be made out. A view of the nerve can be seen through the arm in Plate I. Owing to the position of the diaphragm at this time the course of the nerve is almost directly ventral, passing over the lung anlage which is not represented in the drawing. Later, as pointed out by His and Mall (Mall, '01), the points of origin and insertion of the nerve draw gradually apart, due, on the one hand to the descent of the diaphragm and the lengthening of the thoracic cavity, and on the other hand to the subsequent elevation of the cervical nerves which accompanies the development of the structures of the neck. It is thus that there results the long caudal course of this nerve that is characteristic of the adult.

The brachial plexus is shown in Plate I by representing the arm as transparent. In the region of the fifth cervical to the first thoracic nerves there is an exuberant growth of both the anterior and lateral terminal branches, resulting in a solid flattened mass of fibres, which in turn is split by the skeletal anlage into two laminæ, from which the various nerves arise. Arising from the anterior or ventral lamina one can recognize the nn. musculocutaneous, medianus and ulnaris, and from the posterior or dorsal lamina the nn. axillaris and radialis. These nerves pass down into the arm and break up in the muscle masses, which they are to supply.

The lumbosacral plexus as compared with the brachial plexus is somewhat retarded in its development. It is formed by the fusion of the trunks of the five lumbar and upper three or four sacral nerves. These nerves and their ganglia, as with the cervical nerves, are enlarged as though stimulated to extra growth by the presence of the limb bud. The nerves unite into a flattened mass of fibres which enters laterally into the base of the leg bud, the division into anterior and lateral terminal branches being lost in the formation of the plexus. The further course of the fibres is determined by the framework of the leg. Owing to the cell masses of the bony pelvis and the femur the fibres become grouped into four bundles arranged in two pairs, each consisting of a median and lateral trunk. Of the upper pair the median trunk corresponds to the obturator nerve, and the lateral the femoral nerve.

The lower pair corresponds to the sciatic nerve, and its median bundle constitutes the future tibial nerve, and the lateral the common peroneal. From these larger nerves smaller branches split off and become isolated as discrete nerves, and enter the muscle masses between which the main trunks lie.

The Sympathetic System.

The ventral migration of the cells derived from the neural crest, that are destined to become sympathetic ganglion cells, is completed by the end of the first month. The elements derived from the successive segments have by that time fused together, on each side of the body, to form a longitudinal column of proliferating cells, situated lateral to the aorta and directly in front of the developing bodies of the vertebræ.

This column extends as a rather sharply outlined continuous cellular strand from the occipital region to the level of the lower sacral vertebræ. The differentiation of the individual cells is already under way and nerve fibre formation can be recognized throughout its length, being most pronounced in the thoracic and lower cervical region. This process however has not advanced far enough to produce a breaking apart of the column into segmental nodes, as is characteristic of the adult ganglionic chain.

Dorsally the column remains in connection with the nerve roots and spinal ganglia by means of the *rami communicantes,* which consist of sharply outlined fibrous bundles, varying from one to three bundles to each segment. The rami communicantes are largest and best developed in the thoracic and lumbar regions. In the cervical region they are least well developed, and owing to the slanting course of the upper cervical nerves they could not be satisfactorily traced in sagittal sections for the upper three segments.

Ventrally in the region of the sixth to the eleventh thoracic segment a definite fibro-cellular plexus extends forward to form the splanchnic nerves and cœliac plexus. The splanchnic nerves extend almost directly forward. As is the case with the phrenic nerve their caudal course is brought about later by the subsequent caudal displacement of the viscera relative to the bodies of the vertebræ. At this time the diaphragm and caudal surface of the heart lie opposite the first and second thoracic vertebræ, and the stomach is opposite the fifth to tenth thoracic vertebræ so that the cœliac region is directly ventral to the origin of the splanchnic nerves from the ganglionated cord.

The cardiac plexus and the cranial sympathetic ganglia owing to the more complicated architecture of those regions could not be outlined with any accuracy. The cephalic end of the ganglionated cord can be traced median to the hypoglossal nerve to the region situated between the ganglion nodosum and the wall of the pharynx. Its extension along the internal carotid artery and commuication with the ganglia of the head could not be made out.

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PLATE I. Lateral view of a wax plate reconstruction of a 10 mm. human embryo (No. 3, Huber collection), showing the origin and distribution of the peripheral nerves. The ganglionic masses are represented by darker and the fibre bundles by lighter shading. For purposes of orientation the diaphragm and some of the viscera are shown. The arm and leg are represented as transparent masses into the substance of which the nerve branches may be followed. The original model is enlarged 40 diameters and the drawing is about 12 diameters.

GEORGE L. STREETER

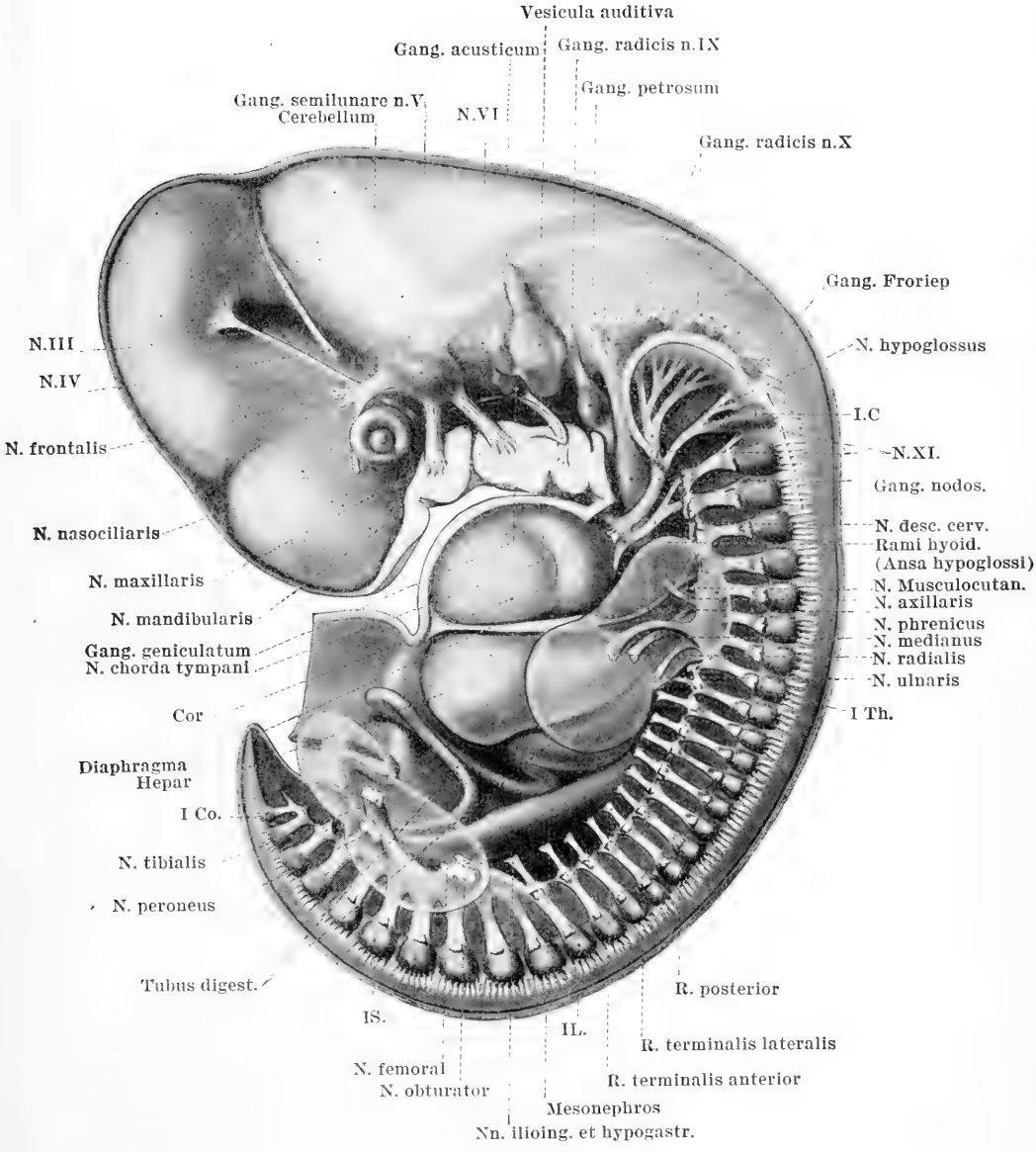

PLATE II. Median view of a model of the cranial nerves in the same embryo shown in Plate I. A portion of the spinal cord is represented and above that everything is cut away, excepting the sensory bundles and motor nuclei of the different nerves, together with that portion of the marginal zone which is to form the funiculus anterolateralis. The somatic motor nuclei are colored red, and it can be seen that they form a column that is practically continuous with the cells of the ventral horn of the spinal cord. Enlarged about 30 diameters.

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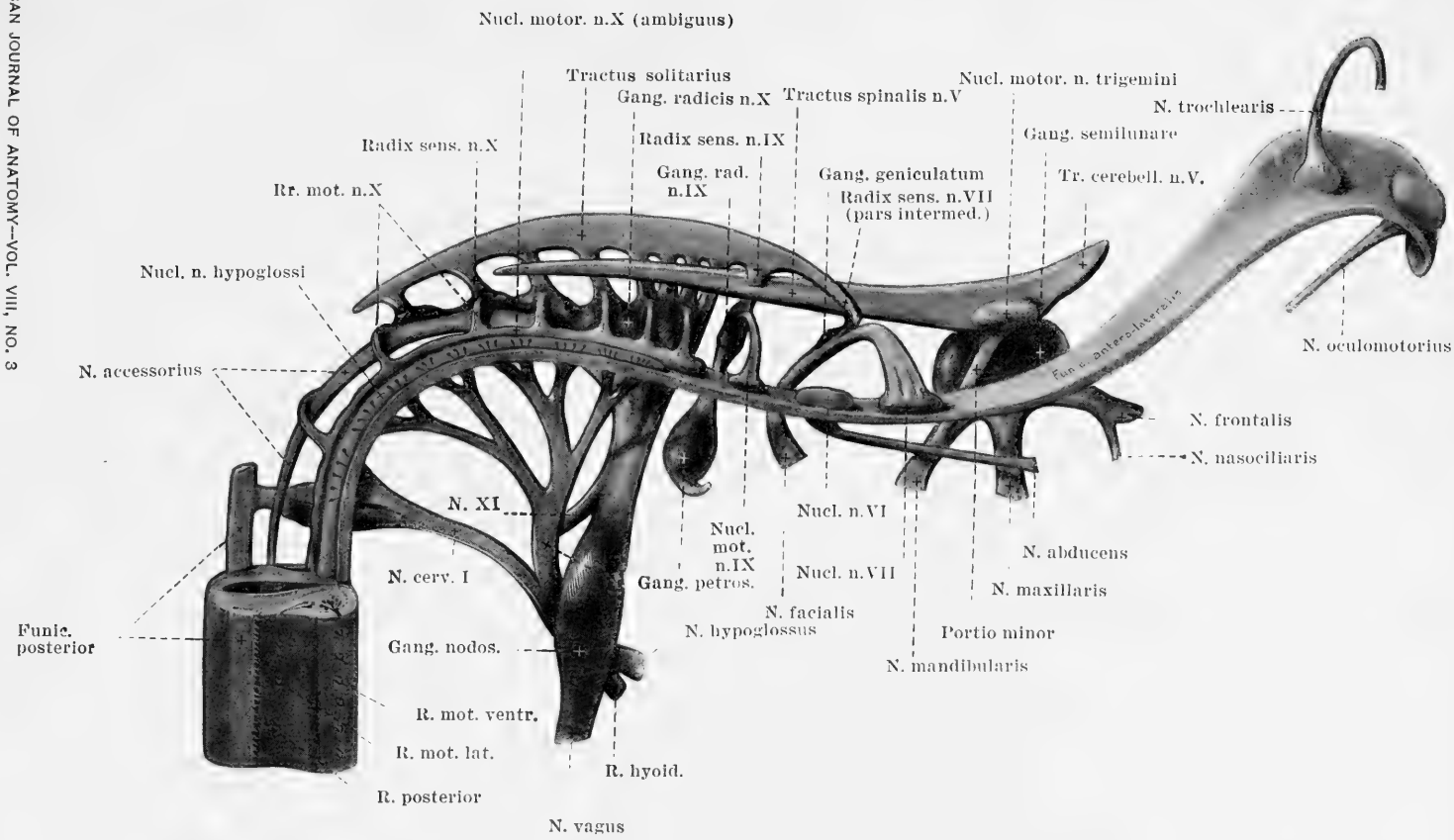
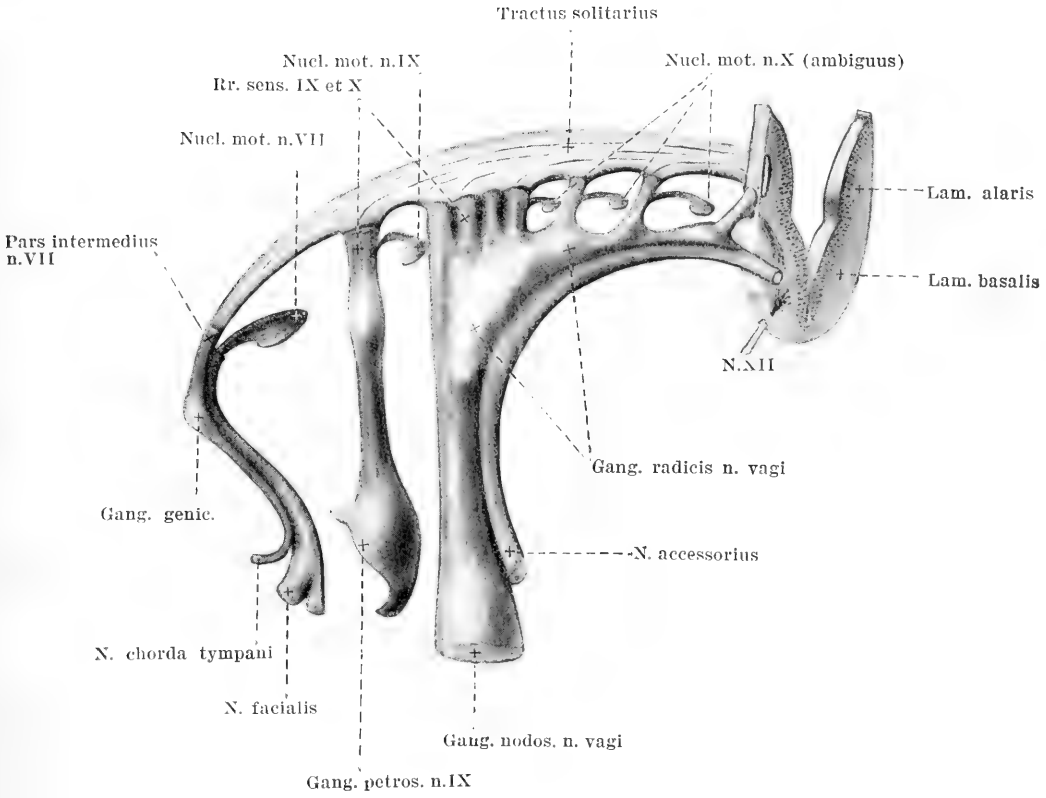


PLATE III. Reconstruction of the facial, glossopharyngeal and vagus nerve group in the same embryo shown in Plate I, showing the series of motor nuclei of origin and the tractus solitarius. It can be seen how the latter is formed by the sensory roots on entering the marginal zone of the neural tube, analogous to the dorsal funiculi formed by the dorsal roots of the spinal cord. A section of the neural tube is included in the reconstruction to show its relation to these different structures. Ganglionic masses are represented by lighter shading than the fibre bundles, and the point at which the rootlets enter the neural tube is indicated by dark rings. Enlargement about 35 diameters.


Tractus solitarius
Nucl. mot. n.IX
Rr. sens. IX et X
Nucl. mot. n.X (ambiguus)
Nucl. mot. n.VII
Lam. alaris
Pars intermedius n.VII
Lam. basalis
N.XII
Gang. radicis n. vagi
Gang. genic.
N. accessorius
N. chorda tympani
N. facialis
Gang. nodos. n. vagi
Gang. petros. n.IX

ON THE ORIGIN OF THE MESENTERIC SAC AND THORACIC DUCT IN THE EMBRYO PIG.

BY

WALTER A. BAETJER.

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The modern literature on the development of the lymphatic system may be said to begin with the publications of Ranvier[1] in 1895. Prior to this time, the most widely accepted theory was that the earliest lymphatics existed as spaces in the mesenchyme, which gradually became confluent and formed lymphatic ducts. The first break from this idea came as early at 1868, when Langer[2] published his observations on the lymphatics in amphibians. He noted that the lymphatics in tadpoles did not resemble tissue spaces, but had rounded endothelial-lined ends, which often had long strands of endothelium coming from them. This gave them the appearance of developing blood-vessels, and Langer interpreted his observations to mean that lymphatics grow like blood-vessels by the sprouting of endothelium.

Ranvier noted the same appearances in the developing lymphatics in tadpoles and in pig embryos and also interpreted them to mean that the lymphatic vessels grow by budding. This made the original theory seem even more doubtful and suggested the close association between the lymphatics and the veins. The proof of the venous origin of the lymphatics—suggested by Ranvier—was not definitely established, however, until the work of Dr. Sabin[3] on pig embryos in 1902. In this study it was first shown that the lymphatic system begins by the formation of sacs or hearts, which arise from the veins. Four of these sacs were described—two in the neck and two in the posterior portion of the body, from which lymphatic vessels grew out and invaded the rest of the body.

[1]Ranvier. Comptes-Rendus de l'Academie des Sciences, Tome 121, 1894, 1895 and 1896, and Arch. d'Anatomie, 1897.

[2]Langer. Sitz. d. k. Akad. d. Wissensch., Bd. LVII, 1868.

[3]Sabin. Am. Jour. Anat., Vol. I.

This view was later confirmed by Dr. Lewis[4] in a paper on the "Development of the Lymphatic System in Rabbits," published in 1905. He worked out in more detail the origin of these sacs, showing them to come from transformed veins. He also stated that they arose in several places in the body and described two more sacs, viz., one in the root of the mesentery and one along the external mammary vein.

In the present work, which has been guided by Dr. Sabin, further evidence will be offered in favor of the direct venous origin of the lymphatics from a study more especially of the origin of one part of this system—the mesenteric sac. For this work serial sections were made of embryos from 16 mm. to 30 mm. long, in which the blood vascular system had been injected, and of embryos from 33 mm. up with lymphatic injections. From this time the primitive system is complete and can be injected through the thoracic duct without difficulty.

In the study of the origin of this system it has been found that there are certain primitive sacs existing in different regions of the embryo which represent the earliest lymphatics. As has been previously shown (Sabin, Lewis, McClure and Huntingdon) the first of these appears in the cervical region, near the internal jugular vein, in the pig, between 14 and 16 mm (Sabin). In a later stage—21 mm.—according to the reconstruction, made by Lewis, definite lymphatic vessels have arisen in three regions (Fig. 8).[5]

(*a*) In the cervical region in association with the jugular veins.

(*b*) Along the vertebral column, dorsal to the aorta, in the exact location of the developing thoracic duct.

(*c*) In the root of the mesentery, just ventral to the renal anastomosis of the sub-cardinal veins. At this stage the lymphatics exist independently of each other and of the veins, as definite, well formed spaces in the embryonic syncytium and lined by endothelium similar to that of the veins.[6]

Between these stages, in embryos 15 mm., in which lymphatics are found only in the cervical region, and in those 23 mm., where they exist

[4]Lewis. Development of Lymphatic System in Rabbits, Am. Jour. Anat., Vol. V, No. 1, 1905.

[5]Lewis, Amer. Jour. Anat., Vol. V, No. 1, 1905.

[6]In general, the study of my own specimens agrees with the reconstruction, though I think this condition occurs at a later stage—23 mm.—since at 21 mm. the lymphatics in the region of the thoracic duct have not yet been differentiated. However, this difference may be due to variations in the methods of making measurements.

in the three areas mentioned above—an embryo can be found (between 21 and 22 mm. in length) with lymphatics in the cervical region and in the mesentery before there is any evidence of similar vessels in the location of the future thoracic duct. At this stage and in all the succeeding ones up to 23 mm., all of the vessels dorsal to the aorta can be completely injected through the umbilical artery or vein, though the branches of the azygos veins are in the exact location of the thoracic duct which replaces them in the later stages from 23 mm. upwards. Below 21 mm., true lymphatics exist as such only in the cervical region, the mesenteric sac being represented by a plexus of capillaries in free communication with the veins. This is well shown in Figs. 1 to 4, which represent sections through the mesenteric sac. The capillaries at these stages are all engorged with blood and injection mass, and in all the sections large openings into the veins can be easily made out.

Before proceeding, however, to the consideration of the origin of this sac, which is indeed the principal object of this paper, several points may be set forth concerning the origin of the thoracic duct proper. This work, however, which is still incomplete, is to be the subject of a future article; therefore, only those points will be stated here which have a direct bearing on the main subject of this paper.

It has been shown that the lymphatics in the cervical region are derived directly from the veins, and this conclusion leads us naturally to expect that the primitive thoracic duct and mesenteric sac would in all probability be found to have a similar origin. This seems to be definitely established for the mesenteric sac; but for the thoracic duct, though all the evidence now at hand seems to favor a like origin for this branch of the lymphatic system, still it does not as yet seem as conclusive as could be desired.

The thoracic duct proper, or the part of the lymphatic system dorsal to the aorta, is not seen until the mesenteric sac is almost completely differentiated from the veins, this area being occupied by numerous branches of the azygos veins, all of which can be completely injected. Lewis, in his work on the development of the lymphatics, concludes that "lymphatic vessels develop along the course of the azygos veins apparently from independent venous outgrowths, all of which unite to form a continuous system, later acquiring new and permanent openings into the veins." The evidence which could be gathered from my own series, I think, in general, supports this conclusion, for sections taken from the same levels show all the vessels dorsal to the aorta injected in an embryo

of 20 mm., while in the stage between 22 and 23 mm. the uninjected duct occupies the same relative positions. Although this evidence does not seem definite enough to warrant an empirical statement as to the origin, it is certainly suggestive, for such a rapid development could hardly be ascribed to new growth and is therefore most logically explained by assuming the presence of pre-formed channels which then become differentiated, such as will later be shown to be the case in the mesenteric sac. The evidence, then, in connection with the thoracic duct, is that it is preceded by a series of veins from which it is suddenly rather than gradually transformed into lymphatics. The question which seems to me of interest is, Does the receptaculum first form as one of the primitive sacs and the thoracic duct grow from it to meet the lymphatics growing down from the cervical region, or does the thoracic duct form from a number of segmental anlagen all homologous to the primitive cervical or mesenteric? Dr. Lewis' figures would seem to suggest the second; but, although the primitive duct is not uniform in calibre and contains numerous dilated areas connected by much smaller trunks, I have been unable to find in any series a stage in which these dilated portions exist as independent sacs. However, it should be added that the connecting trunks are, in some cases, so narrow as to suggest this as a possibility. It will thus appear that there is no evidence whatever that the thoracic duct in the pig forms as Sala[7] has described for the chick.

Sala described the duct in the chick as forming out of solid cords of mesenchyme cells, in which a lumen subsequently developed. Thus, although all the evidence now available seems to indicate the direct venous origin of the thoracic duct, it is not, I think, nearly so conclusive as can be shown in the case of the mesenteric sac..

This sac, located in the roof of the mesentery, between the Wolffian bodies, and just ventral to the renal anastomosis of the sub-cardinal veins, was first noticed by Dr. Lewis in following the transformations of the vena cava inferior in rabbits.[8] In this paper, in his plate illustrating the vessels of this region, the lower portions of the sub-cardinal veins are detached from the rest, and "though colored blue, like the veins, they are described as spaces in the mesentery, suggesting the lymph-hearts of the chick." It is also stated that they may be subcardinal derivatives. In a later work by the same author on the "De-

[7]Sala. Recerche a. lab. di Anat. norm. d. r. Univ. di Roma, Vol. 7, 1900.
[8]Lewis. Amer. Jour. Anat., Vol. I.

velopment of the Lymphatic System in Rabbits," he states that "a portion of the sub-cardinal veins seems to become detached from the rest to form lymphatics," and "that some lymphatics in the mesentery accompanying the superior mesenteric and gastric veins may have arisen as branches of these veins." In his conclusion it is stated that "similar though smaller sacs than the jugular sac arise from the sub-cardinal and mesenteric veins at a slightly later date."

Thus, though the probable early venous connection of this sac is mentioned, no definite account is given of the time and method of origin, nor of its differentiation from the venous system and subsequent connection with the lymphatics dorsal to the aorta—the thoracic duct proper. To trace the origin and development of this sac, serial sections were made of pig embryos in which the blood-vessels had been injected, the embryos ranging in size from 16 mm. to 30 mm.[9] In an embryo of 16 mm. there is as yet no evidence of the blood capillaries which later form this sac, whereas at 30 mm. the sac has been completely differentiated from the venous system and is abundantly connected with the thoracic duct by large channels on each side of the aorta. This is well shown in Fig. 9, which is taken from an embryo of 30 mm.; the aorta is seen suspended, as it were, in lymph.

Cross sections through this sac in an embryo 22 mm. long just after its differentiation, show shreds of tissue extending into the lumen and very irregular margins, presenting a picture highly suggestive of the fusion of many small vessels (see Fig. 7). The early stages were then cut to ascertain whether it was possibly formed by the coalescence of numerous capillaries and thus of direct venous origin, as had already been shown for the cervical lymphatics. This was found to be the case.

At 16 mm. no vessels exist in this region and the mesenteric attachment is a homogeneous network of embryonic connective tissue, while at 17 mm., the next stage examined, a very few small capillaries have appeared (Fig. 1). These are shown in Fig. 1 as small, injected vessels, lying in the root of the mesentery, just ventral to the renal anastomosis of the sub-cardinal veins. Their course is extremely short, running only the length of a few sections, and parallel to the long axis of the

[9]It has been found by H. Mc.L. Evans that all injections should be made through the umbilical artery, whether the embryos are dead or alive, since venous injections are never so complete and are much more likely to cause extravasations which are particularly prone to occur in this region. If the embryo has only recently died, the heart will usually commence beating again as soon as the injection mass reaches it.

embryo. Toward the lower end they turn dorsalward, emptying finally into the renal anastomosis by distinct openings, as shown also in Fig. 1. This is quite in contrast with their mode of venous connection in the later stages in which there is definite fusion into much larger channels before their final termination (Fig. 3). Through the stage of 18 and up to 19 mm. there is a gradual increase in these small mesenteric veins;

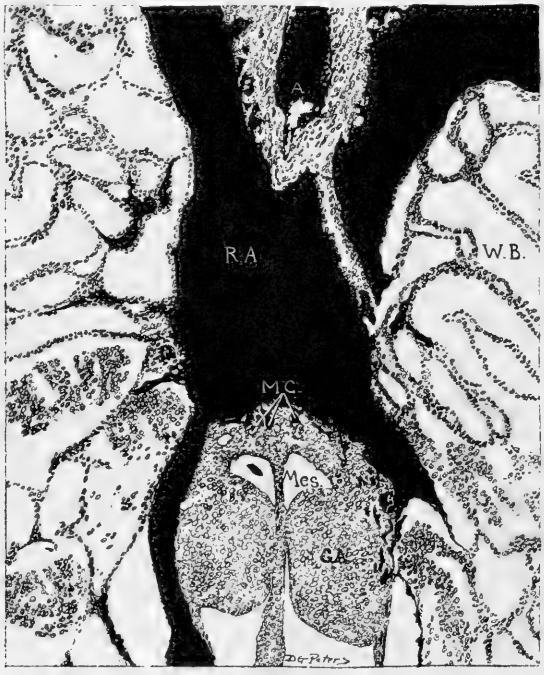

Fig. 1.—Transverse section through the renal anastomosis of the sub-cardinal veins of an embryo pig, 17 mm. long, showing the small veins in the root of the mesentery, which are the anlage of the mesenteric sac *A.*, aorta; *R. A.*, renal anastomosis; *W. B.*, Wolffian body; *M. C.*, mesenteric capillaries; *Mes.*, mesentery; *G. A.*, genital anlage.

they become more numerous and of definitely larger calibre, while at the same time there is an increase in their length (Fig. 2). Fig. 2, taken from an embryo of 18 mm., shows well the initial steps in this process. The region occupied by the minute capillaries in the embryo of 17 mm. (Fig. 1) is seen to contain many more veins, all of which are definitely larger than those seen in the preceding section. A later and

more pronounced stage in this development is shown in Fig. 3 from an embryo of 19 mm. During this time, also, there is a beginning of the process of fusion—a process which eventually leads to the formation of the sac in the later stages—by which many of the smaller vessels first unite to form larger channels before acquiring their venous outlet. Fig. 3 illustrates this process in its inception. In this the root of the mesentery contains many veins of much larger calibre formed by the coalescence of the capillaries seen in the earlier stages. Even now, how-

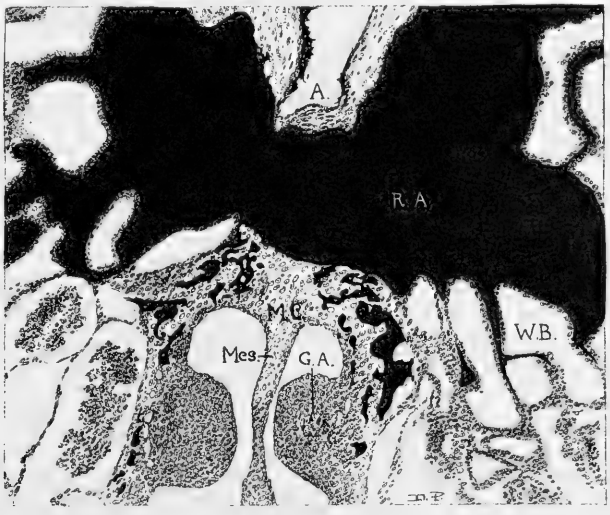

Fig. 2.—Transverse section through the renal anastomosis of the sub-cardinal veins of an embryo pig, 18 mm. long. In this the small capillaries seen in Fig. 1 have become more numerous and of definitely larger calibre. *A.*, aorta; *R. A.*, renal anastomosis; *W. B.*, Wolffian body; *M. C.*, mesenteric capillaries; *Mes.*, mesentery; *G. A.*, genital anlage.

ever, the fusion is not at all marked. The openings into the sub-cardinal veins are much larger than at 17 mm. (Fig. 1), and they are still numerous and quite distinct.

In all these stages, as well as in the succeeding ones, both before and after the complete separation of the sac, conclusive evidence for its venous origin is derived from a special study of the sections through the region of the meso-nephric arteries. Fig. 6 is taken from a section through this region in an embryo of 22 mm. In this the early mesenteric sac is seen occupying the area between these arteries; it is com-

pletely differentiated from the neighboring veins which are filled either with blood corpuscles or the injection mass. In the earlier stages, however, this area is studded with numerous small veins. It is thus evident that this structure, which later becomes an integral part of the lymphatic system, is represented in the earlier stages by a plexus of small veins.

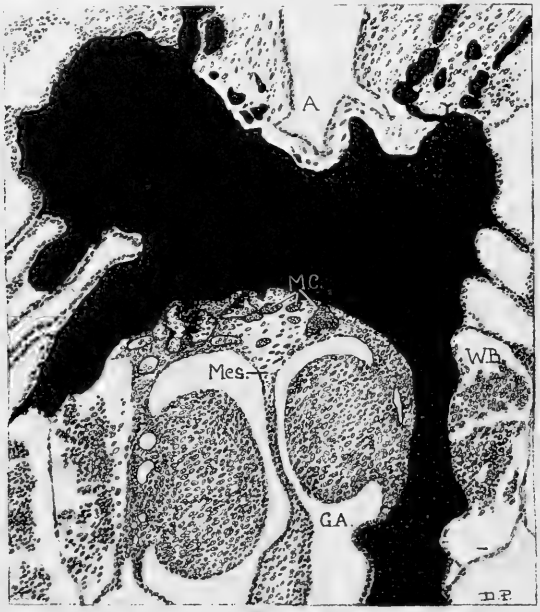

Fig. 3.—Transverse section through the renal anastomosis of the sub-cardinal veins of an embryo pig, 19 mm. long. The veins in the root of the mesentery have fused to form the larger channels seen in this section. This is the beginning of the processes of fusion which leads to the formation of the mesenteric sac in the later stages. At this stage, however, these vessels can all be traced definitely into the renal anastomosis. *A.*, aorta; *R. A.*, renal anastomosis; *W. B.*, Wolffian body; *M. C.*, mesenteric capillaries; *Mes.*, mesentery; *G. A.*, genital anlage.

Up to this time, *i. e.*, 19 mm., the increase both in the number of capillaries and the amount of fusion, has been very gradual. From now on, however, the development in both of these phases goes on with great rapidity; in fact, the active process in the formation of the sac may be said to begin here. Between 19 and 20 mm. the number, calibre and length of these vessels become markedly increased: there is much

greater fusion with the formation of several definite channels bearing a close resemblance to the sac in the later stages; but still having large openings into the veins. This is shown in Figs. 4 and 5; in Fig. 4, representing a section through the renal anastomosis of the sub-cardinal veins, in an embryo of 20 mm., the root of the mesentery is occupied by

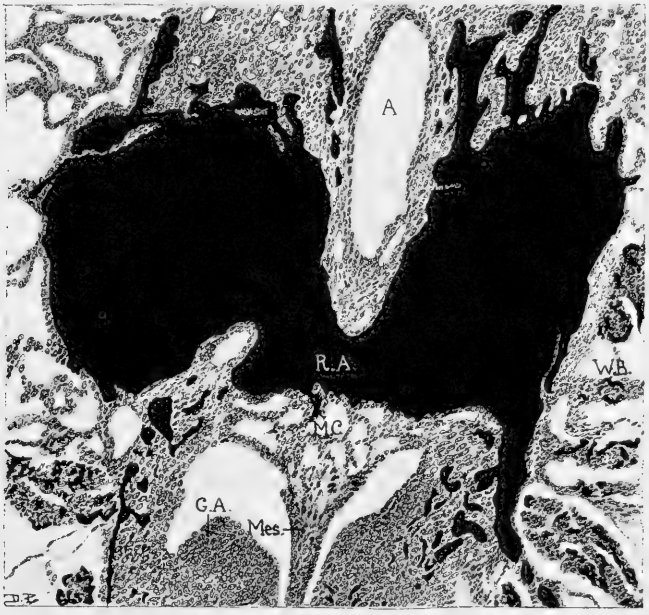

FIG. 4.—Transverse section through the renal anastomosis of the sub-cardinal veins in an embryo pig, 20 mm. long. In this section the venous channels in the root of the mesentery are beginning to show definite evidences of fusion and sac formation, though they are still connected with the veins, as is shown in the figure. *A.*, aorta; *R. A.*, renal anastomosis; *W. B.*, Wolffian body; *M. C.*, mesenteric capillaries; *Mes.*, mesentery; *G. A.*, genital anlage.

large venous channels between which there are extensive communications. At this stage there are still numerous openings into the veins from which the vessels can all be definitely injected, but not as easily as in the earlier embryos, since the venous connections are now being gradually obliterated. One of these openings is shown in the figure, with the ink entering the sac. In Fig. 5, taken from a section a little lower down in

the same embryo, the sac is even more definitely formed. It also shows that the sac is still injected from the vein. The drawing shows the beginning of the mesonephric arteries arising from the aorta, the area between them being occupied by the large channels still definitely connected with the veins, whereas, in Fig. 6, from a section through the

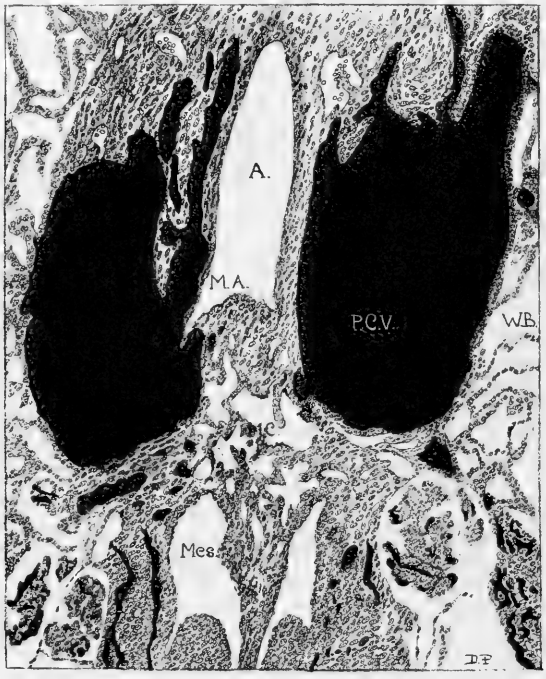

Fig. 5.—Transverse section through the beginnings of the mesonephric arteries in an embryo pig, 20 mm. long. The section shows the beginnings of a definitely formed sac which, however, can still be traced into the veins. The venous connection at this stage, however, is gradually becoming obliterated. *A.*, aorta; *P. C. V.*, post-cardinal veins; *M. C.*, mesenteric capillaries; *Mes.*, mesentery; *W. B.*, Wolffian body; *M. A.*, beginnings of mesonephric arteries.

same level in a 22 mm. embryo, the sac has lost almost all venous connection and has become a definite part of the early lymphatic system.

This active process of development continues between 20 and 21 mm. until, at the latter stage, there is formed a definite sac with irregular margins, due to the coalescence of numerous capillaries; and similar in

appearance to that seen in Fig. 7, though this is taken from an older embryo. At the 21 mm. stage, however, there are still definite venous openings, although they are gradually becoming lessened by a gradual process of differentiation which becomes complete between 22 and 23 mm., before the appearance of any uninjected vessels in the region dorsal to the aorta, thus leaving the sac, for a short time, independent of either venous or lymphatic connections (Figs. 7 and 8). Fig. 7 shows this sac, with its irregular margins, located in the root of the mesentery just

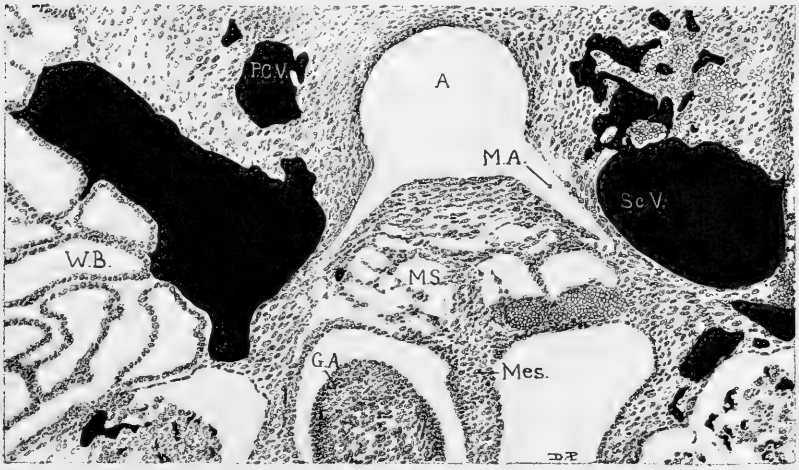

Fig. 6.—Transverse section through the mesonephric arteries in an embryo pig, 22 mm. long. The mesenteric channels at this stage were uninjected, as shown in the figure, while the adjoining veins were filled with blood or injection mass. The venous connections of the sac have been entirely obliterated. *A.*, aorta; *W. B.*, Wolffian body; *S. C. V.*, sub-cardinal veins; *M. S.*, mesenteric sac; *Mes.*, mesentery; *M. A.*, mesonephric arteries; *P. C. V.*, post-cardinal veins; *G. A.*, genital anlage.

ventral to the sub-cardinal veins, that is, in the exact location of the venous plexus in all the earlier stages. It has lost all venous connections and has not yet acquired any communication with the rest of the lymphatic system, but exists for a short time, as an independent sac in the embryonic mesenchyma. Fig. 8 is a section from a lower level in the same embryo and shows the beginnings of the mesonephric arteries with the area between occupied by an independent sac which has replaced the large venous channels of the preceding stages.

Between 23 and 25 mm. the thoracic duct appears, extending at first from about the level of the renal anastomosis up to a point approximately opposite the arch of the aorta. It is bilateral in the thoracic region, but fuses below the diaphragm to form a much dilated channel, just dorsal to the aorta—probably the primitive receptaculum. From 25 mm. on the sac gradually develops its connection with the rest of the

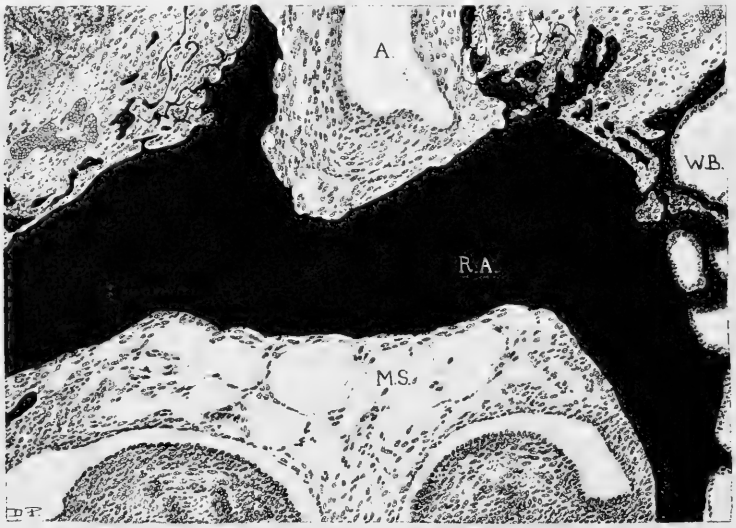

FIG. 7.—Transverse section through the renal anastomosis, in an embryo pig, 23 mm. long. This is the first appearance of a definite sac in the exact location of the venous plexus in the earlier stages. It will be noticed that the irregular margins suggest the fusion of many small vessels. At this stage no connection can be traced between the sac and either the lymphatic system or the veins. *A.*, aorta; *R. A.*, renal anastomosis; *M. S.*, mesenteric sac; *W. B.*, Wolffian body.

lymphatic system in the following manner: small capillaries grow from the sac and primitive receptaculum; these are shown in the earliest stage in Fig. 8 as small vessels extending up from the sac, on each side of the aorta, where they eventually meet and anastomose, finally forming definite channels along the lateral margins of the aorta, complete by 30 mm. (Fig. 9) from which stage they can be definitely injected by way of the thoracic duct.

Prior to this time, however, when the embryo is between 25 and 26 mm. in length, communication is established between the early thoracic

duct and the cervical lymphatics, so that when the embryo reaches 30 mm. the three integral parts of the lymphatic system have all become united to form a completed duct. The connection between the duct and the cervical lymphatics is established as follows: In an embryo between 25 and 26 mm. the duct, which is at first bilateral, extends up to a point about opposite the arch of the aorta, where the two main trunks become fused. The cervical lymphatics, by this time, have grown down

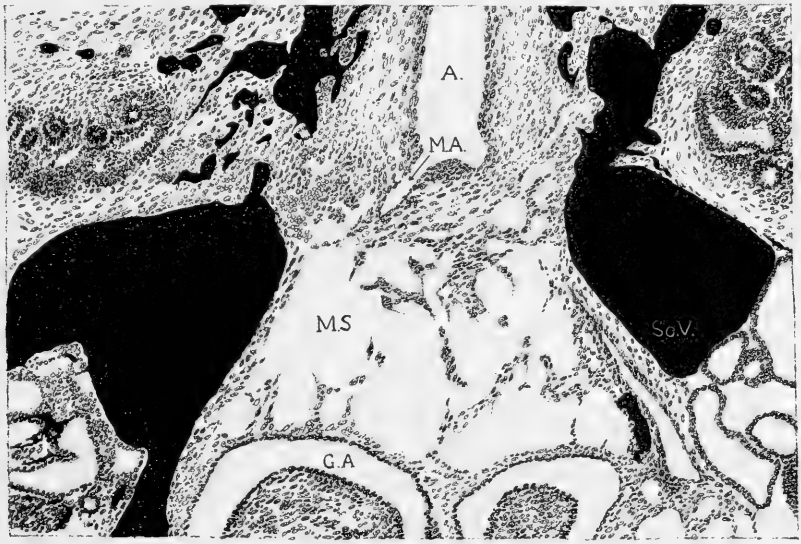

FIG. 8.—Transverse section through the beginnings of the mesonephric arteries in an embryo pig, 23 mm. long. The figure shows the definite mesenteric sac in the region between the mesonephric arteries which was occupied by the venous plexus in the earlier stages. *A.*, aorta; *M. S.*, mesenteric sac, showing the upgrowth of capillaries around the aorta; *S. C. V.*, sub-cardinal veins; W. B., Wolffian body; *G. A.*, genital anlage; *M. A.*, mesonephric artery.

to this same level and connection between the two is established by small anastomosing channels, scarcely larger than capillaries. Gradually, as development takes place, these become distended, until a duct of uniform calibre is formed when the embryo reaches a stage, above 33 mm., from which time complete injections of the lymphatic system can be made without difficulty. Such an injection is shown in Fig. 10, made from a cleared specimen 5.5 cm. long.

This specimen gives a good idea of the primitive lymphatic system. The cervical lymph sac is shown now turning into lymph nodes. The

thoracic duct appears as a plexus of vessels along the aorta in which one can see two definite channels, one on either side. Or one may say that the duct is double with numerous anastomoses. Between the kidneys and reproductive organs is the large mesenteric sac from which vessels

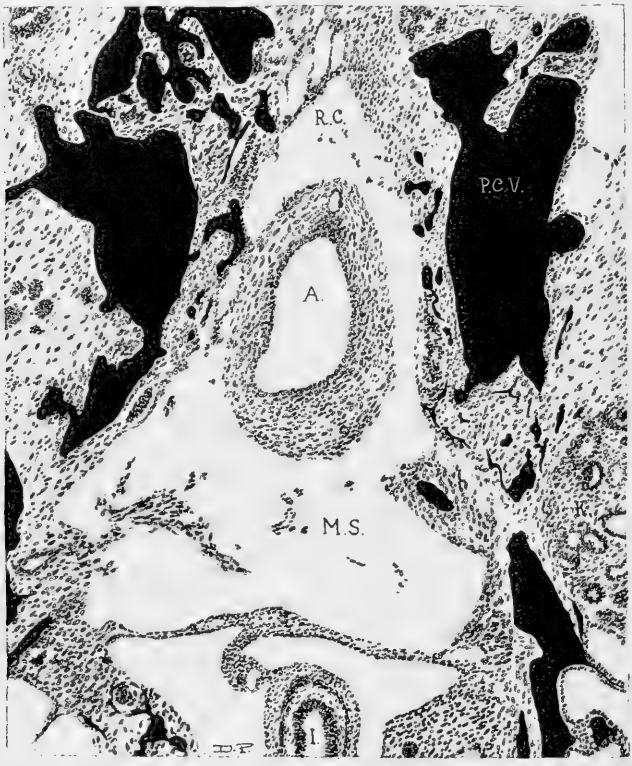

Fig. 9.—Transverse section through the early cisterna chyli and mesenteric sac in an embryo pig, 3 cm. long. The section shows the connection of the receptaculum chyli and the mesenteric sac, by large channels along the lateral margins of the aorta. *A.*, aorta; *C. C.*, cisterna chyli; *K.*, kidney; *M. S.*, mesenteric sac; *I.*, intestine; *P. C. V.*, post-cardinal vein.

spread to the capsule of the kidneys. The cisterna chyli is directly behind the mesenteric sac, separated from it by the aorta and hence cannot show in the figure. The posterior lymph sacs are opposite the lower end of the Wolffian bodies, and from these sacs vessels are seen passing to the legs.

To sum up briefly, then, the following conclusions may be noted:

1. The first lymphatics appear in the cervical region near the internal jugular vein, in the pig, between 14 and 16 mm. (Dr. Sabin).

2. The thoracic duct appears first at 23 mm., and is located in the exact position of the branches of the azygos veins in the earlier stages. In all probability, it is derived from branches of these veins.

3. The mesenteric sac begins as a mass of blood capillaries, lying ventral to the renal anastomosis of the sub-cardinal veins. They become fused into a definite sac at first having extensive venous openings, which later become gradually obliterated, thus making the sac independent at one time of either venous or lymphatic connections.

4. By a growth and fusion of capillaries from both the sac and the lower portion of the thoracic duct proper, the former becomes a definite part of the lymphatic system.

FIG. 10.—From a cleared specimen of a lymphatic injection in an embryo pig 5.5 cm. long. The two main ducts in the thoracic region are seen to fuse into single channels both below the diaphragm and above the arch of the aorta. Numerous channels are seen crossing the aorta. For the lymphatics below the diaphragm, the drawing is slightly misleading, for the specimen was exceedingly transparent, and includes lymphatics of two levels. This complicated area will be made more clear in a paper of Dr. Heuer's soon to be published in this Journal. Between the two kidneys and Wolffian bodies is the large mesenteric sac, lying in front of the aorta; the leader marked *C.C.* runs to this mesenteric sac. The cisterna chyli dorsal to the aorta, is entirely concealed by the mesenteric sac. The ducts running anteriorly from the posterior lymph sacs empty into the cisterna chyli dorsal to the mesenteric sac; they do not empty into it as they appear to do in the figure. *C.*, cervical lymph sac; *C. C.*, mesenteric sac dorsal to which is the cisterna chyli; *D.*, primitive thoracic ducts; *W. B.*, Wolffian bodies; *T.*, testes; *K.*, kidneys; *P.*, posterior lymph sac.

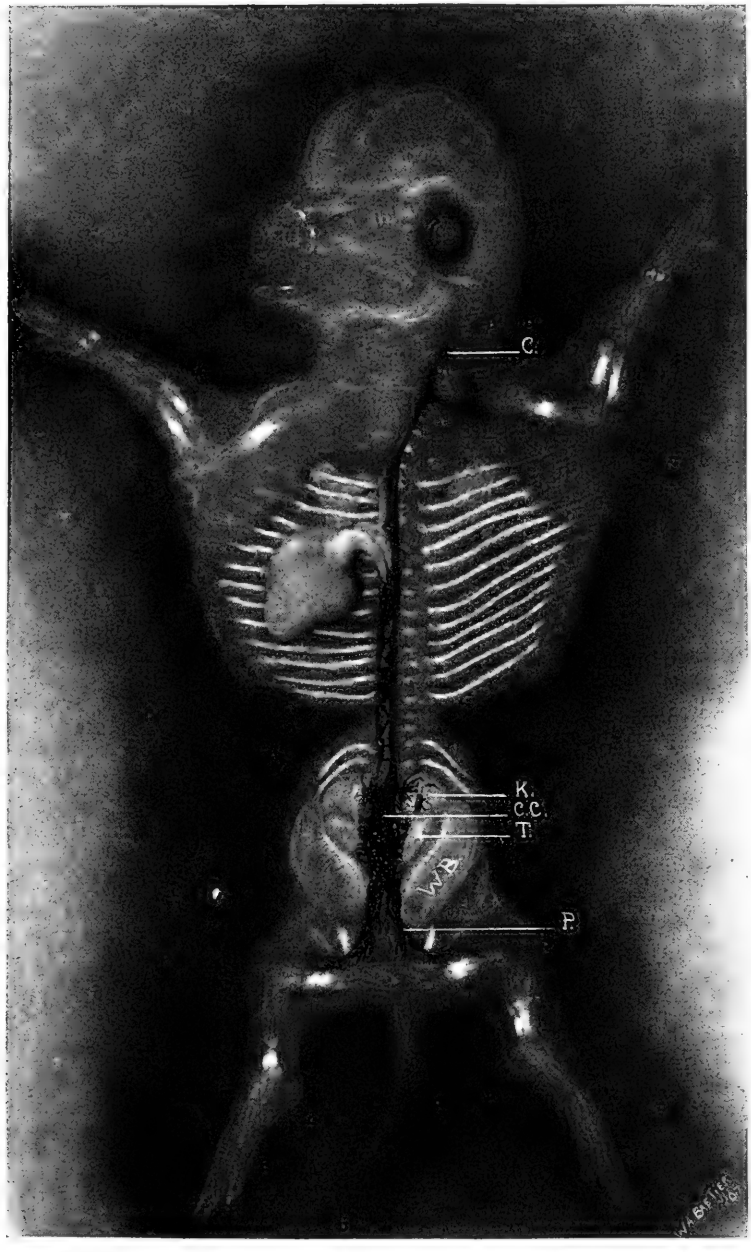

Fig. 10

THE GROWTH OF THE BRAIN AND VISCERA IN THE SMOOTH DOGFISH (MUSTELUS CANIS, MITCHILL)

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Current ideas regarding the growth of animals are based to a considerable extent upon observations on the weight or length of the entire organism. And yet it is well known that the proportions of many external parts regularly change during growth and that at least one internal organ, the brain, does not increase in weight at the same rate as the whole animal. The question comes quite naturally then whether other parts than the brain may not also have their own rates or cycles of growth which may differ more or less from the type of growth given by the entire organism. Physiologists are showing that in many instances certain organs or tissues may show regular, sometimes recurrent, growth cycles quite independent of the growth of the body as a whole and we are led to inquire whether the normal growth of an animal may not be actually a complex of growth cycles of component parts. It is quite possible to examine this question from the morphological as well as from the physiological side, and the present paper represents an attempt to discover whether the brain and viscera of the dogfish grow similarly or in diverse ways, as somewhat independent units of growth.

We are remarkably deficient in our knowledge regarding the normal growth of the viscera or of parts of the body other than the brain. Doubtless much valuable information of this kind regarding man lies concealed in hospital and clinical records. But, as far as I have been able to discover, the meagre data collected by Welcker and Brandt, '02, and by Vierordt, '06, represent the extent of our knowledge regarding the growth of the viscera in man and other vertebrates.

It seems that this lack of information concerning the growth of parts has led to a partial misconception of what is involved in the growth of

the animal body, and that the growth of one or two bulky tissues has been mistaken often for the growth of the organism. Further, some of the problems of growth have been overlooked because of the failure to bear in mind the physiological distinction between determinate and indeterminate growth among animals. The birds and mammals are unusual among vertebrates in that they continue to live for a long time after maturity without continuing to grow meanwhile. This is certainly true of man and seems to be true of the other mammals; and yet the mammals are the forms whose growth has been studied most extensively and from which many fundamental conceptions of growth have been derived. The problem of growth is somewhat different among all of those lower forms whose growth is indeterminate and continues, though slowly to be sure, throughout life, and which represent a more primitive condition in this respect. The present paper presents a fairly complete series of data regarding the increase in weight of the brain and certain of the viscera in a form which grows indeterminately, and suggests a possible interpretation of their significance for the general problems of growth.

Summary

A series of 315 dogfish (Mustelus canis) including specimens from birth (length 32.8 cm., weight 76.2 grams) up to a female 135.1 cm. in length, weighing 8434 grams, has been examined with a view toward getting precise information regarding the relative growth of the brain and viscera. Accurate weighings were made of the brain, heart, rectal gland, pancreas, spleen, liver and gonads. It is found that these viscera as well as the brain are relatively largest in the smaller individuals and that they decrease in size relatively throughout life although they do not cease to increase in actual weight. The period of maximum relative size of these parts is about that at which the growth of the whole organism is most rapid.

While the ages of these fish can not be determined exactly it seems that the dogfish of one meter in length, weighing approximately 2750 grams, is probably about five years old. Females are not ordinarily mature before this size is reached, although the males may mature considerably before this. Absence of the time factor in these observations is not important because their factors, such as food and temperature, are known to be of more importance than age in determining the size of fish.

The weights of the different organs are plotted for each individual separately and smooth curves derived. Each organ seems to have its own rate of growth more or less independent of the others, only the general features of its growth being adapted to that of the entire organism.

While the weight of the whole animal is increasing by the addition of definite equal amounts the heart also increases by the addition of equal increments, but the other organs, except the gonads, increase by the addition of gradually decreasing increments. Peculiarity in the growth of the liver is explained by the accumulation of fat in this organ. Peculiarities in the growth of the gonads apparently are due to the fact that at first these organs do not have a reproductive function; later a second cycle of growth appears which coincides with the approach of sexual maturity during which these organs are actually reproductive.

The sexes can not be distinguished with respect to either the absolute or relative weight of these parts, excepting the gonads.

It is not the organism then, but the organ or tissue that is the growing unit, the growth of the organism being a composite resultant of the growth of its parts. The muscles and supporting tissues form about 75 per cent of the total weight, and it is chiefly the increase of these parts which is measured when the weight of the total organism is taken as the basis for describing growth. The growth of these predominating tissues masks the differing rates of growth of parts of co-ordinate importance though of lesser bulk and an erroneous conception of the growth of organisms results.

Comparison is made with other data and certain general conclusions suggested. The muscles and supporting tissues seem to outgrow the brain and viscera, a relation leading ultimately to a loss of physiological balance within the organism. We should regard the condition of determinate growth found in the birds and mammals as secondary and as arising from the primary condition of indeterminate growth as an adaptation such that the muscles and connective tissues cease their growth while the more slowly growing brain and metabolizing organs are still competent to carry on the work of the whole mass of the organism.

The hypothesis is suggested that the regulation of the normal growth of individual tissues or organs may be carried on through specific internal secretions as is known to be the case with the growth of certain occasionally developing organs or in certain pathological growth phenomena. The evidence here given is purely morphological and therefore indirect.

Material and Methods

The material from which these data were drawn was secured at the Laboratory of the Woods Hole Station of the Bureau of Fisheries.[1] The data were collected with quite another purpose in view, but the present questions have arisen and may be considered at this time.

The data are given in full in Table III, pp. 343-350.

The determinations were made with the accuracy usual in statistical work; the weighings were made to 0.01 gram. The organs determined were the brain, heart, rectal gland, pancreas, spleen, liver and gonad. These parts were removed within one-half hour after the fish ceased to react to touch, and in practically every case the heart was still beating when it and the other organs were removed for weighing. The attachments of the viscera were cut through along the surfaces of the organs and the organs rolled gently in a towel until the blood was expressed. The brain was sectioned from the cord *in situ,* in a transverse plane extending just along the posterior tip of the cerebellum. Anteriorly the olfactory tracts were cut off along the contours of the hemispheres. The infundibulum and pituitary body were included, but the cranial nerve roots were removed along the surface of the brain and the outer membranes removed. This of course does not give a complete brain, but the limits chosen seemed to give the best compromise between completeness of brain and rapidity of removal. This last factor might be one of considerable importance on account of the rapidity with which the weight of the brain changes after death. In the heart no satisfactory landmark could be found along which to section the sinus venosus from the veins nor from the auricle: consequently the entire venous end of the heart was removed along the auriculo-ventricular groove which is very definite. Anteriorly the heart was sectioned at the junction of the conus and truncus. What is referred to as "heart" includes therefore only the ventricle and conus arteriosus. These parts make up by far the greatest part of the weight of the heart and at the same time are the chief functional elements in the fish. The rectal gland was removed as nearly as possible along the line where its duct commenced.

In preparing the plates the weight of each organ in each individual was recorded separately. The curves were derived from these records

[1]I take pleasure in acknowledging my indebtedness to Commissioner George M. Bowers, of the Bureau, and to Director Francis B. Sumner, of the Laboratory, for the privileges of a research room and a large share of the dogfish material collected during the seasons of 1906 and 1907.

by calculating a series of average weights of each organ in successive groups of individuals, and the line formed by connecting these averages was then smoothed to a curve so as to reduce to a minimum the plus and minus deviations of the averages. The groups from which the averages were derived varied in extent from 100 to 1,000 grams in different regions of the entire group, according to the rate at which the character of the curve was changing.

The fish themselves were taken, with very few exceptions, from a single trap in Buzzards Bay, and in nearly every case they were examined within twenty-four hours after their removal from the trap: during this interval they were kept in tanks abundantly supplied with running water. A few specimens had been kept for a few days before weighing in a large floating car in very favorable conditions. In determining total weights the fish were dried off with a towel and the weight of stomach contents subtracted: the ovaries and oviducts, even when containing embryos, were included.

The total number of fish examined was 315 (176 females, 139 males). Of these, the brains of 65 and the gonads of 15 were not weighed. These fish did not form a "random sample," but were of sizes selected so as to give as complete and uniform a series as possible. Practically all of the larger individuals taken were examined, but only a small proportion of the smaller and medium sizes. Consequently many of the usual statistical constants employed would be of no comparative value as descriptive of this group and they have not been determined. As may be seen from the plates the fish ranged in size from those just born, having an average weight of 76.2 grams and average length of 32.8 cm., up to a female weighing 8434 grams, length 135.1 cm. The specimens examined at birth, of which there were thirteen, were born in the laboratory from a single female (I believe this is the maximum number of young recorded for this fish) and it should be borne in mind that in speaking subsequently of the condition of certain organs "at birth," these specimens alone are referred to. Since these were all obtained from a single female and that the largest taken during two seasons' collecting, the weights found may not represent accurately the precise average condition at birth.

The series of fish examined shows, then, an increase in weight of over 110 times and in length of over four times. From a small number of fish collected wholly at random the average weights and lengths were found to be about, males, 1050 grams, 73 cm.; females, 1800 grams, 87

cm., or, including both sexes, about 1425 grams, 81 cm.: probably these figures are fairly close to the actual averages. It is to be regretted that the exact ages of these fish can not be told. I have been unable to find any statement regarding the time rate of growth of any of the Elasmobranchs. While we may nevertheless continue to use the expression "rate of growth" in speaking of the brain and viscera, it must be remembered that not the time rate but the comparative rate of growth is meant, the weight of the entire organism serving as the basis of comparison.

The Data

The Brain.—At birth the average weight of the brain is found to be 0.855 gram. After birth, as shown in Plate 1, its weight increases rapidly, but at a slightly diminishing rate, so that in fish of about average (not middle) size the brain weighs approximately 3.5 grams. Among the larger individuals the diminution is much slower but is continued, though the growth of the brain does not cease during life. The heaviest brain weighed 7.2 grams. While the total weight had increased over 110 times the brain had increased but 8.4 times. The curve shows that this heaviest brain was somewhat larger than the expected weight, which would be only about 6.4 grams, giving an increase of 7.5 times.

The curve showing increase in absolute weight of the brain is, however, less significant than that of its relative weight: this also is shown in Plate 1. At birth the ratio of brain weight to body weight is very high—1.116 per cent. But this falls very rapidly while the animals are increasing up to 300 or 400 grams. Then gradually the ratio decreases until in fish of average size it is only 0.25 per cent. This decrease continues at a diminished rate throughout life, so that it is still falling in the largest specimens examined: in the largest it was but 0.085 per cent. In other words the brain of this largest fish was, compared to the total weight, only one-thirteenth as large as in those just born.

It is not possible to distinguish between the sexes with respect to brain weight. The heaviest male examined weighed 3010.5 grams, or considerably less than one-half the heaviest female, but the weights of the brain, both absolute and relative, in males and females of the same total weight were not sensibly different, as can be seen from inspection of the plates where the sexes are charted distinctively. The curves given by the brain weights are remarkably smooth and the individuals grouped closely about the curve.

The Heart.—At birth the average weight of the heart is 0.078 gram. Almost from this time the increase in weight is uniform. Plate 2 shows this as the only instance among the organs measured of a perfectly regular increase in weight, the line of absolute weights being a straight line after passing the region representing a total weight of about 170 grams. This means of course that equal increments are added successively as the total weight increases by the addition of equal increments. The heaviest heart weighed 6.75 grams, showing a total increase in the series of 84 times.

The curve of relative weights is not so simple. At birth the ratio is 0.11 per cent. Just after birth the heart grows more rapidly than the entire organism, and this relation continues until the total weight is 160-170 grams—double the weight at birth. This maximum ratio is about 0.12 per cent, a comparative increase of about 9 per cent. (One individual shows a ratio of 0.133 and two others 0.130.) From this maximum the ratio decreases, at first rapidly then more slowly, until in fish of average size it is only about 0.087—considerably less than at birth and about two-thirds the maximum. As with the brain the ratio continues to decline steadily though slowly throughout the series, and in the largest fish falls to 0.08 per cent. That is, compared to the total weight, the heart of the largest fish is only two-thirds as large as at its maximum size or less than three-fourths as large as at birth.

There is no distinction between the sexes in either absolute or relative weight of the heart.

The Rectal Gland.—The average weight of the rectal gland at birth is 0.0304 gram, the heaviest weighed 1.62 grams—an increase of over 53 times. Between these two extremes we find, as shown in Plate 3, the weights distributed along a nearly straight line much as with the heart except that there seems to be a tendency among the largest specimens for this curve to rise somewhat more rapidly.

The curve given by the relative weights of this gland is of much the same character as that of the brain, and of the heart after its maximum point. At birth the ratio averages 0.0398 per cent. At first this falls rapidly, then more slowly to a ratio of about 0.0225 in fish of average size, and after this much more slowly to 0.0192 per cent in the largest individual. In this specimen the rectal gland is relatively a little less than one-half as large as at birth. After a weight of 2500 grams is reached this curve drops scarcely at all, the line being practically parallel with the base.

Here again there seems no certain distinction between the sexes, although it is possible that in the largest males the rectal gland is slightly smaller than in females of corresponding sizes. The plate shows that in males of 2000-3000 grams the records for the males are mostly below those of the females, although to be certain of a difference here a larger number should be examined.

The Pancreas.—The average weight of the pancreas at birth is 0.061 gram: the maximum weight observed is 7.78 grams. The distribution of weights between these extremes is quite uniform, but Plate 4 shows that this is along a slightly curved line. The total increase in the pancreas weight was more than 127 times.

The curve of relative weights is quite similar to that of the heart. At birth the ratio is 0.08 per cent; it increases very rapidly until the total weight reaches about 200 grams when it reaches a maximum of 0.137 per cent. Then falling more slowly than the heart it is about 0.105 in fish of average size, higher still than at birth, and finally drops to probably about 0.075 per cent. The largest specimen measured showed an actual ratio of 0.092, but inspection of the curve shows that this is considerably in excess of the expected average as indicated by fish of 5000 to 7000 grams, among which it averages 0.0787 per cent. We may therefore assume about 0.075 as the probable final ratio for comparative purposes. This is not far below the ratio at birth, but it is only about one-half the maximum.

There is no distinction between the sexes in either absolute or relative weight of the pancreas.

The Spleen.—At birth the average weight of the spleen is 0.097 gram. Even at this time there is indicated the condition of great variability which continues throughout the series. Thus at birth the extremes in weight are 0.06 and 0.15 gram among individuals whose total weights vary only between 69.5 and 84.0 grams. And we find that while the curve given by the serial weights is regular—see Plate 5—the individual weights are distributed about it much less closely than in any of the organs yet considered. We find the spleen of the heaviest fish is not the largest absolutely. The largest spleen weighed 12.36 grams, and was found in a female weighing 3638 grams, less than half the weight of the heaviest fish. This was an exceptionally large spleen and for purposes of comparison we should consider rather the condition shown by the curve to be more typical. Thus at 8400 grams total weight the spleen averages about 9.75 grams, giving an increase in the entire series of more than 100 times.

At birth the ratio of spleen weight to total weight is 0.126 per cent. This ratio rises very rapidly just after birth and in fish of about 200 grams it reaches an average of about 0.475, that is it has nearly quadrupled. This is the most rapid initial rise observed in any of these organs. The extreme variability is again shown by the range of the ratios among individuals of approximately 200 grams, the limits being 0.257 and 0.895; this latter ratio is about six times the maximum ratio found at birth. From this point the ratio diminishes gradually throughout the series much as in the pancreas, falling in fish of average size to 0.3, and finally among the largest specimens to 0.106 per cent, or slightly less than at birth and only about one-fourth the maximum average ratio.

There is no distinction between the sexes in either the absolute or relative weight of the spleen.

The Liver.—The weight of the liver at birth averages 2.4 grams. As with the spleen the variability of this organ is so great that the condition in a single specimen may differ very considerably from the condition shown by the examination of a large number to be typical. Plate 6 shows that at 8000 grams the average weight of the liver is about 365 grams. This would show an increase of 152 times. The liver of the largest fish weighed 339.7 grams, while the heaviest liver weighed 557 grams, and was from a fish weighing 6811 grams. Between the extremes of the series the rate of increase was seen not to be quite regular, but gives a rather complex curve unlike that given by any other organ examined.

At birth the average ratio of liver weight to total weight is 3.12 per cent. This rises rapidly to a primary maximum of 5.5 per cent at a total weight of about 200 grams, the usual point of these maxima. It then declines as usual, but ceases when about 4.2 in fish of 700-800 grams and then commences to rise a second time, more slowly now, to a second maximum of 7.4 per cent in fish of about 3700 grams. From this point the ratio falls again until, among the six largest individuals it reaches about 5.5 per cent—about the same as at the first maximum. As will be pointed out later it seems possible to explain the peculiar form of this curve in such a way as to show that the liver really does not differ essentially from the other organs described with respect to its comparative rate of growth.

There is no difference between the sexes in either the absolute or relative weight of the liver.

The Gonads.—At birth the gonads of the two sexes are not unlike in weight either absolutely or relatively. The average weight is 0.274

gram, and the average ratio to total weight is 0.358 per cent. But from birth onward the two sexes become entirely distinct in both respects and therefore must be described separately.

Male.—In the male the weight of the gonads increases rapidly as shown in Plate 7 to a maximum average of about 29 grams: the heaviest testes weighed 31.8 grams. The total increase is nearly 106 times.

The relative weight of the testes increases rapidly after birth from 0.358 to a first maximum of 0.775 per cent among males weighing about 400 grams. Then after falling to a ratio of 0.60 at about 900 grams it recovers and rises rapidly to a ratio considerably higher than the first maximum and then more gradually to a final maximum ratio of 1.15 (1.03 as averaged from the eight heaviest males). This ratio of 1.03 per cent is nearly three times that at birth and one-third higher than at the first maximum. This is the only organ measured whose weight continues throughout the life to increase relatively to the total weight.

Female.—From the time of birth the gonads of the females increase at a somewhat slower rate than do those of the males. The rate is only approximately uniform, so that the line given by plotting the weights (Plate 7) is not a simple curve. The gonad weights of the larger females are not strictly comparable with each other because, at the season when they were weighed (July and August), some of the ovaries still contained one or more large yolk-filled ova, while from others the mature ova had been completely discharged so that the weight of the ovary was considerably altered. In Plate 7 the ovaries that contained large ova are enclosed in small circles. Only one female of less than 3600 grams (the exception weighed 2266 grams) was found with large eggs in the ovary. Similarly only one of less than 3250 grams (the exception weighed 1998 grams) contained developing embryos in the oviducts, while all of the 26 specimens observed above this weight contained embryos. The females of this dogfish therefore do not become mature until they have reached a weight of at least 2000 and usually 3000 grams; the length of such fish is roughly 90 and 100 cm., respectively, and their age probably four or five years.

The relative weight of the ovary rises like that of the testes to a primary maximum in fish of about 400 grams. This maximum is not so high as in the male, being only 0.675 per cent. This is followed by a fall to a ratio of 0.43 in fish of about 1700 grams. After remaining at about this point for some time the ratio tends to rise a second time as in the male, though not to the same extent. Probably this

tendency to rise a second time here is periodic and seasonal. For if we consider the distribution of only the ovaries containing large ova we see a considerable rise in relative weight, but the weights of the ovaries from which all mature ova have been discharged do not give an increasing ratio but one that is practically uniform. Probably therefore this general curve of relative weights is a composite and should be resolved into two components as in Plate 7, Curves A and B.

Discussion of the Data

Before attempting to interpret these data or to compare them with other more or less similar data from other forms we may compare the data concerning the various organs among themselves.

Of course these curves do not contain a known time factor and this must be borne in mind during their consideration and in comparing them with other data. The measurement of a large number of dogfish taken at random might give us some information regarding the average time rate of growth for the first few years of life, but so far as I know we have no such data. Of the specimens which I examined the first eighty were collected at random, since they included practically all of the fish taken in almost daily hauls of the trap for six weeks. Upon plotting these fish according to weight and length we get curves with several maxima in their early parts, indicating the total weight and length with age as follows:

Age	Weight in Grams	Length in Cm.
Birth	75	32.5
1 Yr.	300	45.0
2 Yr.	750-800	63.0
3 Yr.	1400	78.5
4 Yr.	2200-2250	90.0
5 Yr.	2750	99.0

There is considerable overlapping, and after the fifth year the individuals are so scattered that they form a more or less continuous and irregular line. The distribution commences to become uneven after what is apparently the second year. It can not be told with much probability whether or not the sexes grow at the same rate, though it seems likely that the males at first grow faster than the females, but after the third

year this relation is reversed. Probably the actual average weights and lengths at different ages would be found to differ somewhat from these figures, but this is the best approximation I can make with the available data. This is precisely the type of distribution which has been found repeatedly in the measurement of teleosts. (See, for example, Moenkhaus, '95, and Fulton, '01, '06).

It is undoubtedly true that here, as in the teleosts observed, age is not the chief factor in determining size, but that, as in so many invertebrates, the factors of food and temperature are the most important. Therefore to relate total size with age in these and similar forms would not add much to the interpretation of these size relations. As affecting the size of the brain and viscera probably the age is of still less importance, so that for these organs we are upon a more instructive basis in considering their weights as compared with that of the entire organism without reference to age. Consequently the absence of a known time factor is not the serious matter it might seem at first thought or probably would be were we considering a higher vertebrate such as a bird or mammal.

As compared with these curves in which total weight irrespective of age is alone the basis of comparison, the curves given by the time rate of increase would differ in their precise form, since different lengths of time would be required to cover what are here indicated as equal distances along the base line. If the time element could be introduced the curves would probably be shortened chiefly in the region between the total weights of 1000 and 2000 grams and somewhat less below and above these weights, and then lengthened considerably from the middle part onward.

Considering in the first place, then, the absolute weights of the organs measured, we find, first, that while the curves are all of essentially the same character, yet, second, each is distinguished by certain details of form, and, third, excepting only the liver and gonads, they are all of simple character with no indication of being formed by two or more dissimilar elements or cycles. No attempt has been made to describe any of these curves mathematically. With the exception of the curve of gonad weights which is obviously of special character, it is possible to arrange the curves in a series between the members of which the differences are minimal.

Commencing with the spleen (Plate 5) we have a curve which is distinctly concave to the base line throughout its entire course, al-

though the concavity decreases considerably toward the upper end. The curve most nearly similar to this is that of the brain (Plate 1) in which the concavity is well marked, but does not extend over the entire curve, the upper end being straight though at an angle with the base. Following this we have the curve of the pancreas (Plate 4), which is considerably less concave and in which the entire upper part has become straight. This tendency to straighten is continued in the curve of the rectal gland (Plate 3) where only the very beginning shows any concavity and that very slight. Finally we reach the condition found in the heart (Plate 2) where the line becomes straight almost from its very beginning. The curve given by the liver weights (Plate 6) is more like this last than any other, but is not simple in character for reasons to be mentioned presently. This tendency for the concave curves to straighten is carried to an extreme in the gonad curves (Plate 7) which actually become convex to the base; this is most pronounced in the curve of the testes.

Of course the alteration here of a concavely curved line into a straight line indicates that an organ passes from a condition in which it grows by the addition of constantly diminishing increments, to one of growth by the addition of successively equal increments, the total weight meanwhile increasing in either case by the addition of equal amounts. The spleen, for example, throughout its growth increases by the addition of constantly decreasing increments, while the heart almost from the first grows by the addition of equal increments. The other organs show the various intermediate conditions described. The obliquity of this line to the base is determined by the size of the increment added, just as the amount of the curvature is determined by the rate at which the increments are decreasing. The rectal gland is the only one of the viscera except the gonads which gives a curve becoming convex to the base, and this occurs only at its extremity, this means that this organ increases, among the largest females, by the addition of increments of increasing size.

We may conclude then that these curves though all of the same general type, are individually distinct so that the rates of increase in weight of these organs are not determined by precisely the same factors or, at any rate, by factors operating with equal intensity at corresponding periods throughout this series of organs. This is shown also by the curves showing the relative weights of these organs which seem more instructive and which aid in the possible interpretation of these curves just described.

These curves of relative weight are again all of the same general type though individually distinct. The heart, pancreas and spleen (Plates 2, 4, 5) are essentially alike in showing first a rapid increase in relative weight followed by a somewhat less rapid fall and then a long and slow but steady decline through to the end of the series. Individually these differ in the extent of the initial rise, in the rate and duration of the first and second phases of decline and in the total amount of decline. In the brain and rectal gland (Plates 1, 3) the initial phase of rapid rise is omitted, the entire curve resembling in general the declining parts of the preceding curves. Of all the curves, that of the rectal gland shows the most nearly horizontal line in its latter part. The first parts of the curves given by the liver and gonads (Plates 6, 7) are similar to those first mentioned in showing the initial rapid rise and similarly this is followed by a considerable decline. This decline, however, is checked and the curves soon become somewhat irregular, the testes showing a very pronounced rise, the ovary and liver considerably less.

It is hardly necessary to point out that the relation between these curves and the base line of body weights expresses the relation between the relative rates of growth of the particular organ and the entire body. Should these lines be parallel the two are growing at relatively equal rates; when the curve rises or falls the particular organ is growing respectively faster or slower than the body as a whole. The growth of an organ by the addition of constantly equal increments, as described above, would give a curve or line, depending upon the actual size of the increment, tending to approach the base line, which simply expresses the fact that equal increments added become smaller relatively as the organ and the body increase in size. With certain initial size relations among organ, increment and total weight, addition of constantly equal increments would give a curve showing first a rapid rise and then a slower and long continued fall, much as we find in some of these curves, for example, in the heart, which increases regularly at the rate of 0.85 gram per 1000 grams total weight. Should the added increments constantly decrease in amount the curve would approach the base line more rapidly, or should the increments increase the curve might become parallel with the base as in the rectal gland, or it might even rise as in the testes.

In discussing the possible significance of these curves it is convenient to consider the liver and gonads separately later. It is evident that

during a certain early period, the exact time and extent of which may vary, the brain, heart, rectal gland, pancreas and spleen grow at a faster rate than do the other parts of the body: and that after this period these organs grow at a slower rate than the other parts. As other parts we must include chiefly the muscular and skeletal elements, gonads and probably fat. The conditions of the excretory system and of the peripheral parts of the circulatory and nervous systems are unknown in this form, but these constitute relatively small parts of the total weight with which these other organs are being compared, and in forms where something is known about them they too grow more slowly. The alimentary canal seems to share this relation and in the dogfish its length increases at a constantly diminishing rate.

It appears therefore that while the various tissues or organs grow at different rates, those forming the greater part of the bulk of the body, namely, the locomotor and supporting tissues, continue throughout life to increase in mass at a more rapid rate than do the brain, heart and chief viscera. Ultimately, of course, were this relation continued, a condition would be reached where these parts mentioned would become physiologically incompetent to carry on the work of the constantly increasing mass of the body. That is, the muscles and connective tissues actually outgrow their controlling and metabolizing sources, the physiological balance of the organism becomes unstable and death may result naturally or the animal may become an easy victim to adverse circumstances.

Many features of the curves are partly explainable by assuming that the mass of an organ is related in a general, though not a precise, way to the extent of its functional activity. Thus at the time of birth the relative size of the heart and digestive glands is increasing rapidly and this increase continues for a time after birth, while the young fish are undergoing the most critical period of their existence and are making the most numerous and rapid adjustments of their lives. The young contained in the oviducts of the mother are almost inactive and food is supplied abundantly and in a condition which permits of its easy assimilation. Immediately after birth the small fish must capture and prepare for assimilation their own food and the activity of the neuromuscular and digestive tissues is enormously increased. Probably the relatively immense size of the brain at birth is a provision for this period which comes on so abruptly, and the initial phase of rapid increase in relative size of this organ which we have noted is absent from our

curves, is actually thrown forward into the latter part of "fœtal" life and is only apparently omitted. It is not now possible to consider the rectal gland from this point of view because we have no positive knowledge regarding its function, but the similarity between its curve of growth and that of the brain is worth noting, though probably merely accidental.

Following this period of rapid and extensive adjustment comes that of the most rapid growth which occurs during that time the animal is dependent upon its own organs of direction and metabolism. During the year of embryonic or "fœtal" life it attains a weight of approximately 75 grams. During the first year of postnatal life, if our determination of time rate of growth is correct, it grows to a weight of about 300 grams—an increase of four times. During its second year, however, the fish only little more than doubles its weight. It is, therefore, when of from 75 to 300 grams weight that, as an independent organism, it is growing the most rapidly (as measured by Minot's method) and that all its independent nutritive processes must be relatively at their maximum, and it is just at this time that the metabolizing organs are relatively the largest. The spleen gives an excellent single example of this relation; in the fish this is the chief hæmatoplastic organ and during this period of rapid growth the circulating tissues must be of prime importance, and correspondingly we find the spleen relatively very large. After this early period of rapid growth increase in bulk is slower and the relative size of the metabolizing organs decreases. But as already mentioned, late in life the brain and viscera cease their growth more rapidly than the muscles and supporting tissues, which make up about 75 per cent of the total weight. This relation is obviously non-adaptive, but may, probably will, be found quite frequent if not typical among indeterminately growing forms.

Donaldson, '95, has noted from the fragmentary observations of Bischoff a similar relation in man and pointed out that there the muscular system has grown more extensively than the brain and nutritive system, suggesting that this was because the constructive processes become less active in older individuals. His suggestion is well supported by these more complete data from the dogfish, although here the problem is somewhat different because the muscles and connective tissues do not stop growing at a definite time as in man and other mammals.

We may now attempt to interpret briefly the peculiar growth relations of the liver and gonads. The liver seems to differ from the other

digestive organs and to agree more nearly with the muscular and skeletal tissues with respect to its comparative rate of growth in that it does not show on the whole a pronounced relative decrease in weight. The first part of the liver curve (Plate 6) is almost precisely like those of the other organs, but the usual steady decline following the maximal relative size is replaced by only a brief period of decline and then the liver weight rises again to a fairly high level, tending to fall again only among the very largest specimens. It seems probable that this peculiarity is the result, at least in large part, of the storing of fat in this organ. Most higher vertebrates and some lower forms, under good nutritive conditions, lay up fat not only within many tissues but quite usually within or around some of the organs contained in the body cavity, often in large masses. In the dogfish one notices at once the complete absence of fat tissue in this region. The liver, however, particularly in the larger specimens, contains large quantities of fat or oil, as the manufacturers of cod-liver oil could testify, and everyone who has used these animals in the laboratory can not have failed to observe this annoying fact.

In order to fix this point Dr. C. L. Alsberg, of the Harvard Medical School, has very kindly made, at the Bureau of Fisheries Laboratory, a series of determinations of the amount of fat in livers taken from dogfish of different sizes. His results show clearly, first, that the amount of fat does increase rapidly with the size of the fish or liver to an extremely high percentage in the larger fish; and, second, that livers above or below the average weight in fish of a given size have relatively higher or lower percentages of fat respectively.

In the dogfish, therefore, as in the teleost (Fulton, '06) the liver must be regarded not as a simple glandular organ, but, in the older individuals, largely as a fat reservoir. This fact offers an interpretation of the form of its growth curves. Only in the younger fish is the liver chiefly a glandular structure, and in such fish we find the growth curve typical for such parts. In animals of 600 to 800 grams we find the accumulation of fat masking the actual condition of growth of the liver tissue proper, so that apparently but not really this organ seems to afford an exception to the rate of growth typical of the viscera. If we could subtract the amount of stored fat from the total weight we should have left a series of weights representing actual liver substance, which would give a curve probably not unlike those already described for the other viscera. The extreme variability of the liver may also result largely from this same fact, since the amount of fat stored up would depend

quite largely upon the constantly varying nutritional conditions of the fish.

The somewhat similar form of the growth curves of the gonad weights must of course have a totally different significance. The gonads (Plate 7), while at first like the other viscera, are unique in showing later both an absolute and a relative increase in weight throughout life; this occurs earlier and is more pronounced in the testes. The gonads are the only organs whose curves of growth give evidence of being composed of two overlapping cycles: in the males a second growth cycle commences when a total weight of 800 to 1000 grams has been reached, and in the females when the total weight reaches 2000 to 3000 grams. The periods at which this second increase in size of the gonads occur, namely, of sexual maturity in each case, give a clue to its cause and real nature.

The first cycle which is in progress at birth, is that during which these organs reach their primary maximum soon after birth; this probably is equivalent to the only cycle present in the growth of the other organs and occurs at about the same time. During this cycle the gonads are not reproductive in function; they are growing as more or less undifferentiated mesodermal organs, not wholly undifferentiated, for they must be producing internal secretions which affect the rate of growth of certain other parts in such a way as to form at any rate the secondary sexual characters. As this phase of growth commences to wane just as it does in the other viscera, the gonads become truly reproductive in structure and in function and as such organs they enter upon a second cycle of growth which carries the size of these parts to a much higher point, and which is never completed in the sense that it reaches a maximum and then declines during life. This phase of growth is more pronounced in the testes than in the ovaries because the latter are not so largely composed of strictly reproductive tissue, but contain relatively a much larger amount of connective tissue.

We have already mentioned the apparently composite character of the latter part of the growth curve of the ovary. These weights were being determined during the season of ovulation and in Plate 7 the curves A and B show respectively the average weights of the ovaries before and after ovulation. There must be consequently a regular rhythm in the weight of the ovary which extends over a period of one or two years—it is not certain whether this dogfish can produce young annually or only biennially, although probably the latter is the case. The curve of ovaries which have recently discharged their ova drops quite to the horizontal,

indicating that they just maintain their relative size. It is only the ovaries containing large maturing ova, filled with yolk, that show clearly the second growth cycle; this agrees with the interpretation offered of their peculiar growth curve.

Comparison with other Data

Upon attempting to consider these data comparatively we meet serious limitations at once. The growth of the brain has been studied quite extensively in mammals, chiefly in man (see Donaldson, '95, for references) and in the guinea pig and the rat, which are typical for the group, and in frogs of various species (Donaldson, '98, '03, '08, Donaldson and Shoemaker, '00). Concerning the growth of the viscera we seem to have no sufficiently extended data for comparative use except for man, and these are not homogeneous and are far from satisfactory. The data collected by Welcker and Brandt, '02, are the best, but these observations are based upon such a small number of individuals that their usefulness is very limited. In dealing with such variable structures, records of single individuals of a given size may be very far from representing the actual average condition.

The work of Donaldson ('95, '98, '03, '08) has made it well known that in mammals after birth and in frogs after metamorphosis the brain does not grow as rapidly as the remainder of the body, so that it becomes relatively smaller as the animal becomes larger or older. Dubois, '98, (this paper contains a good bibliography up to 1898), Dhéré and Lapicque, '98, Donaldson, '03, Beck, '07, Hatai, '08, and Robertson, '08, have proposed formulæ according to which the weight of the brain can be calculated quite accurately from the weight or weight and length of the body or some other external characters. All of these formulæ are of such character as to show that in a given species the brain becomes relatively smaller as the individual increases in size. To illustrate, Vierordt, '06, publishes data (quoted by Donaldson, '95, from a previous edition of Vierordt) showing that in human males the brain at birth composes 12.29 per cent of the total weight, while at 25 years of age only 2.16 per cent. A similar series of data for females gave 12.81 and 2.23 per cent respectively. During an increase of more than 21 times in total weight the brain had increased only about 3.5 times. Welcker and Brandt, '02, give a few data from several sources which show practically the same decrease. They give measurements also upon the human

TABLE I.

Actual and Relative Brain Weights in Large and Small Individuals of Several Species.

	Age	Total Weight in Grams	Brain Weight in Grams	Brain Weight Per Cent. of Total Weight	Increase in Total Weight	Increase in Brain Weight	Relative Size of Brain in Largest and Smallest
Man W. and B., '02	3 mo. embryo 6 mo. embryo Just born 16 yrs. Adult Average, 5 ♂	12.51 491.0 2360.5 33940.0 58200.0	2.538 92.0 380.0 1406.0 1410.0	20.29 18.74 16.10 4.14 2.42	.... 24.6 times	.... 3.7 times	.... 15.0%
Man Vierordt, '06	Just born Adult	3100.0 66200.0	381.0 1431.0	12.29 2.16	21.3 times	3.76 times	17.6%
Dog W. and B., '02	2 hrs. 113 days	230.6 4788.6	7.65 ± 80.1	3.3 ± 1.67	20.7 times	10.5 times	53.6%
Fowl W. and B., '02	Just hatched Adult Average, 2 ♂	29.65 1595.7	0.92 3.8	3.10 0.24	53.8 times	4.1 times	7.7%
Bullfrog Donaldson, '98	..... Adult	1.32 313.0	0.025 0.215	1.89 0.068	237.0 times	8.6 times	3.6%
Frogs Average three Species. Donaldson, '08	..... Adult	12.7 41.6	0.0613 0.0995	0.488 0.238	3.2 times	1.6 times	49.4%
Salamander W. and B., '02	3 days Adult	..... 23.6	..... 0.045	2.68 0.193	.....	.....	7.2%
Stickleback. W. and B., '02	....	0.406 1.447	0.008 0.022	1.97 1.49	3.6 times	2.75 times	75.6%
Dog fish	Just born Adult ♀	76.2 8434.0	0.855 7.2	1.116 0.085	110.7 times	8.42 times	7.6

fœtus showing that at three and six months the percentage weight of the brain is 20.29 and 18.74 respectively, at birth 16.10 and adult 2.42 per cent.

For the bull-frog (Rana catesbiana) Donaldson, '98, gives data showing that while the total weight is increasing from 1.32 up to 313.0 grams the relative weight of the brain falls from 1.89 to 0.068 per cent. And in three other species of frogs (R. pipiens, R. esculenta, R. temporaria) the same author, '08, gives data showing that the brain falls from 0.57, 0.465, 0.43 per cent to 0.24, 0.24, 0.23 per cent respectively, while the total weights were increasing from 11.6, 12.4, 14.1 grams to 47.0, 45.0, 32.8 grams respectively. We should note that in determining the total weight of the frogs the ovaries were included only when not pigmented, if pigmented their weight was subtracted. If these had been included throughout, the ratios given for the large individuals would be still lower.

And we have seen that in the dogfish the brain decreased from 1,116 to 0.085 per cent of the total weight during growth from birth to maximum size.

Obviously these figures can not be used comparatively because the relative ages and conditions are so unlike, but just to emphasize the fact of this universal and very considerable falling off in relative brain weight these data and some others are condensed in Table I.

The idea that the viscera, like the brain, show a relative decrease during growth is perhaps less familiar. Most of the available data have been collected and tabulated by Welcker and Brandt, '02, and some additional data for man by Vierordt, '06. These are partially given in a condensed form in Table II. In considering this table it should be noted that only in the frog and dogfish are the figures the result of the examination of a considerable series of specimens so that the truly representative character of those included in the table is certain. In the other forms often only a single individual has to serve, and when we consider the great normal variability of the weight of viscera we see that these figures may not give very precise information. Nor except in man and the fowl have we information as to the relative size of these parts at different stages of growth. In these two instances we have a few scattering data given by Welcker and Brandt, '02, from their own and various other sources. These data suggest that in these forms more complete observations would show that many of the viscera would give curves showing a rise and fall as in the dogfish, but facts are so scanty that nothing definite can be said on the point. Incomplete as

TABLE II.

WEIGHT OF ORGANS, PER CENT OF TOTAL WEIGHT, IN SMALL AND LARGE INDIVIDUALS OF VARIOUS SPECIES. COMPILED LARGELY FROM THE TABLES OF WELCKER AND BRANDT, '02.

	MAN			DOG (Dachshund)		FOWL		FROG (R. esculenta)		SALAMANDER (S. maculosa)		STICKLEBACK (G. aculeata)		DOGFISH (M. canis)	
	One male 3 mo. embryo.	One male just born.	Average of five adult males.	One male 2 hrs.	One female 113 days.	One male just hatched.	Average of two adult males.	One female	Average of two males	Average of two specimens 3 days.	Average of two specimens ♂ and ♀	One specimen	Average of three specimens.	Average of thirteen specimens just born.	One female
Total weight in grams...	12.51	2360.5	58200.0	230.62	4788.6	29.65	1595.7	5.725	66.5	.....	23.58	0.406	1.447	76.2	8434.0
Skeleton.....	46.2	18.03	18.02	14.05	13.95	67.15	11.69	10.03	10.35	70.72 incl. sp. cord.	71.48 incl. sp. cord.	15.76	16.97	.....	.....
Muscles.....		23.30	45.00	34.87	41.94		54.53	51.02	53.74			48.52	50.49	.....	.....
Skin.....	8.39 (?) fat	20.33 incl. fat	Vierordt 17.77 incl. fat	21.29 incl. fat	16.58 incl. fat	10.66 incl. fat	18.86 inc. fat	12.84	14.99			3.94	5.34	.....	.....
Brain.....	20.29	16.10	2.42	3.3±	1.67	3.10	0.24	0.46	0.18	2.68	0.19	1.97	1.49	1.116	0.085
Heart.....	0.63	0.72	0.62	0.96 incl. large vessels	0.75	0.91	0.61	0.40	0.28	0.58	0.265	0.25	0.17	0.11 (max. = 0.12)	0.08
Spleen.....	.....	0.44	0.28	0.23	0.18	0.07	0.09	0.04	0.17	.....	.....	0.25	0.17	0.126 (max. = 0.475)	0.106
Adrenals.....	0.54	0.35	0.02	.....	.....	.....	.....	.....	.....	.....	.....	....	.....	Rectal 0.0398	Gland 0.0192
Pancreas.....	0.45	0.15	0.17	0.23	0.42	.....	0.18	0.28	0.17	.....	.....	....	.....	0.08 (max. = 0.137)	0.092 (prob. = 0.075)
Liver.....	8.13	5.00	2.52	5.94	4.23	3.17	1.88	2.48	4.00	3.26	8.02	2.22	2.62	3.12 (max. = 5.5)	4.02
Kidneys.....	0.66	0.73	0.52	1.36	1.06	1.08	0.59	1.06	0.37	1.59	0.95	0.74	2.91	.....	.....
Gonads.....	0.10	.....	0.11	.....	.....	0.003	0.52	0.37 ♀	0.26 ♂	.....	.....	....	.....	0.358	1.03 ♂ 0.40 ♀ (0.68)
Blood.....	3.56	.....	3.97	5.85	6.08	.....	2.30	2.18	3.59	.....	.....	0.49	3.38	.....	.....

the data are they represent the state of our knowledge and are given in the table for what they are worth.

The net result is to show that among the vertebrates generally the parts which increase relatively the most during growth are the skeleton and muscles and perhaps the skin and subcutaneous tissue. Together these make up roughly three-fourths of the total weight. The viscera as well as the brain show a falling off at various rates.

Conclusion

We see then that it is a general law among vertebrates that the organism does not grow entirely as a unit but as the resultant of the growth of its parts, and that these component parts of the body do not all grow at the same or corresponding rates. What is ordinarily measured and described as growth of the organism is really not growth of the whole organism, but the growth chiefly of the locomotor, supporting and protective tissues, and probably frequently of fat also. The curve of growth of an organism is a composite affair made up of many dissimilar components, with the growth of those mentioned as the predominating elements. Such curves therefore may be misleading unless this relation is borne in mind, since disproportionate importance is thus allowed to elements of the body which should be considered of only co-ordinate importance. Indeed it is not clear why, in the growing organism, the condition of the brain and viscera should not be the more significant, and yet the growth of these parts is almost completely masked by the increase of the bulkier muscles, skeleton and skin.

It seems that some confusion has arisen in the study of growth through the failure to remember that in all of those forms whose growth has been studied most extensively, growth is determinate: the organism reaches, about the time of sexual maturity, a fairly definite average size, then stops growing and may continue to live for a considerable time thereafter. This is true for mammals and birds at least and perhaps also for some of the lower vertebrates. In some forms the organism or parts of it may actually diminish in weight. But among fishes quite another condition prevails: growth is indeterminate and the fish may continue to increase in weight, slowly it is true, as long as it remains alive, with an average food supply. This seems to be the condition among most invertebrates, except insects, and has been demonstrated in the teleost fishes (Fulton, '01, '06), and from these data it must be true

also of the dogfish. Observation of many of the lower vertebrates in nature (Fulton, '01, '06) and in captivity, such as the giant salamander and some reptiles, shows that these grow indeterminately; Agassiz's, '57, observations upon Chrysemys are typical. As a recent example of the failure to make this distinction we might mention the work of Robertson '08, who has devised certain formulæ for the description of growth and has brought out the very suggestive fact that the growth curve of an organism or organ or tissue is similar to that given by an autocatalytic reaction. These formulæ hold good upon the assumption that the organism or organ has a definite period of growth at the end of which increase in size ceases. This is true for the higher vertebrates, but for all the indeterminately growing forms we can not determine any such "final weight" of the body or organ upon which to base a formula. We could not assume the maximum discovered size as the "final weight" because this is subject to such extreme variation; in the dogfish, including both sexes, we might find the "final weight" anywhere from 2000 to 8000 grams and even higher.

We have already suggested, since the muscles, supporting tissues and skin increase relatively much more rapidly than the other parts and since this relation continues through life, that a time must come at which the brain and metabolizing organs become incompetent as physiological elements in the organism and death must result. As showing that this relation is not one of mere bulk alone, we might recall some of the observations of Hardesty, '05, on the frog. Here the number of spinal ganglion cells as well as the number of dorsal and ventral root fibers increases throughout growth, but inspection of his data shows that this increase is at a constantly diminishing rate so that the relative number of ganglion cells is constantly decreasing. Thus in a frog of 7.0 grams there are in the ganglia of the V, VII, IX nerves respectively 103, 77.8, 549 cells per gram of body weight, while in a frog of 63.4 grams the corresponding numbers are 15.9, 18.1, 72.7, although the actual numbers of cells contained have increased 41, 111, 20 per cent respectively. In general the same is true for the number of fibers in the dorsal and ventral roots. Hardesty points out that this increase in number of ganglion cells is opposed to the tradition regarding the nerve cells of vertebrates which is supported by Hatai, '02, who found in the rat no increase in the number of ganglion cells during growth, but only increase in the number of mature fibers.

Beddard, '03, found in a giant salamander which died in the Zoological Society's Gardens that the only visible cause of death was the small

TABLE III.

THE DATA. WEIGHTS, IN GRAMS, OF TOTAL FISH, BRAIN AND VISCERA

MALES.

SERIAL NUMBER	TOTAL	BRAIN	RECTAL GLAND	HEART	PANCREAS	SPLEEN	GONAD	LIVER
C	69.5	0.77	0.03	0.08	0.06	0.09	0.22	1.77
L	71.3	0.885	0.03	0.08	0.055	0.085	0.24	1.78
J	71.8	0.805	0.025	0.075	0.055	0.085	0.24	1.96
E	76.7	0.81	0.02	0.07	0.06	0.095	0.27	2.45
I	78.2	0.84	0.035	0.085	0.06	0.09	0.26	2.76
H	78.8	0.85	0.04	0.095	0.065	0.15	0.275	2.79
D	79.1	0.851	0.04	0.086	0.065	0.12	0.31	2.325
A	80.3	0.86	0.03	0.09	0.06	0.08	0.32	2.73
247	124.6	1.04	0.04	0.155	0.13	0.52	0.57	6.68
168	128.8	0.99	0.045	0.13	0.18	0.43	0.51	5.52
206	157.3	1.11	0.05	0.185	0.205	0.555	0.915	9.13
197	160.9	1.18	0.055	0.175	0.225	0.585	0.84	7.51
214	172.5	1.22	0.05	0.21	0.21	0.77	0.99	7.45
185	186.0	1.14	0.055	0.205	0.25	0.53	0.925	8.57
231	198.5	1.17	0.085	0.25	0.29	1.31	1.10	12.54
205	214.8	1.36	0.065	0.25	0.265	0.66	1.36	11.78
198	223.0	1.35	0.07	0.25	0.32	1.07	1.46	11.16
229	232.5	1.35	0.08	0.22	0.30	0.91	1.62	11.21
238	242.5	1.415	0.08	0.26	0.335	2.17	1.89	12.67
216	248.2	1.33	0.10	0.28	0.405	0.92	1.48	10.98
252	252.0	1.35	0.085	0.26	0.30	1.16	1.93	12.68
224	279.0	1.23	0.11	0.315	0.325	1.55	2.05	16.17
64	281.0	....	0.09	0.29	0.47	1.70	2.48	16.00
225	282.0	1.45	0.10	0.28	0.34	1.12	1.73	14.23
59	311.0	....	0.12	0.32	0.45	2.10	2.47	18.71
62	324.0	....	0.12	0.32	0.37	1.25	2.00	17.40
294	348.0	1.51	0.11	0.39	0.41	1.39	2.76	24.40
38	362.0	....	0.07	0.31	0.25	0.95	0.85	7.89
122	368.6	2.08	0.09	0.355	0.52	1.25	2.11	12.75
125	425.7	2.065	0.14	0.49	0.72	1.51	2.30	17.92
112	435.0	2.21	0.105	0.44	0.60	1.33	3.23	14.00
164	437.0	2.21	0.13	0.42	0.62	1.38	2.60	19.42
227	458.0	2.085	0.105	0.485	0.495	1.78	4.035	19.92
124	528.0	2.19	0.175	0.57	0.73	2.23	4.69	24.25
26	537.0	....	0.15	0.56	0.76	3.22	4.82	15.74
20	558.0	....	0.12	0.53	0.75	2.07	3.50	19.26
175	560.5	2.23	0.205	0.57	0.65	2.39	7.60	31.98
228	594.0	2.21	0.16	0.555	0.76	3.05	4.40	23.57
27	610.0		0.15	0.55	0.70	2.21	3.80	21.54

TABLE III. (Continued.)

THE DATA. WEIGHTS, IN GRAMS, OF TOTAL FISH, BRAIN AND VISCERA

MALES

Serial Number	Total	Brain	Rectal Gland	Heart	Pancreas	Spleen	Gonad	Liver
157	616.3	2.625	0.175	0.605	0.83	3.11	3.71	33.53
43	628.5	....	0.12	0.57	0.63	2.37	4.31	27.34
180	632.7	2.78	0.195	0.615	0.785	1.90	3.81	18.13
28	663.5	....	0.16	0.50	0.80	3.17	4.50	23.06
128	678.3	2.33	0.205	0.65	0.85	2.42	3.85	22.41
41	680.0	....	0.22	0.58	0.69	3.24	6.12	32.74
22	693.5	....	0.16	0.56	0.73	2.135	3.92	26.64
106	707.0	2.44	0.16	0.70	0.91	2.39	3.95	22.91
39	715.0	....	0.18	0.60	0.86	4.21	5.31	39.69
170	735.0	2.555	0.22	0.655	0.95	2.39	4.03	25.79
19	743.0	....	0.20	0.67	1.025	5.73	6.86	34.36
45	772.0	....	0.15	0.60	0.66	2.39	3.84	40.44
6	779.0	....	0.18	0.865	0.88	2.46	....	30.65
220	793.5	2.92	0.245	0.79	0.955	3.205	4.05	24.92
258	816.7	2.48	0.22	0.77	0.985	4.275	6.11	34.05
303	818.0	2.25	0.22	0.71	1.18	2.38	6.80	56.2
223	839.0	2.76	0.22	0.72	1.03	3.16	4.48	53.0
259	842.0	2.68	0.22	0.865	1.08	3.25	5.02	36.36
262	845.5	2.66	0.22	0.71	0.80	2.87	3.95	41.03
89	863.7	2.95	0.23	0.86	1.14	2.71	5.13	37.76
63	878.0	....	0.21	0.72	0.81	2.35	4.10	52.0
61	893.0	....	0.19	0.81	0.87	4.045	4.69	49.79
79	900.4	2.76	0.21	0.78	0.81	2.76	4.79	40.4
10	908.0	....	0.27	0.74	0.86	2.87	....	32.31
99	912.5	2.81	0.29	0.96	1.48	3.34	5.18	43.0
1	917.5	....	0.20	1.00	1.12	2.61	....	46.87
277	938.0	2.365	0.26	0.91	1.39	5.625	5.41	58.8
270	946.0	2.92	0.23	0.91	0.89	3.96	6.55	57.7
215	958.0	2.98	0.23	0.935	0.97	2.50	6.73	39.1
177	970.8	2.99	0.295	0.98	1.105	3.78	5.37	42.1
246	999.5	2.58	0.24	0.85	0.78	3.80	5.03	72.5
131	1024.5	3.035	0.28	1.03	1.14	3.765	6.70	38.3
80	1087.5	2.95	0.24	1.05	1.17	3.17	8.08	32.4
249	1088.0	2.87	0.25	1.10	1.11	3.34	6.08	35.6
162	1106.0	3.02	0.29	0.99	1.29	3.52	7.36	40.4
21	1112.5	....	0.23	0.97	1.01	4.48	9.47	74.39
23	1123.0	....	0.235	0.85	1.30	3.80	5.70	47.15
2	1124.5	....	0.26	0.95	1.405	4.70	....	52.75
3	1150.0	....	0.27	1.06	1.16	2.93	....	44.77

TABLE III. (Continued.)

THE DATA. WEIGHTS, IN GRAMS, OF TOTAL FISH, BRAIN AND VISCERA

MALES

SERIAL NUMBER	TOTAL	BRAIN	RECTAL GLAND	HEART	PANCREAS	SPLEEN	GONAD	LIVER
245	1162.0	2.97	0.21	1.07	1.035	3.29	7.57	67.0
11	1194.5	....	0.29	1.09	1.32	3.54	....	59.08
85	1208.4	3.28	0.31	1.05	1.47	3.67	7.08	36.75
178	1221.3	3.18	0.28	1.28	1.11	3.47	6.33	39.7
29	1246.5	....	0.26	1.07	1.15	2.82	8.13	57.15
149	1259.5	3.09	0.29	0.98	0.96	4.21	7.13	58.1
137	1277.0	2.99	0.285	1.22	1.425	3.24	8.01	89.8
296	1291.0	3.325	0.29	1.095	1.81	3.48	7.02	75.7
209	1300.0	3.55	0.36	1.23	1.535	3.275	10.045	64.8
171	1315.5	3.47	0.30	1.13	1.27	4.53	7.96	79.6
14	1324.0	....	0.27	1.07	1.26	3.95	....	68.11
46	1327.0	....	0.33	1.11	1.62	2.90	8.69	73.56
5	1337.0	....	0.24	1.24	1.525	3.56	....	59.55
78	1338.5	3.84	0.29	1.19	1.64	4.87	11.81	77.4
181	1370.0	3.21	0.30	1.10	1.36	3.07	7.53	44.5
286	1400.0	3.50	0.30	1.28	1.63	3.49	8.95	59.3
56	1416.0	....	0.23	1.05	1.175	4.45	9.52	86.87
17	1452.5	....	0.30	1.27	1.56	3.55	12.51	80.01
47	1453.0	....	0.30	1.14	1.40	3.90	9.57	80.0
34	1454.0	....	0.27	1.20	1.40	5.18	9.55	79.99
172	1462.0	3.53	0.32	1.54	1.62	4.00	11.07	58.5
136	1463.0	3.655	0.33	1.32	1.72	5.13	13.61	50.1
154	1468.5	3.92	0.32	1.42	1.79	4.90	12.71	56.1
121	1471.0	3.42	0.27	1.31	1.28	3.50	14.20	77.7
109	1481.0	3.64	0.28	1.21	1.47	4.55	10.62	90.9
293	1495.0	3.47	0.37	1.42	1.65	3.91	13.47	94.3
179	1512.3	3.55	0.39	1.32	1.88	5.08	14.18	92.2
156	1521.0	3.87	0.305	1.24	1.67	3.30	11.00	59.0
261	1529.5	3.52	0.30	1.29	1.26	4.56	12.38	76.8
13	1563.0	....	0.31	1.30	1.83	4.65	....	80.29
160	1567.7	4.17	0.285	1.36	1.72	3.34	13.46	82.2
92	1625.0	3.71	0.33	1.55	1.765	2.61	13.42	64.0
297	1651.0	3.32	0.36	1.425	1.61	4.45	13.56	114.2
218	1655.0	4.235	0.37	1.45	1.30	4.715	15.13	79.4
7	1681.0	....	0.41	1.36	1.81	4.55	....	92.34
213	1749.0	3.62	0.345	1.60	1.80	5.29	19.55	103.7
113	1756.3	3.82	0.42	1.60	1.85	5.69	17.12	66.4
248	1760.0	3.51	0.34	1.24	1.29	3.39	12.78	79.7
90	1760.6	4.13	0.45	1.48	2.13	5.79	16.09	54.7

TABLE III. (Continued.)

THE DATA. WEIGHTS, IN GRAMS, OF TOTAL FISH, BRAIN AND VISCERA

MALES

SERIAL NUMBER	TOTAL	BRAIN	RECTAL GLAND	HEART	PANCREAS	SPLEEN	GONAD	LIVER
219	1821.0	4.095	0.35	1.965	1.77	5.09	17.16	93.8
291	1860.0	3.64	0.33	1.50	1.96	5.66	20.40	96.3
95	1914.5	4.01	0.39	1.65	2.01	5.59	20.59	108.1
93	1975.9	3.89	0.44	1.11	2.07	4.52	14.59	66.4
83	1986.0	4.88	0.40	2.17	2.00	6.31	23.28	85.0
256	2002.0	3.98	0.335	2.005	1.87	5.45	19.97	79.5
266	2046.0	4.385	0.41	1.88	2.21	4.69	23.89	136.3
166	2046.0	4.24	0.45	1.815	2.32	5.24	18.99	87.7
115	2070.5	4.06	0.47	2.06	2.24	5.41	16.00	88.5
165	2130.0	4.46	0.41	1.50	2.345	5.85	19.63	147.0
114	2185.5	4.28	0.48	1.81	2.24	6.05	21.63	70.1
273	2197.0	4.15	0.405	1.89	1.31	7.41	20.06	136.0
52	2302.0	....	0.40	1.67	1.96	5.64	20.78	148.16
140	2398.5	4.81	0.48	2.23	3.23	5.62	24.65	86.4
111	2464.5	4.74	0.43	2.70	3.07	6.63	28.36	104.2
240	2482.5	4.37	0.455	2.015	2.55	7.27	31.80	140.0
268	2563.0	4.02	0.46	1.96	2.225	5.00	24.22	97.8
69	2590.0	4.80	0.50	2.33	2.28	4.75	22.70	141.0
44	2649.0	....	0.47	2.25	2.24	7.56	26.83	175.59
108	2651.0	4.99	0.50	2.39	2.29	8.44	29.30	136.4
67	2791.0	4.77	0.45	2.72	2.35	7.08	29.15	204.8
94	3010.5	5.38	0.61	2.94	3.46	4.95	23.97	171.9

FEMALES

K	71.7	0.83	0.025	0.075	0.06	0.06	0.25	1.95
F	71.7	....	0.02	0.085	0.06	0.095	0.23	1.96
B	75.0	1.02	0.03	0.085	0.07	0.10	0.27	2.50
G	83.1	0.84	0.035	0.08	0.06	0.09	0.35	2.51
M	84.0	0.905	0.035	0.100	0.065	0.120	0.325	3.720
232	152.1	1.07	0.05	0.17	0.20	0.57	0.60	7.48
196	159.5	1.10	0.065	0.20	0.20	0.50	0.88	7.92
167	160.0	1.07	0.06	0.18	0.27	0.36	0.855	8.19
186	189.0	1.27	0.06	0.215	0.23	0.50	0.93	9.17
187	189.0	1.39	0.07	0.245	0.245	0.54	0.94	9.08
57	208.0	....	0.08	0.27	0.27	0.80	1.06	13.33
195	209.0	1.42	0.065	0.25	0.305	1.245	1.02	11.87
191	217.5	1.155	0.065	0.22	0.32	1.02	1.075	11.02
169	220.8	1.315	0.085	0.26	0.275	1.50	1.39	13.45

TABLE III. (Continued.)

THE DATA. WEIGHTS, IN GRAMS, OF TOTAL FISH, BRAIN AND VISCERA

FEMALES

SERIAL NUMBER	TOTAL	BRAIN	RECTAL GLAND	HEART	PANCREAS	SPLEEN	GONAD	LIVER
253	221.0	1.285	0.07	0.28	0.33	1.60	1.52	13.63
53	226.0	....	0.09	0.23	0.34	1.56	1.50	11.82
37	238.0	....	0.09	0.25	0.32	1.07	1.45	10.79
50	240.0	....	0.10	0.24	0.38	1.18	1.64	11.87
194	251.4	1.35	0.08	0.27	0.30	0.725	1.27	14.39
204	259.7	1.40	0.07	0.27	0.35	1.01	1.41	12.09
237	269.5	1.37	0.08	0.28	0.33	0.71	2.10	12.00
221	308.5	1.385	0.10	0.30	0.41	0.95	1.54	17.01
58	333.0	....	0.12	0.35	0.46	2.11	2.72	18.74
300	345.5	1.54	0.12	0.395	0.45	0.85	1.95	19.44
288	352.5	1.45	0.12	0.37	0.49	1.51	2.25	23.13
132	390.7	1.96	0.10	0.43	0.56	1.41	4.71	16.63
144	441.4	2.44	0.135	0.465	0.68	1.29	2.88	18.29
25	482.5	....	0.13	0.49	0.81	1.48	1.97	16.14
289	485.0	1.81	0.145	0.55	0.62	1.405	2.63	35.45
202	513.5	2.36	0.16	0.57	0.58	2.15	3.65	15.88
199	513.7	2.33	0.12	0.545	0.66	1.59	3.93	19.95
176	525.0	2.28	0.16	0.53	0.81	1.91	2.56	23.68
188	527.5	2.56	0.15	0.56	0.635	1.97	3.065	20.53
51	547.0	....	0.15	0.61	0.65	2.25	3.37	23.46
150	550.3	2.315	0.16	0.555	0.70	2.06	2.795	23.19
123	552.7	2.46	0.15	0.485	0.70	1.81	3.03	18.45
287	555.0	2.00	0.13	0.55	0.675	1.90	3.00	21.53
126	561.5	2.325	0.16	0.54	0.87	1.79	2.75	19.27
159	574.0	2.35	0.14	0.63	1.01	2.745	4.61	25.08
207	630.5	2.23	0.19	0.65	0.615	2.29	3.95	33.00
16	699.0	....	0.17	0.61	0.94	3.24	3.02	23.88
31	699.0	....	0.18	0.58	0.69	2.02	5.21	23.15
60	710.0	....	0.21	0.61	0.81	1.45	2.86	25.48
161	747.0	2.53	0.23	0.75	1.10	2.98	4.80	48.8
35	761.0	....	0.22	0.70	1.00	3.24	4.72	45.19
183	771.0	2.42	0.195	0.80	0.86	3.465	4.57	34.6
182	809.4	2.38	0.18	0.70	0.86	1.86	3.77	36.1
84	824.4	2.87	0.18	0.67	0.93	2.15	5.32	23.64
36	829.0	....	0.23	0.70	1.07	2.42	6.75	34.78
54	837.0	....	0.22	0.63	0.97	2.81	5.20	50.64
15	868.0	....	0.27	0.825	1.10	5.74	....	37.10
65	874.0	....	0.18	0.70	0.85	2.25	4.32	51.03
158	890.3	2.93	0.24	0.86	1.185	3.04	4.86	39.3

TABLE III. (Continued.)

THE DATA. WEIGHTS, IN GRAMS, OF TOTAL FISH, BRAIN AND VISCERA

FEMALES

SERIAL NUMBER	TOTAL	BRAIN	RECTAL GLAND	HEART	PANCREAS	SPLEEN	GONAD	LIVER
203	919.5	2.815	0.21	0.865	0.95	2.97	4.355	53.2
163	939.5	3.24	0.23	0.80	1.20	1.69	2.86	30.14
174	988.0	2.97	0.25	0.91	0.95	3.10	3.30	45.3
299	995.0	2.90	0.25	0.85	1.01	2.91	5.35	43.0
155	995.5	3.0	0.23	0.93	1.08	3.27	4.91	41.05
302	1000.0	2.56	0.27	0.82	1.26	2.87	6.60	71.8
276	1014.0	2.88	0.255	0.82	0.945	2.55	5.76	54.9
230	1026.0	3.23	0.27	1.03	1.63	3.96	4.42	46.1
102	1042.4	3.13	0.275	0.95	1.32	4.65	3.82	40.3
235	1064.0	3.19	0.27	0.895	1.10	3.07	6.05	49.3
88	1073.2	3.11	0.33	0.94	1.32	3.72	5.00	74.4
135	1085.0	3.08	0.27	0.96	1.125	3.15	4.76	35.24
153	1086.0	3.17	0.22	0.99	1.18	2.85	4.37	29.33
98	1130.0	2.93	0.20	0.81	1.07	2.70	4.57	34.25
234	1143.0	3.18	0.27	1.08	1.02	5.275	5.16	66.0
201	1145.0	3.29	0.27	1.02	1.18	3.00	7.00	53.6
127	1163.1	3.14	0.265	1.05	1.78	4.935	6.79	52.52
104	1176.0	3.06	0.28	0.95	1.28	5.07	6.19	102.0
236	1187.0	3.575	0.275	1.11	1.36	4.40	5.08	53.8
226	1196.5	3.07	0.255	1.08	1.30	4.54	4.65	76.5
55	1230.0	....	0.32	1.02	1.23	3.82	7.45	60.90
210	1249.0	3.455	0.25	1.23	1.19	5.35	4.57	90.4
118	1267.0	3.16	0.28	1.13	1.30	3.45	5.42	67.8
97	1295.5	3.36	0.34	1.06	1.87	4.47	6.24	66.2
33	1296.0	....	0.27	1.09	0.95	3.77	7.17	74.49
9	1297.5	....	0.35	1.11	1.23	4.43	....	95.49
151	1303.5	3.76	0.31	1.45	1.72	4.70	7.89	64.75
72	1310.6	3.41	0.28	1.17	1.32	2.79	5.81	43.5
75	1312.5	3.66	0.29	1.02	1.23	2.81	4.91	41.6
298	1343.0	3.11	0.25	1.26	1.56	3.25	6.54	81.3
260	1352.0	3.735	0.31	1.255	1.70	4.02	8.92	59.2
200	1371.0	3.66	0.29	1.26	1.48	5.24	6.88	53.6
278	1392.0	3.11	0.315	1.17	1.46	4.09	7.47	102.5
272	1412.5	3.21	0.36	1.215	1.24	4.67	7.35	65.3
134	1439.0	3.90	0.35	1.32	1.34	3.35	8.0	44.4
285	1440.0	3.49	0.32	1.22	1.50	2.61	5.19	79.5
24	1488.0	....	0.32	1.18	1.55	4.35	7.29	76.34
12	1500.0	....	0.30	1.21	2.04	3.80	....	111.59
251	1500.0	3.27	0.375	1.23	1.45	4.85	6.51	103.5

TABLE III. (Continued.)

THE DATA. WEIGHTS, IN GRAMS, OF TOTAL FISH, BRAIN AND VISCERA

FEMALES

SERIAL NUMBER	TOTAL	BRAIN	RECTAL GLAND	HEART	PANCREAS	SPLEEN	GONAD	LIVER
8	1519.5	....	0.35	1.27	1.69	4.72	....	83.21
279	1537.0	3.48	0.38	1.34	1.61	5.97	6.03	77.1
129	1538.3	3.95	0.36	1.50	2.04	4.19	7.50	57.9
76	1550.0	3.37	0.285	1.29	1.53	3.77	5.38	69.2
71	1575.2	3.43	0.37	1.265	1.52	3.25	6.83	62.9
265	1603.0	3.24	0.285	1.32	1.58	4.47	5.84	95.0
292	1617.0	2.98	0.37	1.36	1.59	3.98	7.35	155.5
77	1642.0	3.72	0.38	1.30	1.645	4.98	7.01	166.7
86	1660.0	3.61	0.31	1.50	1.76	4.75	7.0	80.7
250	1688.0	3.96	0.34	1.40	1.74	6.00	9.24	94.0
103	1736.5	3.83	0.40	1.56	1.52	4.59	9.83	84.0
301	1737.0	3.205	0.385	1.325	1.60	5.21	8.53	141.0
119	1761.0	4.05	0.36	1.50	1.83	2.69	7.23	38.8
73	1789.5	4.14	0.39	1.56	1.77	4.27	6.02	59.7
152	1791.0	4.06	0.345	1.82	1.91	3.82	7.77	86.2
269	1795.0	3.34	0.405	1.38	2.13	3.53	5.44	129.5
130	1795.0	3.98	0.38	1.41	1.90	4.94	9.15	105.1
211	1803.5	4.19	0.42	1.88	1.89	4.68	10.22	106.6
100	1847.0	3.98	0.33	1.44	1.55	4.26	6.59	81.7
146	1890.0	3.73	0.375	1.72	2.35	4.595	9.12	81.4
244	1913.0	4.21	0.34	1.49	1.89	4.16	5.25	120.5
295	1948.0	3.51	0.365	1.69	1.55	5.48	10.94	148.5
184	1952.8	4.17	0.46	1.60	1.49	3.50	9.14	57.0
145	1998.0	4.24	0.45	1.915	2.40	6.30	13.47	74.3
40	2090.0	....	0.44	1.80	2.01	3.97	6.37	103.0
105	2107.0	3.88	0.445	2.06	2.44	4.78	9.51	121.9
120	2115.0	3.945	0.41	1.60	2.34	5.30	11.58	93.0
48	2130.0	....	0.43	1.50	1.64	5.21	8.55	109.34
49	2146.0	....	0.62	1.79	1.72	5.26	8.85	113.94
173	2175.0	4.05	0.49	1.82	1.87	4.57	13.74	75.2
212	2219.0	4.24	0.40	1.98	2.23	4.955	9.48	115.7
32	2230.0	....	0.35	1.75	1.75	6.13	11.20	143.76
101	2266.0	4.46	0.42	2.21	1.61	5.50	30.28	75.6
290	2290.0	3.83	0.46	1.585	2.57	6.28	10.78	180.0
42	2302.0	....	0.45	1.86	2.42	5.51	7.62	171.51
133	2330.5	4.36	0.42	2.00	2.49	5.075	11.70	105.3
74	2332.0	4.29	0.405	1.97	2.55	4.79	13.06	98.1
4	2350.0	....	0.48	1.96	2.77	5.22	....	145.76
208	2380.0	4.35	0.44	2.055	2.28	5.775	13.15	157.4
110	2394.3	4.39	0.50	1.93	2.51	5.61	9.86	152.1
143	2427.5	4.39	0.51	2.38	2.61	5.40	11.35	149.8
275	2432.0	3.57	0.43	1.87	1.95	5.70	8.61	163.5

TABLE III. (Concluded.)

THE DATA. WEIGHTS, IN GRAMS, OF TOTAL FISH, BRAIN AND VISCERA

FEMALES

Serial Number	Total	Brain	Rectal Gland	Heart	Pancreas	Spleen	Gonad	Liver
264	2534.0	4.24	0.54	2.05	1.82	4.08	9.78	139.4
91	2610.7	4.63	0.43	2.175	2.49	4.71	9.38	104.8
66	2642.0	4.3	0.45	2.5	2.1	4.2	9.5	129.0
142	2652.0	4.815	0.65	2.73	3.30	5.13	12.17	96.7
30	2860.0	....	0.51	2.05	2.32	6.70	13.25	175.2
274	2865.0	4.30	0.65	1.975	2.25	4.88	9.13	166.8
87	2900.0	4.52	0.66	2.27	2.28	7.00	11.8	230.5
141	2911.0	4.94	0.49	2.265	3.00	5.39	10.20	159.6
257	2960.0	4.57	0.67	2.66	2.19	6.50	15.09	232.2
239	3001.0	4.62	0.50	2.30	2.95	6.90	14.075	169.1
222	3039.0	5.33	0.58	2.96	3.48	5.17	11.63	228.3
242	3114.0	4.73	0.86	2.98	3.00	7.14	13.77	206.8
148	3250.0	4.61	0.66	2.59	2.48	6.60	18.0	154.6
192	3304.5	4.745	0.56	2.47	2.91	5.535	19.16	171.3
241	3312.0	4.80	0.60	2.62	2.925	6.46	14.59	326.5
189	3490.0	4.80	0.60	2.84	2.92	6.73	26.91	196.8
255	3513.0	4.87	0.80	2.98	3.08	8.14	18.90	325.5
271	3522.0	4.63	0.63	3.08	2.66	7.67	15.81	366.8
96	3581.0	4.71	0.77	2.92	3.20	8.28	15.50	253.0
254	3609.0	4.82	0.53	3.55	2.62	6.04	16.59	117.0
243	3638.0	5.08	0.74	3.64	4.98	12.36	27.91	368.3
193	3760.0	5.01	0.705	3.10	4.345	6.23	15.90	419.0
117	3810.0	5.34	0.65	3.31	3.59	8.96	27.27	206.2
147	3995.0	4.91	0.81	3.30	4.17	7.44	32.57	401.5
107	4152.5	5.28	0.655	3.30	3.56	8.96	26.04	357.6
233	4172.0	5.08	0.72	3.72	3.50	10.25	17.82	283.3
116	4264.5	5.35	0.75	4.15	6.52	8.90	23.65	329.5
82	4275.0	5.63	0.94	4.05	4.03	6.08	47.5	188.0
217	4420.0	5.105	0.845	4.255	3.845	7.95	26.84	270.2
284	4510.0	5.16	0.78	3.53	3.91	8.47	17.30	247.0
263	4540.0	5.39	1.32	5.35	3.645	8.87	19.53	403.0
281	4550.0	5.48	0.905	3.98	3.47	8.27	26.77	259.5
68	4600.0	5.32	0.81	3.39	3.90	5.66	46.5	175.0
18	4754.0	....	0.93	3.36	3.46	8.33	23.60	355.95
139	4862.0	5.68	0.96	3.90	4.56	9.95	26.53	274.0
267	4863.0	4.98	0.92	4.735	4.16	6.34	20.39	274.7
282	5634.6	5.51	0.95	4.36	4.43	7.03	16.26	296.5
280	5850.0	5.95	1.04	4.19	4.02	10.96	29.75	273.3
190	6123.6	5.55	1.17	5.72	5.43	8.57	28.37	394.5
138	6633.0	5.98	1.36	5.93	4.76	10.23	40.17	287.2
283	6790.0	5.915	1.36	5.19	5.84	8.12	24.97	557.0
70	8434.0	7.20	1.62	6.75	7.78	9.00	118.00	339.7

size of the valves of the conus from which the walls of the conus had apparently grown away, thus rendering them incompetent. He found these valves relatively larger in a smaler specimen and in a brief letter to "Nature" suggested that such "normally unequal growth" might be here and elsewhere a cause of natural death. From the facts we have given here it seems that we must expand this idea of "normally unequal growth" to include the general and normal relation, among the lower forms at least, between the locomotor, supporting and protecting tissues on the one hand and on the other the controlling, circulatory and metabolizing organs, either singly or collectively.

From this point of view the condition of determinate growth which we find in higher vertebrates is secondary and is derived from that of indeterminate growth as an adaptation upon the part of the organism, such that the muscles and supporting tissues cease their growth at such a point that the brain and viscera remain competent to maintain a physiological balance. We have seen that in the dogfish the brain and viscera decrease rapidly in relative size after an early maximum until about the time of sexual maturity and after that the decrease is much slower. If only the muscles and connective tissues could be made to stop their growth at that time (*i. e.,* become determinate), the animal apparently might continue to live for a comparatively long time after maturity. Apparently this is just what happens in the higher forms.

The recent work of the physiologists upon growth of certain tissues or organs suggests a mechanism through which this normal growth of the tissue or organ might be controlled and which might account for this comparatively more rapid cessation of growth in the determinately growing forms. They have demonstrated that the growth of occasional organs or tissues often results from the presence of internal secretions or of hormones. For example we might mention the effect of fœtus extract upon the growth of the mammary glands, of ovarian secretion upon the growth of the placenta, and so forth. And also in pathological growths internal secretions are known to be involved, for example, the effect of the thyroid secretion upon growth of the brain or connective tissues and of pituitary secretion upon the growth of bones. Probably the best example of this effect of internal secretion upon the growth of parts is given by the whole group of secondary sexual characters which result from secretions of the gonads. These secretions seem to affect growth in either a positive or a negative way—either by their presence or by their withdrawal after having been present for some time.

It is quite possible, therefore, that the normal growth of the individual tissue or organ may be similarly regulated by the presence or absence of specific internal secretions formed in various parts of the body. Whether these secretions cause growth to continue by their presence or by their absence could be told only through experiment, the relation might differ with different parts, but the general hypothesis of the control of normal growth through internal secretions seems legitimate and may afford a simple explanation of the growth of the organism as a composite collection of more or less independently growing units. The data presented here seem to give morphological evidence of a control of some such nature.

Woods Hole, Mass., August, 1908.

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PLATE 1.

Curves showing the actual and relative increase in the weight of the brain in a series of dogfish (Mustelus canis). In this and in the following plates the sexes and individuals are plotted separately and the smoothed curves drawn from averages.

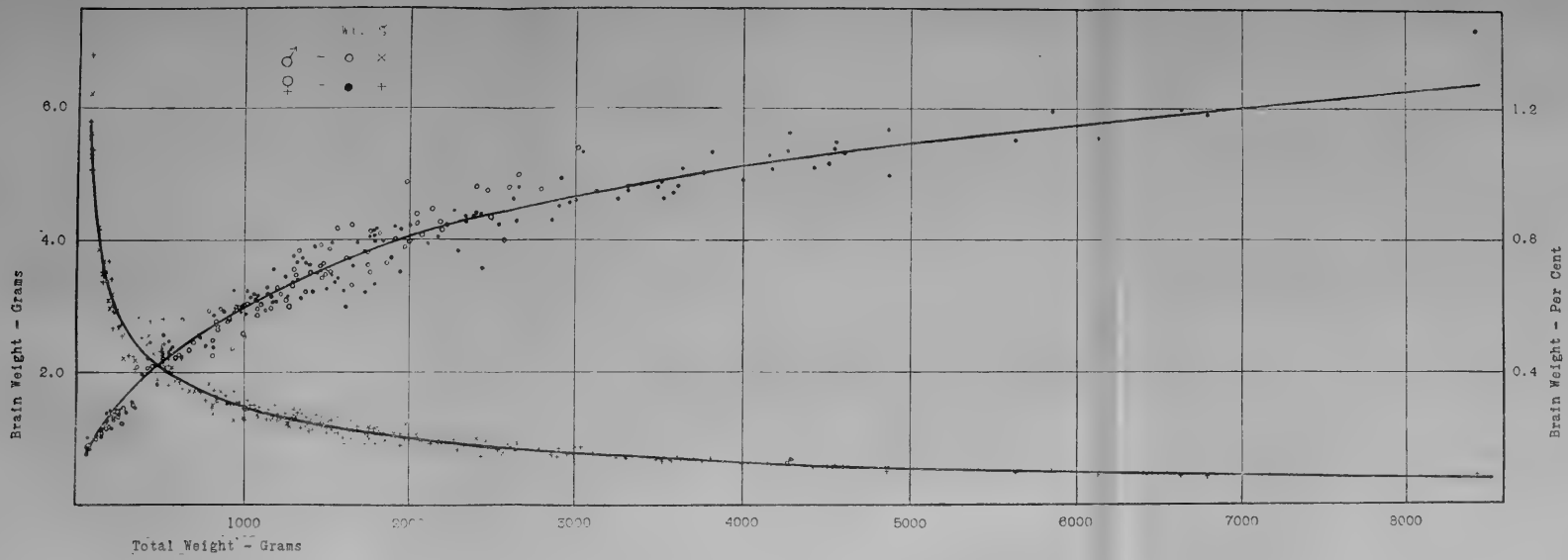

Wt. ♂
♂ - ○ ×
♀ - ● +
6.0
4.0
2.0
1.2
0.8
0.4
Brain Weight - Grams
Brain Weight - Per Cent
1000
3000
4000
5000
6000
7000
8000
Total Weight - Grams

PLATE 2.

Curves showing the actual and relative increase in the weight of the heart.

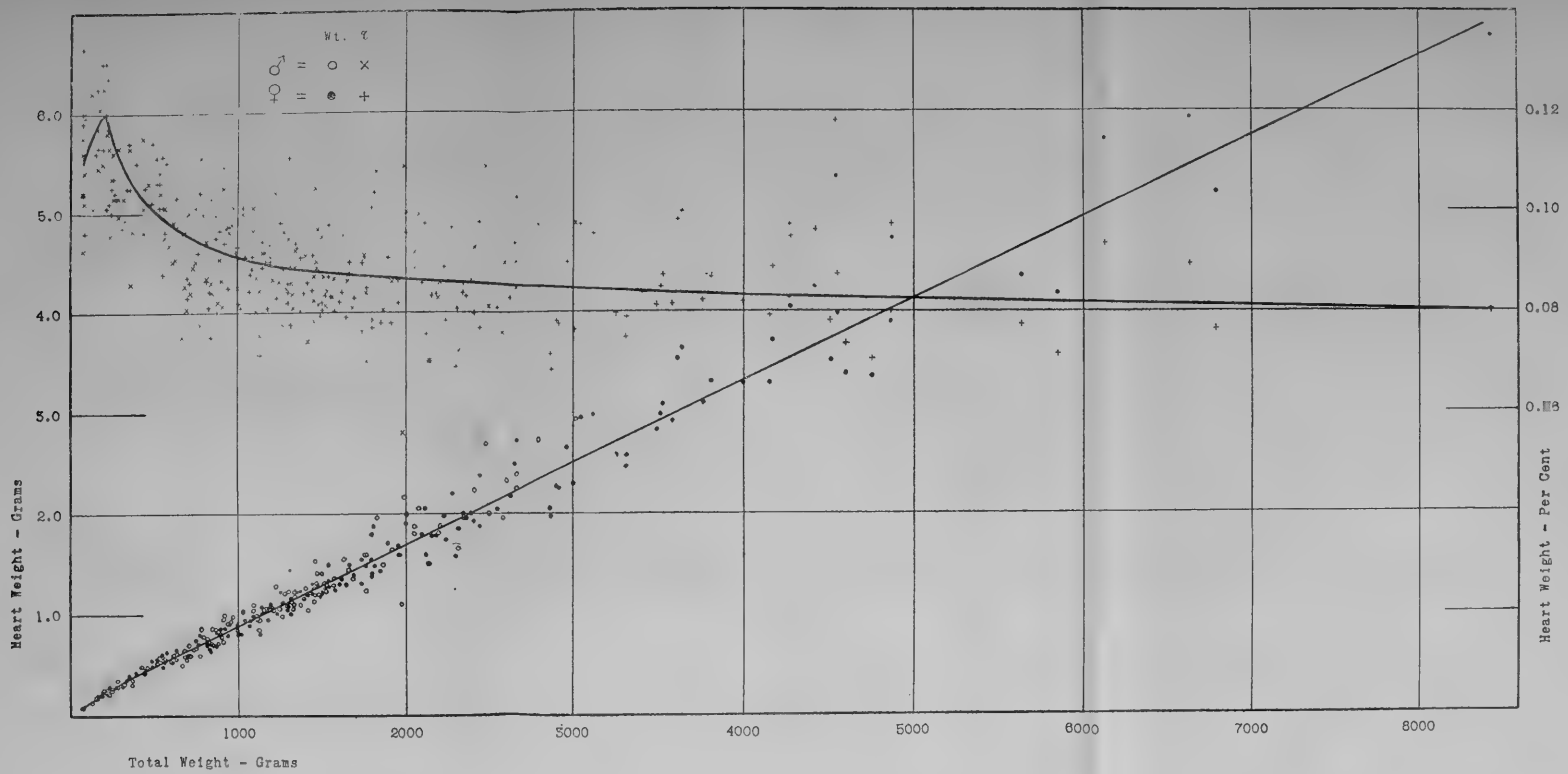

Wt. ♀
♂ = ○ ×
♀ = ● +
6.0
5.0
4.0
3.0
2.0
1.0
Heart Weight - Grams
0.12
0.10
0.08
0.06
Heart Weight - Per Cent
1000
2000
3000
4000
5000
6000
7000
8000
Total Weight - Grams

PLATE 3.

Curves showing the actual and relative increase in the weight of the rectal gland.

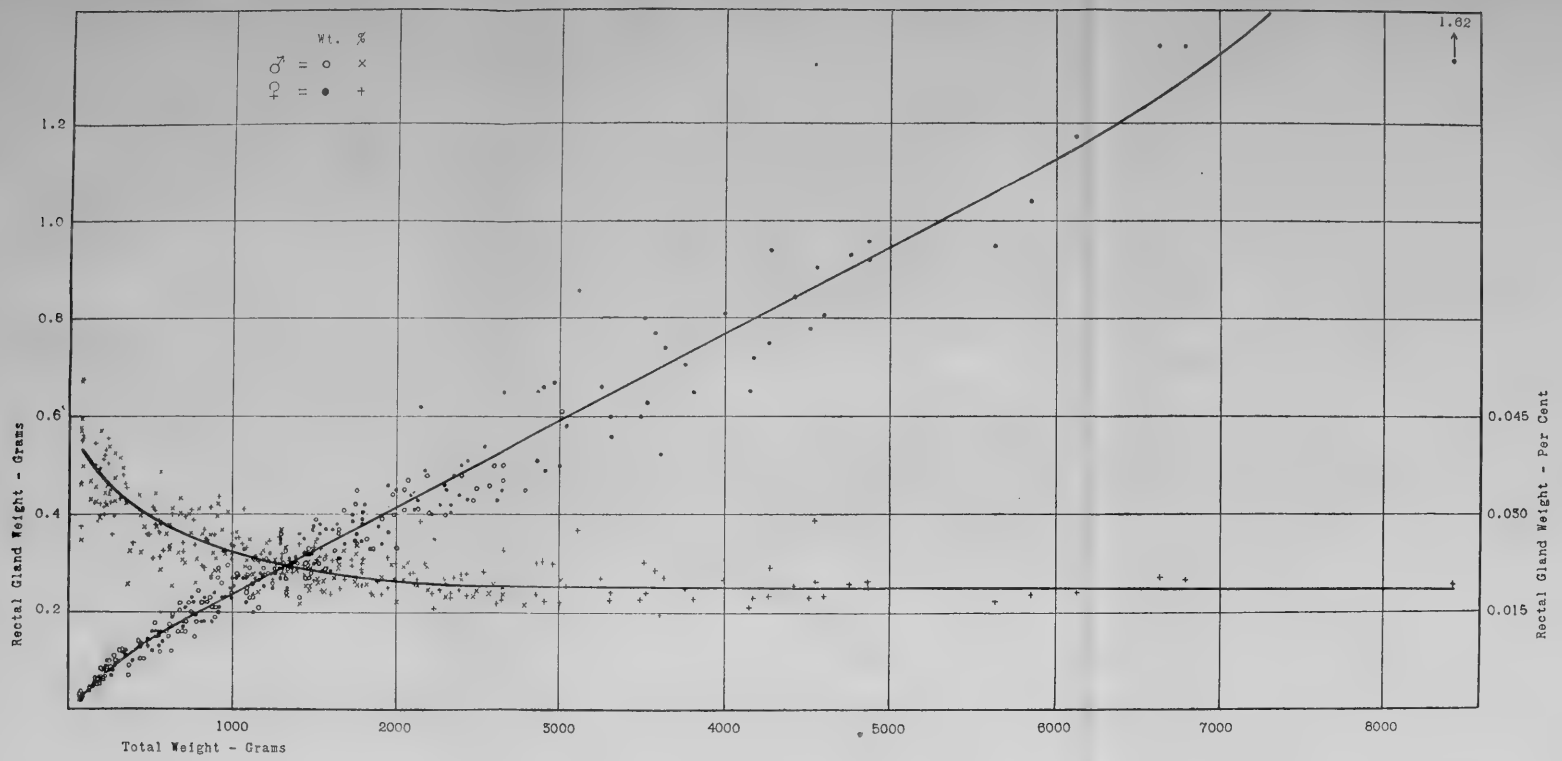

Wt. %
♂ = ○ ×
♀ = ● +
1.62
1.2
1.0
0.8
0.6
0.4
0.2
Rectal Gland Weight - Grams
0.045
0.030
0.015
Rectal Gland Weight - Per Cent
1000
2000
3000
4000
5000
6000
7000
8000
Total Weight - Grams

PLATE 4.

Curves showing the actual and relative increase in the weight of the pancreas.

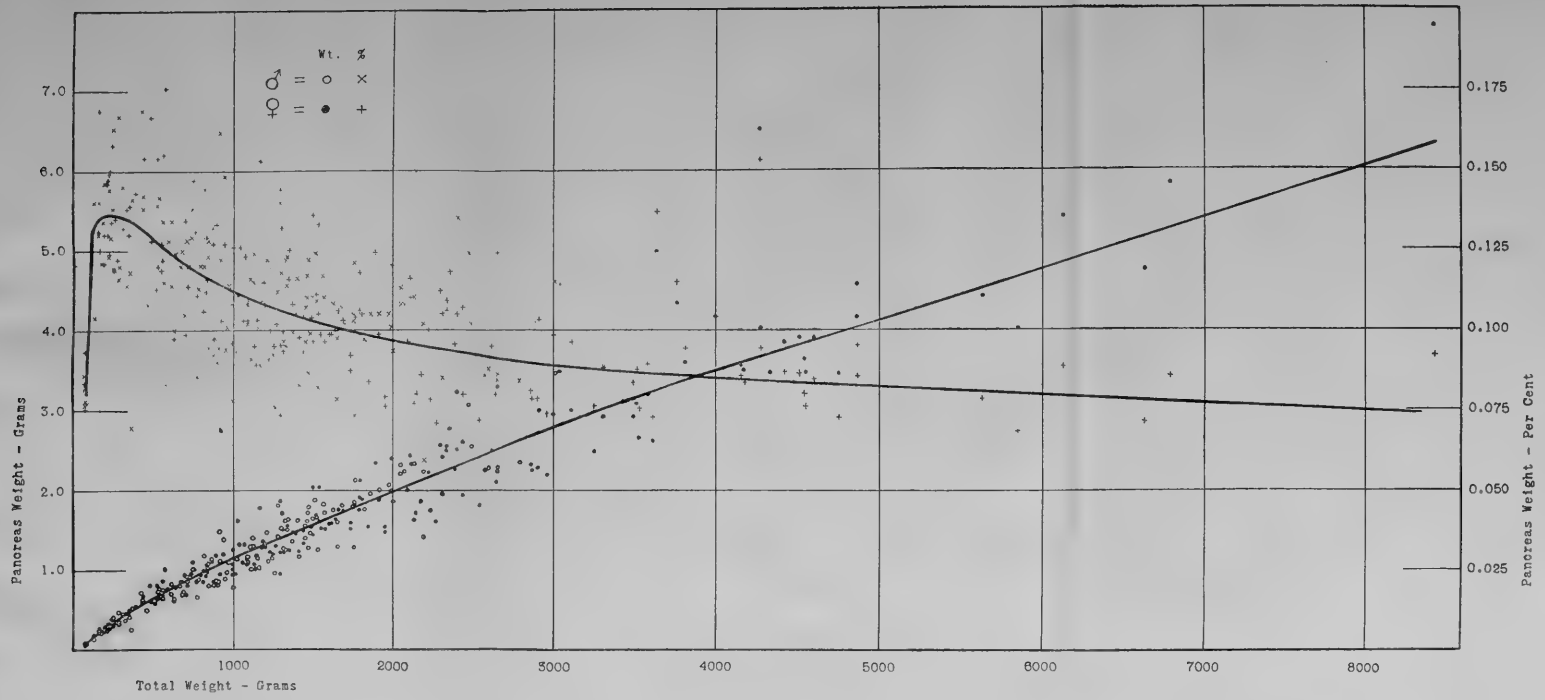

Wt. %
♂ = ○ ×
♀ = ● +
7.0
6.0
5.0
4.0
3.0
2.0
1.0
Pancreas Weight - Grams
0.175
0.150
0.125
0.100
0.075
0.050
0.025
Pancreas Weight - Per Cent
1000
2000
3000
4000
5000
6000
7000
8000
Total Weight - Grams

PLATE 5.

Curves showing the actual and relative increase in the weight of the spleen.

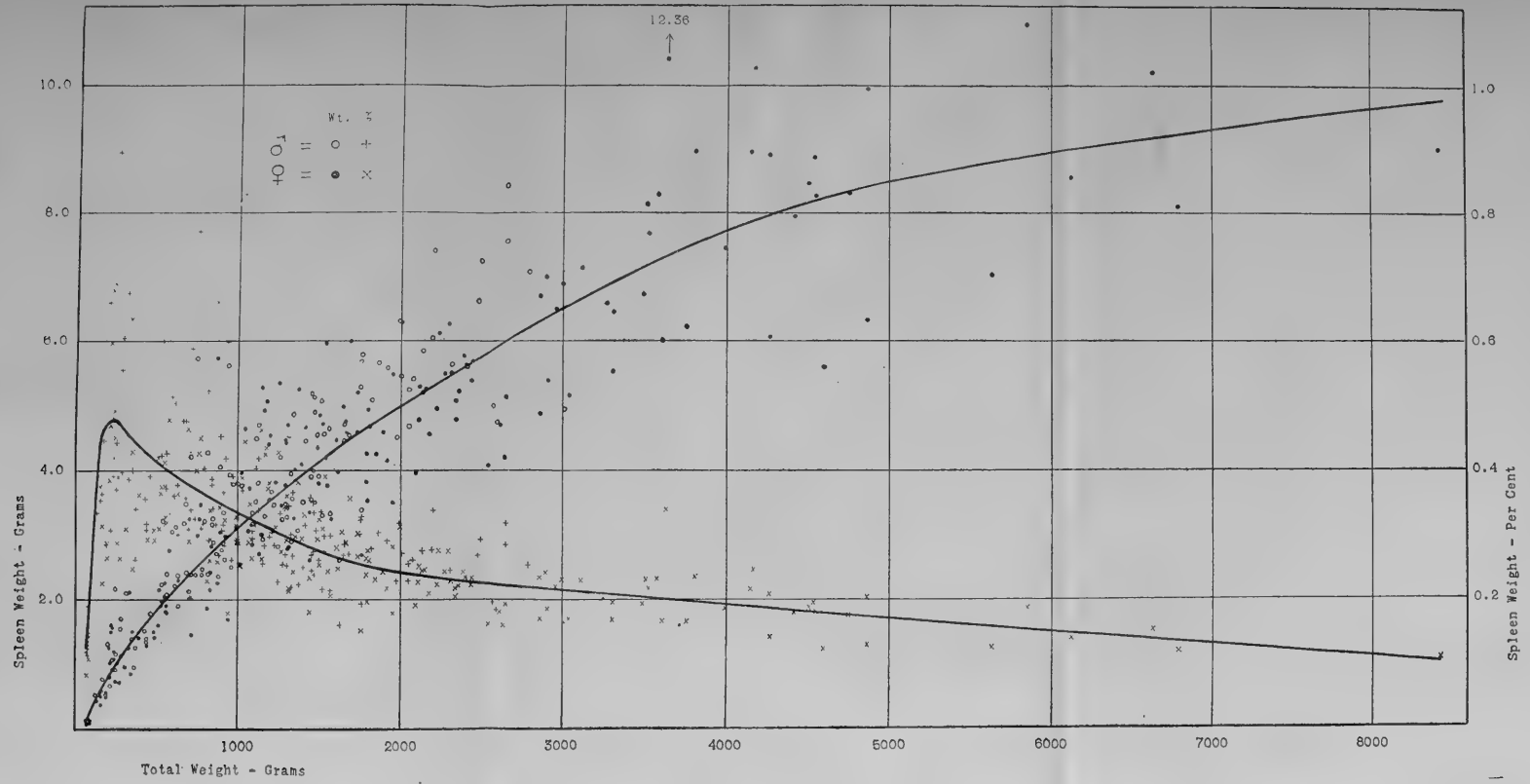

12.36
10.0
8.0
6.0
4.0
2.0
1.0
0.8
0.6
0.4
0.2
Wt. %
♀ ♂
Spleen Weight - Grams
Spleen Weight - Per Cent
1000
2000
3000
4000
5000
6000
7000
8000
Total Weight - Grams

PLATE 6.

Curves showing the actual and relative increase in the weight of the liver.

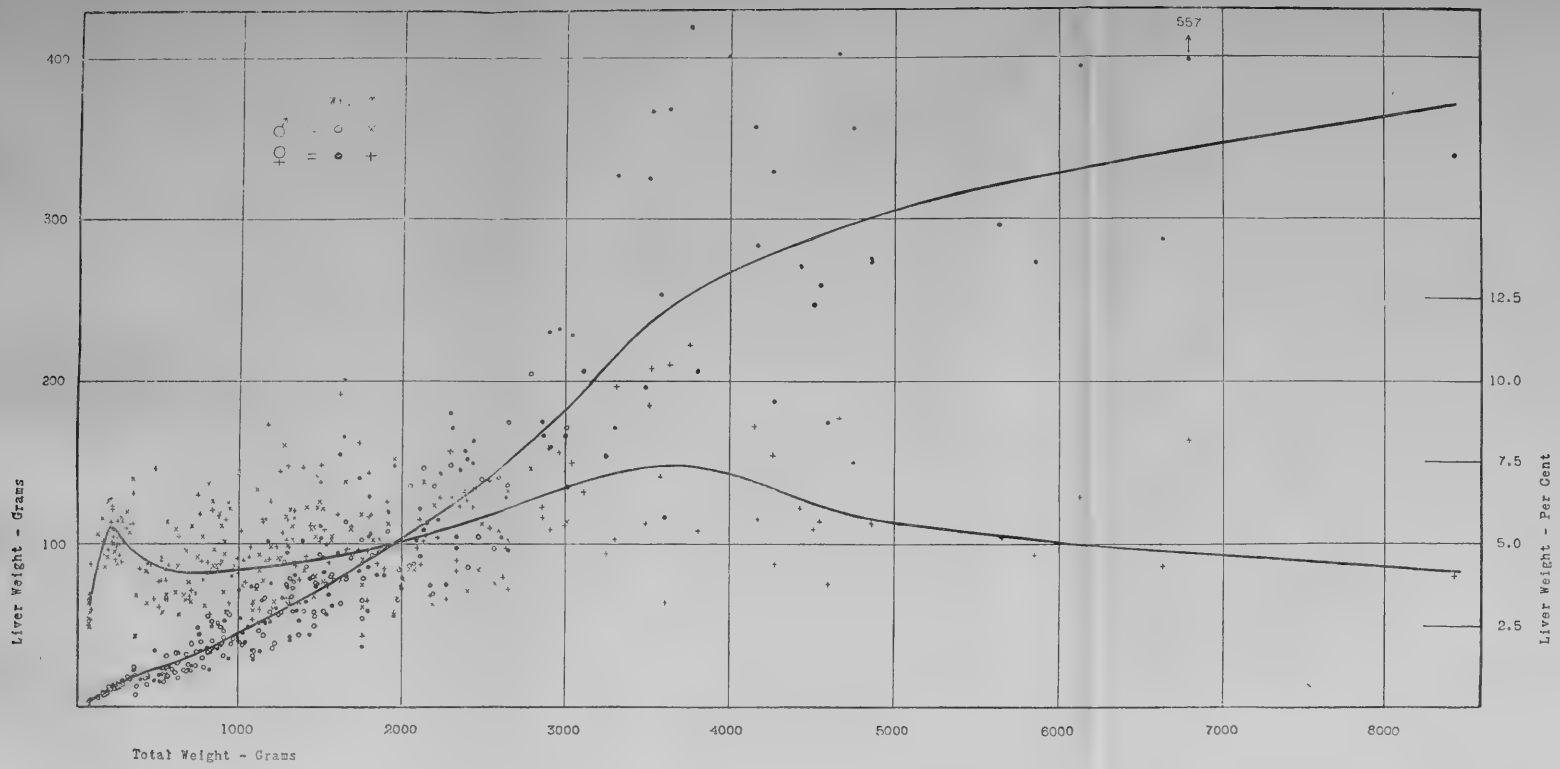
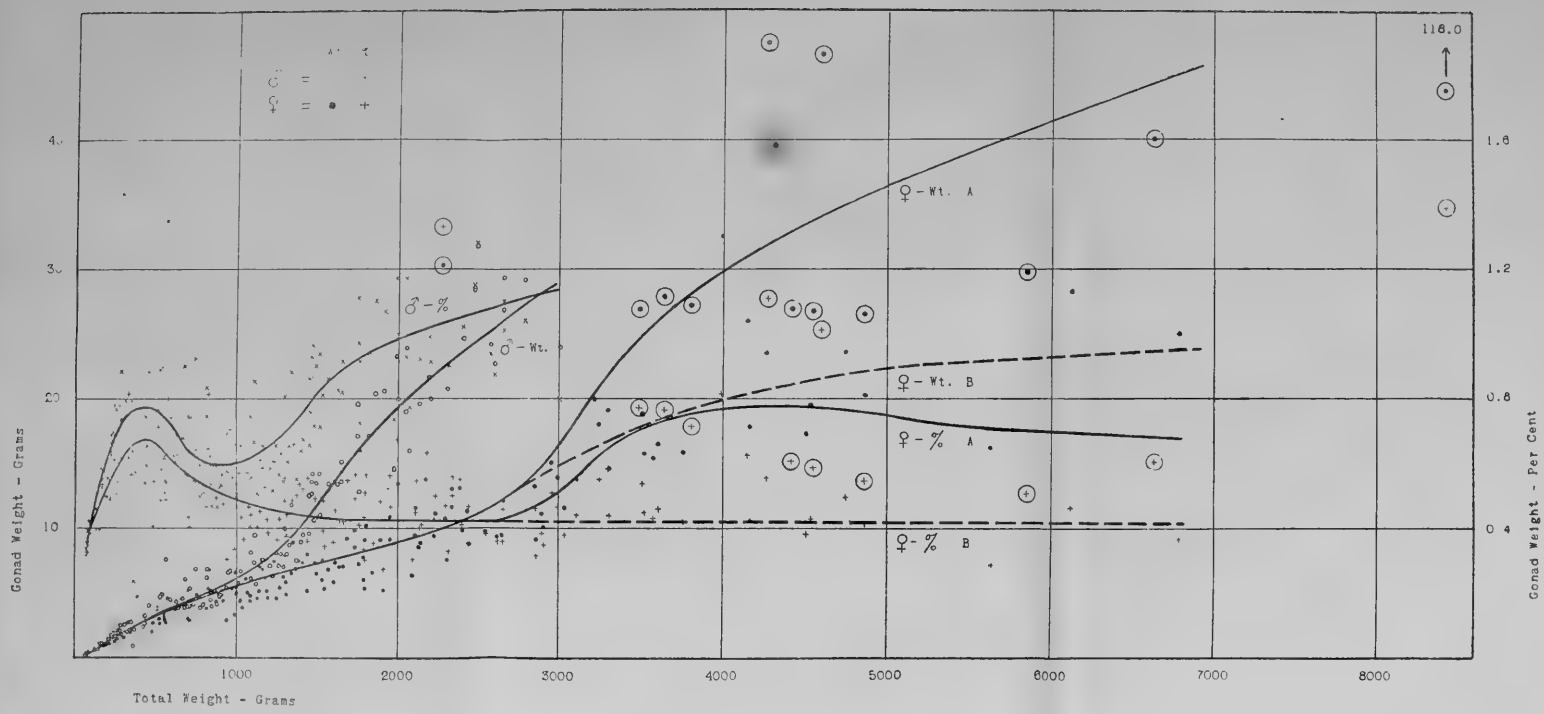

557
♂
♀
400
300
200
100
1000
2000
3000
4000
5000
6000
7000
8000
Total Weight - Grams
Liver Weight - Grams
12.5
10.0
7.5
5.0
2.5
Liver Weight - Per Cent

PLATE 7.

Curves showing the actual and relative increase in the weight of the gonads. The small circles enclose the records of individuals with ovaries containing large yolk-filled ova. Curves A and B show the average maximal and minimal sizes of ovaries before and after the discharge of the ova.


♂ =
♀ =
♂ - %
♂ - Wt.
♀ - Wt. A
♀ - Wt. B
♀ - % A
♀ - % B
116.0
Gonad Weight - Grams
Gonad Weight - Per Cent
Total Weight - Grams
1000
2000
3000
4000
5000
6000
7000
8000
10
20
3
4
0.4
0.8
1.2
1.6

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gol
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THE MORPHOLOGY OF COSMOBIA; SPECULATIONS CONCERNING THE SIGNIFICANCE OF CERTAIN TYPES OF MONSTERS.

BY

HARRIS HAWTHORNE WILDER.

With 4 Plates and 32 Text Figures.

Introduction.

Should one wish to learn the methods of a conjurer, he might vainly watch the latter's customary repertoire, and, so long as everything went smoothly, might never obtain a clue to the mysterious performance, baffled by the precision of the manipulations and the complexity of the apparatus; if, however, a single error were made in any part or if a single deviation from the customary method should force the manipulator along an unaccustomed path, it would give the investigator an opportunity to obtain a part or the whole of the secret. Thus, although the simile must not be pushed too far, it seems likely that through the study of the abnormal or unusual some insight may be obtained into that mystery of mysteries, the development of an organism, an insight denied to those who study only the usual and normal; and this is especially likely to be the case where the abnormalities studied are not deformities, such as are caused by failure of nutrition, mechanical injury, or other external cause, but *where they are due to some modification in the germ itself,* leading the organisms to develop in accordance with laws as definite and natural, though not as usual, as those governing normal development.

That any of the cases usually classed as "monstrosities" can be as natural and symmetrical in their development as are normal individuals, and be thus as legimate a subject for biological investigation, seems not to be generally believed, an attitude which has been fostered by the customary practice of denying them a place in the text-books of general anatomy and embryology, and banishing them to a sort of extra-mural

ghetto among all sorts of malformations and deformities under the general head of "teratology", an *omnium gatherum* in which a few have sought and found valuable material but which for the most part have been left to the curiosity-seekers. Indeed, with the exception of the brilliant suggestion of FISHER, who in 1866 separated the double monsters from the rest, there has been little or no attempt to distinguish between monsters that develop in accordance with the laws of growth inherent in the organism and the various deformities due to external causes. Classifications of monsters are not wanting, indeed the earlier teratologists did little else but classify, each by his own method, but a careful distinction between the two sorts does not seem to have been made.

That this distinction, that between an unusual form of development and a deformity, is a real one, is easily shown. It takes but a moment's consideration to see that such a case as that of the Siamese or other conjoined twins does not belong in the same class with an acephalus, or with a monster showing distortion or truncation of limbs, since the former shows a perfectly normal development in respect to bodily symmetry and the normal condition of the organs and tissues. It is an unusual type of being, but is not a deformity or malformation; and from this standpoint it is but a step to include also all double monsters formed of equal components, the "diplopagi" of my previous paper (1904). At that time I made a sharp distinction between those double monsters in which the components are equal and those in which one component is more or less reduced (*i. e.*, "parasitic" monsters), but since then I have changed my views on this point and include them with equal diplopagi, a point concerning which I shall have something to say later on. Passing this over for the present, however, I may say that what I then recognized of the definiteness and order characterizing the structure and development of diplopagi has been corroborated and emphasized by the opportunities I have since had of investigating many more cases, and their symmetry and regularity in anatomical details have led me to insist upon a sharp distinction between them and other forms of anomalies and to look upon the former as beings as orderly and perfect in their development as are the usual and normal types of being. *Abnormal they certainly are in the sense of not being the usual form in which a given species manifests itself, but they are not deformed.*

Furthermore, it seems also necessary to extend this distinction between orderly and deformed beings so as to include, not only diplopagi with both equal and unequal components, and normal individuals, but also

the numerous cases of primarily symmetrical beings that are less than a normal being, such as cyclocephali and symmeli (cyclops and siren monsters). These, like the diplopagi, are represented by complete series of forms which connect the extreme cases with the normal by imperceptible gradations. The similarity of the two sets of symmetrical abnormalities that lie upon either side of the normal is apparent from the exact correspondence in detail between similarly incomplete members of both sets, such as a median double leg or a median double eye, *whether they represent the two normal components as in the one case or the two supernumerary ones as in the other.*

This recognition of the kinship between these forms of defective monsters and diplopagi seems an important logical step, since it enables us to construct an almost unbroken series (or rather several related series, differing in their geometrical relations) which begin at the most defective cyclocephalus or symmelus; progress step by step until the normal condition is attained, and then again, passing this point, run through the various grades of diplopagi to the stage represented by separate duplicate twins. There are even suggestions of possible extensions of the series beyond this point, for we have not only identical triplets and still higher numbers of separate "duplicate" individuals, but there are also certain cases of monsters which suggest intermediate stages between these and duplicate twins, such as cases of twin births in which one is a normal individual and the other a double monster[1], or cases in which a multiplication involving a part of the organism has progressed beyond the degree of two components and thus represents a stage between two and three components.[2]

This series may be stated as follows, it being borne in mind that the inter-relation of the components may involve more than one geometrical possibility and that the phenomenon may not include the entire body:—

1. Cases in which the entire individual, or the part involved, is less than a normal individual.

[1](a) The "Monstrum Anglicum," born at Fisherton Anger, near Salisbury, England, in 1664 (to Mrs. John Waterman). This was an imperfect female ischiopagus, with legs upon one side only. At the same birth there was a normal daughter who lived to grow up. Licetus, ed. 1665, p. 316.

(b) Fisher's case 43, born near Berlin, Germany, 1773 (to Frau Anna Maria Woblack). This was a male of the "Tocci" type (A VI of my Table, '04, Pl. A). At the same birth there was a normal male child.

Both of these cases are rather old, but seem to have been accepted by later teratologists.

[2]Förster, Taf. IV, Fig. 12, Tricephalus.

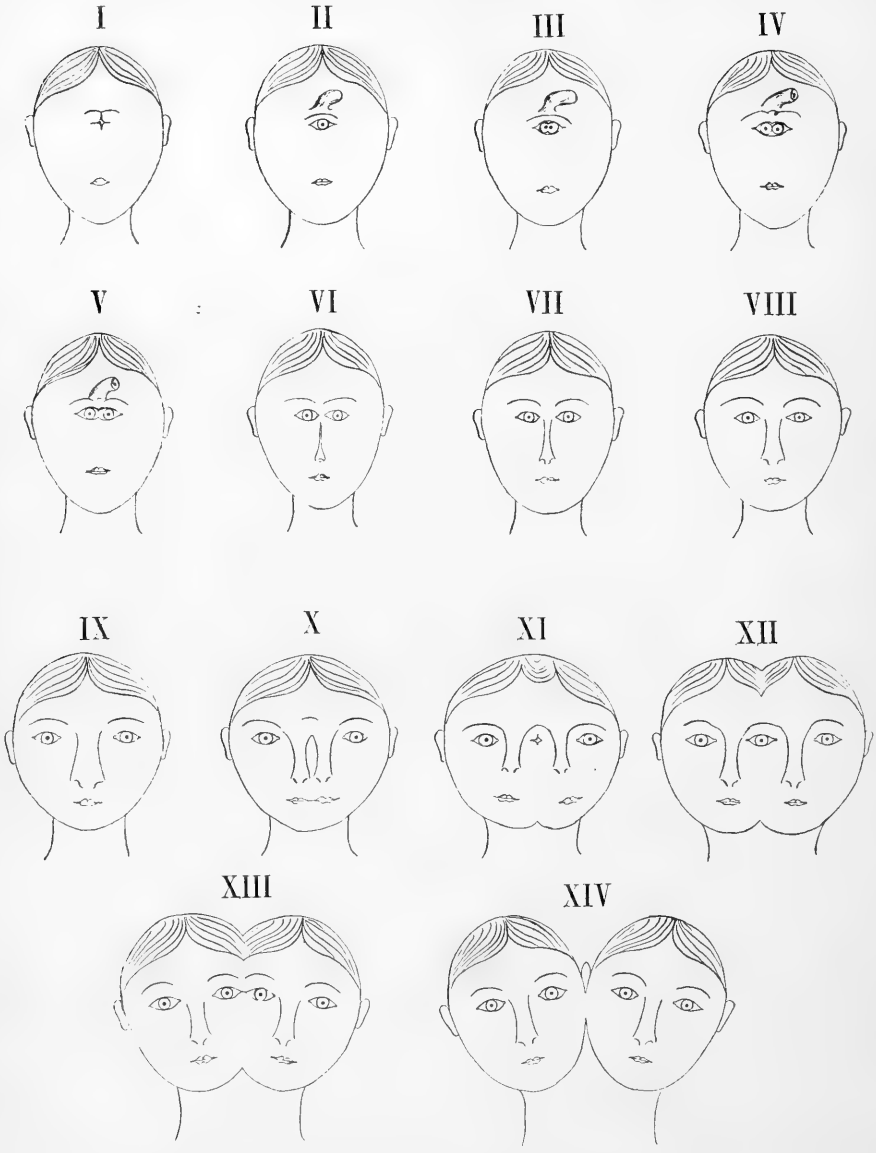


Fig. 1. Diagram showing a related cosmobiotic series.
Stages I-V, Various degrees of Cyclopia.
Stages VII-IX, Normal beings.
Stages X-XIV, Various stages of Diprosopy.

2. A normal individual.
3. Cases in which the entire individual, or the part involved, is more than one individual and less than two.
4. Separate duplicate twins, both normal.
5. (*a*), Separate duplicate twins, one of them a diplopage.
   (*b*), Cases involving a single part, in value between two and three components.
6. Separate duplicate triplets.

Beyond this lie the possibilities of identical quadruplets or even higher numbers, with a tendency to a farther partial duplication on the part of one or more of them, thus continuing the series almost indefinitely.

This idea may be best explained by taking the details of a given organ in an actual series, such a one, for example, as is furnished by the eye-components in a series that includes the various degrees of cyclopy, diprosopy, and normal beings (Fig. 1). In this we may begin with the most reduced type of Cyclops, and find, externally, a mere palpebral slit, symmetrical in outline and with, perhaps, a double set of lacrimal punctæ. This may be followed by cases in which the palpebral opening becomes gradually larger and the median double eye-ball more and more visible. Beyond this the progressive stages are shown by changes upon the eye-ball itself, which becomes continually more visible through an increased palpebral opening; first, a double pupil in an oval iris, two distinct pupils on a figure-8 iris, a double iris on a single sclera, two distinct irides, and finally an eye-ball which is plainly double. (Stages I-V.) In all of these cases the nose, which is prevented from coming down in the usual manner through a downward growth of the fronto-nasal process, remains above the double eye and presents a shape something like a proboscis, decidedly abnormal, but characteristic of all monsters in which there is no space between the eye-components. [Cf. the imperfect face of an unsymmetrical Janus.]

In the next stage, however (stage VI), which closely approaches a normal type, the eye-balls are distinct and a small and narrow nose rudiment, usually with a single median nostril, succeeds in pushing its way down the narrow interval between them, and thus appears in the normal position.

To continue the series further it is necessary to select several types of faces which may be found at any time in an average street crowd. We may begin with an individual with the eyes unusually close together and with the thin file-like nose that always accompanies such a condition

(stage VIII), and end with one that possesses a very broad face, has the eyes far apart, and a broad nose between them (stage IX).

Between these extremes we may find all perceptible gradations, but for our purpose here but one will suffice, an average human face, with eyes and nose of average proportions (stage VIII).

But the series does not end here even, for just beyond the face with the eyes far apart occurs a stage in which there is a slight doubling of the nasal septum or of some other parts of the nose (stage X); then one with two distinct nasal components and a minute palpebral opening between (stage XI). This median eye is in all points similar to that of the type with which we began the series, save that here, if we should analyze the case more completely, we would find that the components of this median double eye would have their potential outer sides together, while in the former case the relation of the eye components is that of a normal pair of eyes, with the inner aspects together. These relations become apparent if we compare members of the series a little more doubled, with the two components of the double eyes more completely developed.

After this the stages that follow, not all of which are shown in the diagram, repeat, in respect to this median double eye, the external appearances shown in the first part of the series; there comes first the doubling of the pupil, then that of the iris, and lastly that of the entire eye-ball, although internally there is always the reverse relationship of the muscles and nerves, as will be shown later on. After the eye-ball is completely doubled there follow several stages in the gradual separation of the ear components, and finally two complete heads upon one neck, a typical Dicephalus. The relations of this form of monster to other forms of diplopagi are too well known to necessitate repetition here, but the reader may be referred to my former paper on the subject, in which is shown a farther continuation of the Dicephalus series, and the relation of this line to the various forms of Ischiopagi.

That such a complete series may be made by the use of both normal and abnormal types, while not in itself constituting a proof of any real relationship between them, is still highly suggestive of a similar cause at the basis of all, and that one which is fundamental, most probably existing in the germ itself. The exact similarity of form, even to minute anatomical details, between parts of the same degree of development on either side of the normal, that is, in both "defective" and "excessive" monsters (*monstra in defectu et monstra in excessu* of the older teratol-

ogists), leads to the conclusion that both sorts of monsters are due to the same cause or kind of cause, and that they should be considered together in any general treatment of the subject, especially in all discussions concerning the cause of these monsters. It seems, furthermore, that all members of this series, both normal and abnormal, are equally subject to definite and orderly laws of development, the impulse to the formation of which lies, in the one case as in the other, within the organism, and leads in all cases to the formation of beings which are primarily symmetrical and free from all pathological tissue or anything which is out of harmony with the organism as a whole. It must be remembered, however, that the word "primarily" is always to be understood in connection with the above statement, for even in the case of perfectly normal germs, later causes, mainly external, may lead to very great deformities, through which the resulting organism is led to deviate from the original goal. Since this is often so in individuals primarily normal, where all the conditions of development have become long adapted to an embryo of a certain definite form and size, how much more likely to become secondarily deformed must be an organism unusual and unwonted in these particulars? If we consider the perfect adaptation of the uterus, the placenta, the yolk-sac, the egg-shell, and the other adjuncts to development that appear in the different classes of vertebrates, we wonder that any embryo of abnormal shape can ever attain an advanced stage without secondary deformations rather than that some of them should become thus. It seems also very probable that monsters vary in their susceptibility to secondary deformation, and that, while certain types usually come to maturity and are even viable, others may inevitably encounter some adverse mechanical principle at an early embryonic stage. Thus the deformed proboscis that represents a nose in several of the types of the series in question, probably develops without deformation up to the time at which the descent of the fronto-nasal process should begin, and the deformity that then begins to make its appearance, although an inevitable one, is due to no deficiency in the germ, but to an unfortunate mechanical relationship which appears at this time Should an embryo of such a monster ever be obtained at a time before the fronto-nasal process begins its downward growth it is safe to predict that there will be nothing in this region which may be considered a deformity, but that the parts will be symmetrically and orderly arranged as in the case of those parts which are not hindered during development.

In carrying on the study of these forms from this standpoint it becomes thus a matter of no moment if or at what time a secondary deformation occurs. If we have either a true double monster or one of a symmetrical series less than a normal individual we must assume that any lack of symmetry or other deformation is secondary in nature and that the embryo was not deformed at first. We must try to look through all such deformations, which by the very nature of the case are bound to occur frequently, and endeavor to find what was the essential condition of the original type which Nature attempted to produce, to learn the intention of the germ, if the expression be allowed. To do this it will be well to consider the nature of the causes which may produce secondary deformation of an abnormal embryo.

Naturally the chief of these in cases where the components are together greater than a single individual, is lack of room, and the commonest result of this disadvantage would naturally be the reduction in size of the less favored component, producing a monster which would be classed under the head of "autosite and parasite," the "parasitic monster" of most authors. In my previous paper I followed the usual custom and sharply distinguished this sort from "true diplopagi," *i. e.*, symmetrical ones. This view I at present reject, and, while not quite prepared to accept all cases of parasitic monsters as deformed instances of primarily symmetrical ones, I feel sure that the most of them are, and that they differ from symmetrical monsters merely in the accidental conditions to which they have individually been subjected during development. The criterion of a true diplopage which should in all cases be insisted on is that of homologous union, that is, that the parts of each component by which they are united to each other should be anatomically the same, a criterion which is indeed difficult of application in cases in which the lesser component is very much reduced, but which is evident in by far the greater number of cases. This would still leave open the possibility of the occurrence of other forms of association, such as that of the secondary fusion of two blastomeres on a common yolk, in which the points of union would be the chance points at which the two embryos first came in contact with one another, and would not be homologous. This latter form of monster is probably common among the Sauropsida, since the occurrence of such fusion in the early stages has been frequently observed, although it is not likely that these cases would be able to develop far. A similar secondary fusion of two geometrically unrelated embryos might account for cases of included fetus (*fetus in*

fetu), and I would wish to remain noncommittal for the present in regard to the majority of dermoid cysts and other embryomata where the parasite is too amorphous to apply the test of homologous union. However, excepting all these doubtful cases there still remains a large class in which the lesser component is properly related to the greater to constitute with it a primarily symmetrical diplopage, though secondarily deformed.

A second cause of deformity, at least as regards bilateral symmetry or equality of components, and one which is especially operative in assisting in the secondary deformation of a diplopage, is found in the striving among the parts during growth for the best physiological efficiency. In a vertebrate embryo certain of the organs, especially those of circulation, and, to a lesser extent, digestion, are physiologically active from a very early period of development. The former, for example, is early called upon to solve certain mechanical problems connected with the transportation of the blood, and although much of the general arrangement of these parts is probably inherent in the germ, the details are mainly left to the exigencies of the particular cases, as is shown by the great amount of individual variation in the adult of a given species, especially in the smaller, later appearing vessels. Now in those diplopagi in which the heart is represented by two separate components, which yet form parts of one system, the problem is presented in a more definite way than in the case of two rival blood-vessels that supply the same part, since there are here two pulsating organs to direct one circulation. It is inevitable in such a case that one of the hearts should early become a little stronger than the other and gain either a control of vessels beyond the median line separating the two components or else secure for its vessels a little more of the blood; in either case the result would soon show in a lack of symmetry between the two components or between corresponding parts, although at first the two components were exactly equal. This point will be brought out farther on by a comparison of the circulation in several cases of the group known as "Janus" monsters, where the asymmetry in the circulatory system is plainly of a secondary nature and due to the causes above outlined. As an instance of secondary asymmetry due to the rivalry among digestive systems I may cite the case of a two-headed lamb (Teras XV of my collection), which had come to full term and lived and fed for perhaps four weeks. Aside from the doubling of the head it appeared absolutely normal, *i. e.*, single, and the two heads were exact duplicates of each other and per-

fect in development.[3] It had, however, probably by chance, used one mouth exclusively in suckling and that exercise of functional activity, even during the brief life of the animal, had given a slight twist to the neck so that the feeding head came to be carried as if it were the continuation of the median axis of the body while the head that took no nourishment lay a little to one side. It cannot be doubted that the persistence of this treatment through several years would have increased this tendency so that in the adult state a person who knew nothing of the early conditions would have classified the case as that of a lamb with a parasitic head.

Since, now, in the case of Sauropsida and Mammalia, so much of the development is gone through with before the incident of hatching or birth, it is to be expected that in most cases of primarily symmetrical monsters there will be found secondary differences at least in the internal organs, at the time of birth, and that these differences will be greatest in those systems which are actively functional from an early period, such as the circulatory and digestive systems; while the least amount of modification is to be expected in such systems as the skeleton and muscles. That such is actually the case will be seen in the descriptive part of this paper where the numerous modifications in the circulatory system of otherwise perfectly symmetrical monsters will be contrasted with the symmetry of median eyes, formed from two components, where each muscle, nerve, or other part is repeated on the two sides with at least as much faithfulness as in the two sides of a normal bilateral being. In the case of the circulatory system the modifications would naturally affect mainly the heart and the main vessels, while the arteries distributed to symmetrical components would be as regular and symmetrical as the nerves or muscles. [Cf. the cephalic arteries in double-headed monsters, as shown by Miss Bishop.]

A third cause, or rather a large class of causes, producing secondary deformation of a primarily symmetrical monster, and one likely to induce all sorts of pathological conditions, is the mechanical hindrance to the carrying out of a given plan of development through the interposition of some organ which either encroaches upon the space required for something else or actually blocks the way and renders farther develop-

[3]This specimen, Teras XV, was one of those used by my pupil, Miss Bishop, in her paper upon the arteries of dicephalous monsters. The exact equivalence of the two head components is well shown in the equivalence of the arterial supply.

ment in a certain direction impossible. Such is the case of the proboscis-like nose given above. Still more serious would be the difficulty if the encroaching organ should hinder the full efficacy of some system of functional importance to the embryo, as for example the circulatory or lymphatic organs. Thus there might arise those evidently pathological beings that fill the pages of general works on teratology, yet in which may still be traced a definite original plan capable of finding a place in some series of symmetrical and non-pathological beings. It is probable, indeed, that certain types of primarily symmetrical monsters have such a mechanical configuration as to render development impossible without becoming secondarily pathological through this cause, and in such cases one must either learn to eliminate the secondary modifications as remarked above or, perhaps, by some fortunate chance, as rare as the discovery of some long-sought link among the strata of the earth's crust, obtain and study an embryo of the type in question representing a stage previous to the appearance of the causes of the pathological condition.

Aside from the above and probably other causes affecting the development of abnormal embryos in general, certain groups of vertebrates are undoubtedly subject to special hindrances due to some peculiar and specific mode of development. The result of this may be that only certain types are possible within a certain group of vertebrates; hence, in completing a given series of symmetrical monsters it may easily happen that a certain stage sought cannot be found in mammals but may be of frequent occurrence among amphibians, or that a stage in the series that always appears in a secondarily distorted condition in birds may be found without such modifications in reptiles. This suggests an explanation of the fact that certain types of monsters are of far more frequent occurrence in some animals than in others, a field of inquiry that would undoubtedly yield much if it were carefully investigated. For example, birds have at least two developmental peculiarities that would tend to modify the development of monstrous embryos, namely, the enormous yolk and the early twisting of the embryo, and as a matter of fact, avian monsters, when hatched, are more limited in variety than those of mammals and are usually unilateral and somewhat distorted. All of these suggested causes of malformation have this in common, that they exert their modifying influence at some time during embryonic life upon what must be at first an undeformed, though abnormal, embryo. It follows, therefore, that we would eliminate these secondary modifi-

cations if we could only study these types of monsters as early embryos. Such material is, however, all but impossible to obtain, but with the gradually increasing use of the embryos of various vertebrates in general laboratory work in colleges and universities, an increasingly large number is yearly sorted over, and thus the chance of such fortunate discoveries is always on the increase. Embryo avian monsters are frequently met with, but these, for the reasons above cited, are rather unsatisfactory material for work, although KAESTNER has turned these very disadvantages into points of much significance and has obtained therefrom highly important results. Early mammalian embryo monsters, of the types referred to in this paper, are almost unknown, but since in my collection I already have two of them, Terata III and XXX, (see p. 369, foot-note; also Fig. 27) such research appears to be quite within our reach.

Aside from the obvious advantages of getting rid of secondary modifications, the study of "teratembryology" offers another, which is very great. Just as certain of the types which belong naturally in a teratological series are bound during later development to meet with certain mechanical difficulties which prevent them from surviving birth, the so-called "non-viable" monsters, it is also very probable that others which exist so far as we know only in a theoretical series actually begin embryonic existence but meet with difficulties which set a term to their life while still embryos. Such forms would then be expelled in a disintegrated condition, or absorbed, and would thus never come within the ken of the teratologist.

If now we may assume that there is a class of monsters which are primarily as symmetrical in structure and as normal in their tissues as are the beings we usually consider normal, and if we may hold that they, as well as normal beings, owe their structure to some germinal variation, there is great need of a distinct term, which is broad enough to include both these forms of monsters which are merely deformities and pathological cases. In defining this term a set of duplicate twins, whether separate or conjoined, should have the value of a single unit.

For such an organism (or set of organisms), whether normal or abnormal, whether less or more than or equivalent to a normal being, and lastly whether perfect or deformed, provided the deformity is due to a secondary cause as explained above, I propose the name COSMOBION *(plural* COSMOBIA*), an orderly living being.* In this term, the meaning of which exactly expresses my idea, the only violence to classic

Greek seems to lie in the formation of a neuter noun, *βίον*, a living thing, from the abstract masculine, *βίος*, life; a formation which is abundantly supported by analogy, and fully in accordance with the genius of the language.[4] Another possible criticism of the word lies in the fact that the word *κόσμος*, *order*, has been commonly used, even by the Greeks themselves, in its derived meaning of the *Universe*. The literal meaning is, however, exactly what I desire, and in addition to being euphonious and simple, it readily admits of the adjective form Cosmobiotic and is applicable to plants as well as to animals if desired. Whether such forms exist among plants I cannot say, but, in order to be analogous, they must belong to the sexual generation and hence be looked for among the lower Cryptogams.[5]

The theory which I have here set forth, and which I may call the *theory of Cosmobia*, is not wholly a new one, since the recognition of certain series of monsters with imperceptible gradations between them has been pointed out by teratologists for a long time. What may be considered new is, first, the recognition of the relationship between the symmetrical anomalies on either side of a normal being; the inclusion among Cosmobia of certain types of secondarily deformed and misshapen monsters resulting from abnormal conditions during development; and, thirdly, the possibility of considering in a single series both these forms with less and those with more than the normal number of parts, including also normal beings. Whether either of these points may be in accord with the actual facts can only be shown through much investigation of the structure of all sorts of Cosmobia, together with experimental work on the artificial production of these forms, a field which, though often tried, has until recently yielded but little.[6] At the best my theory can be

[4]We have already the exactly analogous word Rhizobia, the organisms living in the root nodules of leguminous plants.

[5]The various sorts of double or twinned flowers, fruits, and other parts of plants are phenomena of quite a different kind from cosmobiotic organisms, since the appearance is localized and affects certain parts only. These may perhaps be compared to the doubling of fingers, limbs, or other lateral parts among animals, which, although they may be germinal in origin, do not modify the entire organism.

[6]As far as can be learned from figures and descriptions of artificiall pyroduced monsters, they all seem to be merely cases of deformation, with no genuine Cosmobion among them. In the case of the reported artificial production of "double monsters," like those claimed by Panum or Gerlach, it is probable that these were simply natural cases of monsters, quite frequent among birds, and not due to the experiments. Experiments thus far seem to

nothing more than a working hypothesis, which may point out the direction in which needed work may be done, and its establishment, modification or refutation are a matter of indifference so long as our knowledge of the subject is advanced. Concerning the probability of each of the points suggested the reader must judge after the consideration of the following report, which presents the results of my investigation of the subject.

As material I have had the opportunity of studying the following monsters; the numbers given in connection with them being those under which I have filed them in my notes. These will be used for convenient reference throughout the paper.

I. Pig embryo; Diprosopus tetrophthalmus. [Lambert.]

II. Two-headed snake (Storeria). [Davison.]

III. Human Synote (imperfect Janus), advanced fetus. [Baldwin.]

IV. Human Thoracopagi, one parasitic; advanced fetuses. [Wistar Inst. Coll. No. 2884.] This specimen is figured by Hirst and Piersol, Part IV, Pls. XXXVIII and XXXIX.

V. Chick embryo, two bodies, head apparently single, but imperfectly formed. [Smith College Laboratory, incubated.]

VI. Human Cyclops, child at term. [Wistar Inst. Coll. No. 6956.]

VII. Pig Cyclops, large fetus. [Wistar Inst. Coll. No. 2913.]

VIII. Human Paracephalus. [Wistar Inst. Coll. No. 4926.] This specimen is figured by Hirst and Piersol, Part III, Pl. XXIV.

IX. Pig embryo, perhaps a Cyclops, but very imperfect. [Lambert.]

X. Human Omphalopagi, advanced fetuses. [Wistar Inst. Coll. No. 4996.] This specimen is figured by Hirst and Piersol, Part IV, Pl. XXXV.

emphasize the position taken here, that true cosmobia of all sorts, normal, excessive, and defective, are due to a cause existing in the germ, or applied during the very early stages of development, and it is there that our efforts should be directed if we may hope to produce such an organism artificially, a result that we can hardly expect to reach by purely mechanical means. As the tendency to produce duplicate twins and other sorts of abnormal cosmobia seems inherent in certain organisms, and to be transmitted by heredity, it is quite possible that we may be able to breed certain of the viable forms. In this connection the remarkable experiments of Stockard, which are now being carried on, are of the greatest moment, and will yield important conclusions.

XI. Chicken, newly hatched, Diprosopus triophthalmus, also with four legs, the inner ones smaller. [B. G. Wilder.]

XII. Pig, new-born, Diprosopus triophthalmus. [B. G. Wilder.]

XIII. Duck, adult, with a supernumerary leg. [B. G. Wilder.]

XIV. Pig, new born (?), two bodies in the form of Omphalopagi, but with a single head with double tongue and lower jaw. [Lambert.] From the Barnum Museum of Tufts College.

XV. Lamb, three or four weeks old, with two equal heads. [B. G. Wilder.] Born at Ludlowville, N. Y.

XVI. Chick embryo, perhaps a "Janus." [Smith College Laboratory, incubated.]

XVII. Kitten, new-born; parasitic thoracopagus. [Mead.]

XVIII. Chick embryo, perhaps a "Janus." [Gorham.]

XIX. Chick embryo; double primitive streak. [Gorham.]

XX. Turtle, small Chrysemys; dicephalus. [Mead.]

XXI. Chick, a few days after hatching; double median leg in addition to the normal pair. [Lambert.]

XXII. Chick, a few days after hatching; a supernumerary leg upon one side. [B. G. Wilder.][7]

Of these monsters, which are listed in the order in which they have been received, Nos. VIII, XIII, and XXII are probably not Cosmobia, at least not typical ones, and are hence not considered in any way in the present paper. The others may be placed in groups as follows:—

A. Janus-Omphalopagus group: Nos. III, IV, V, X, XIV, XVI, XVII, XVIII.

B. Diprosopus group: Nos. I, II, XI, XII, XV, XIX, XX.

C. Cyclops group: Nos. VI, VII, IX.

From this material it is my purpose to select for the use of the present paper certain topics, the consideration of which may be of direct bearing upon the theory above enunciated rather than to attempt an anatomical description of the several forms, a kind of work of which

[7]Since the completion of this paper I have received from Professor B. G. Wilder a large and valuable collection of monsters, which arrived too late for incorporation in this list. One of them, however, Teras XXX, is of such value in this connection that it deserves special mention. This is a kitten embryo of 34 mm., with a partially doubled head, and practically the counterpart of Dr. Lambert's diprosopic pig, Teras I. This I have already sectioned and hope to use it later in connection with further work on Teras I. I am also inserting into this paper a drawing of it in connection with the description of this latter monster. (Fig. 27*b*.)

there is already an abundance among teratological literature. Two such topics will be treated in this paper; the *first* of which is a general description of Teras III, with especial treatment of the auditory ossicles and the circulatory system. This monster belongs to the type called "Synote" and I shall refer to it as the "Baldwin Synote" from the donor of the specimen. The *second* topic is a comparison between various types of double eyes, as they occur in all three of the groups given above.

In a work of this nature, more than in perhaps any other, the investigator is dependent for his material upon the thoughtfulness and generosity of others, and it is thus with especial earnestness that I wish here to personally thank those who have so kindly aided me in this respect. Dr. F. D. Lambert, who inspects many hundreds of pig embryos yearly, has sent me everything abnormal which has come under his inspection, and I wish especially to mention the beautiful specimen, No. I, which came to me faultlessly preserved, so that I was able to section the entire specimen and make wax-plate models of several of the parts, an opportunity that has seldom if ever come to the teratologist. The human Synote, No. III, also beautifully preserved, was given me by Dr. James F. Baldwin, the Chief of Staff of Grant Hospital, Columbus, Ohio, who preferred to have the specimen used for scientific investigation rather than to keep it "simply as a curiosity." In using such a valuable specimen I feel the responsibility for good results and only hope that they will justify the sacrifice. An especially valuable aid in my investigations has come from the Wistar Institute of Anatomy, in Philadelphia, largely through the kindness of its director, Dr. Milton J. Greenman, who has loaned me numerous specimens for study and even dissection. Prof. B. G. Wilder, of Cornell University, has been untiring in obtaining for me Cosmobia of various sorts, his most valued contribution being perhaps the diprosopic pig, No. XII, which, delivered at term, belongs in the same series as Dr. Lambert's beautiful specimen, No. I, and thus enables me to trace the later development of this form of monster; the fact that the two differ slightly in the degree of separation of the two components enhances the value of both specimens.[8] The two-headed snake, *Storeria occipitomaculata* (Teras II) was sent me by Dr. Alvin Davidson, of Lafayette, and Drs. Mead and Gorham, of Brown University, have furnished me with several valuable specimens.

[8]One of Professor Wilder's latest specimens, Teras XXX, mentioned in a previous footnote and figured here as Fig. 27*b*, will perhaps vie with Teras XII in point of value. This came too late for proper treatment here, but will serve for later research, especially in connection with Teras I.

PART 1. THE "BALDWIN SYNOTE," A HUMAN MONSTER OF THE IMPERFET JANUS TYPE.

A. *General consideration of the Janus-Omphalopagus Series.* This is an extensive natural series of Cosmobia, certain of the stages of which are among the most frequent of mammalian symmetrical monsters. In this series the two components are placed *vis-a-vis,* that is, with the ventral sides applied to each other, and with always a common umbilicus. Individuals of this series may vary in two ways, not dependent upon each other; (1) in the extent of longitudinal union, and (2) in the amount of lateral torsion of the two components in respect to each other. These will be considered in order.

1. *Variations in the extent of longitudinal union.* The posterior limit of this union is always fixed by the umbilicus, to which it extends in all cases and beyond which it never goes, leaving, posterior to this point, in undeformed Cosmobia, two perfect hinder parts, facing each other. Even in cases with extreme involution of one side (as described under (2)) this peculiarity becomes less and less posteriorly, and by the time the umbilical level is reached the components exactly face each other.

The stages in such a series are shown in the accompanying diagram. (Fig. 2.) Each stage figured rests upon actual cases, and typical examples are indicated by the name of the authority and the date of the descriptive paper, so that the cases can be easily found by refernce to a teratological bibliography. As the diagram represents merely the extent of union longitudinally, each case is represented with the components exactly opposite, that is, with no lateral torsion. The series thus begins with a "Janus symmetros," in which the line of union begins at the vertex and extends, as in all the cases, to the umbilicus. In the second stage the brows, eyes, and noses become free, although the latter may be hindered from full development through lack of room. In the third stage the face is free as far as the chin, and in the fourth the heads and necks are free and the union begins at the manubrium sterni. In the stage following the union begins at the mesosternum, but in the next it involves the xiphisternum alone. The extreme type of this series is one in which the entire sternum is free and the soft parts alone are involved. Such were the famous "Siamese twins," Chang and Eng.

Beyond this there is introduced a stage in which the united parts include only extra-embryonal structures, as, for instance, a portion of the umbilical cord or even the placenta alone. Such a case would be a true Cosmobion, but as the united structures are cast away at birth

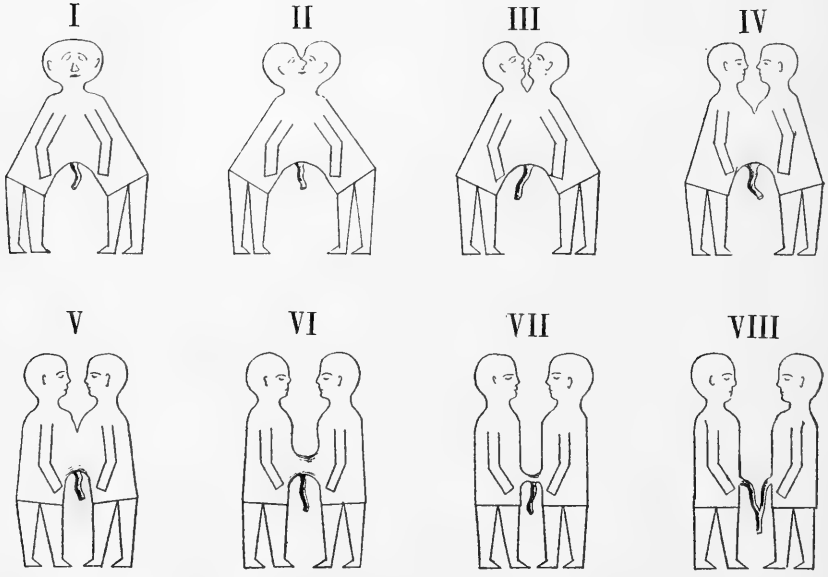


Fig. 2. A related series of Diplopagi, the "Janus-Thoracopagus" series (monophaliens, G. St. Hilaire): drawn in diagrammatic form from recent cases, as follows:

I. PROSOPOPAGUS. The "Baldwin Synote," described in this paper.
II. GNATHOPAGUS. Williamson, 1895.
III. TRACHELOPAGUS. Fraser, 1890.
IV. STERNOPAGUS. Sebart, 1896-97.
V. THORACOPAGUS. Scott, 1889.
VI. XIPHOPAGUS. Boettcher, 1871.
VII. OMPHALOPAGUS. The "Siamese Twins," b. 1819; d. 1874.
VIII. URACHOPAGUS. Any genuine case of "Duplicate Twins."

In the last case (VIII) the united part does not usually involve the free portion of the umbilical cord, but is confined to the placental portion. If the portion of cord shown be considered to represent the entire extra-embryonal part of the embryo, the diagram correctly expresses the condition. Such twins are thus properly double monsters in which the parts in common are extra-embryonal and are cast away at birth.

there results a pair of free components, in short, duplicate twins! During early embryonal life, when there is no clear distinction between embryonal and extra-embryonal parts, it would be without question a Diplopage, but the subsequent abandonment of those parts in which the union occurs leaves the two components free from each other, a difference of no moment to the morphologist but a most vital one from the standpoint of the individuals concerned.

As the terms that have been applied to the various stages of this series are numerous and varied, I have hoped to simplify matters a little by suggesting a series of terms, the most of which are already in use, which designate the condition in the simplest way; namely, using in each case the Greek term for the point at which the union begins anteriorly, joining to this the usual term for a monster with two components, —*pagus,* (πήγανυμι). The term *omphalo-* is often added to the compound, as "Thoraco-omphalopagus," but this is hardly necessary as the umbilicus must of necessity always form the posterior limit of such monsters. We have thus the terms, *Cephalopagus, Gnathopagus,* etc., as given in the diagram, a set of terms which may be freely added to if we wish to express grades between those given.

2. *Variations in the amount of lateral torsion of the two components; with involution of certain of the parts upon the less favored side.* It rarely happens that the components so exactly face each other in the head region that the two resulting compound lateral faces are perfectly equal. Such a case is called a "Janus symmetros" and is one of the greatest teratological rarities. Usually in this region there is what may be termed a lateral torsion, with the result that the compound face upon one side is complete while that upon the other suffers a greater or less involution, that affects the median parts at least, but, with a greater degree of involution gradually affects parts that are more laterally placed. The series formed by this principle is shown in diagrammatic form in Fig. 3, which begins with a Janus symmetros and ends with so complete a degree of involution that the external features of the face are entirely suppressed upon the imperfect side, giving the compound head the external appearance of a single one, facing in a direction that is really lateral in respect to the actual position of the components. This extreme condition is that realized by my Teras XIV, a pig with eight legs, two bodies, and apparently a single head placed sideways with respect to the bodies. In all cases the torsion is most pronounced anteriorly and becomes gradually less towards the umbilicus, at which point it disappears and the two bodies are opposite each other.

B. *The Baldwin Synote and its place in the series.* This monster [Plate I] is an "imperfect Janus" (Cephalopagus) of the degree of torsion represented by Stage V of the diagram [Fig. 3]. The face

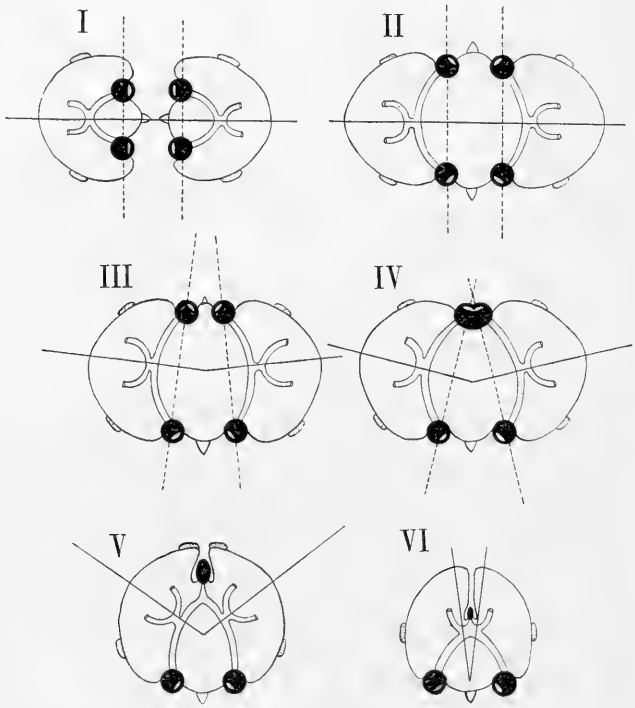


FIG. 3. Diagram showing different degrees of lateral torsion (involution) of monsters of the Janus group.

I indicates the relation of the two components; the others represent actual cases, as seen in cross-section at the level of the eyes. II is a "Janos symmetros," in which the two components are exactly opposite, and the two faces are consequently equal and perfect. III to V are the common types, in which one face is more or less suppressed, thus suggesting the employment of such words as "anterior" and "posterior," "front' and "back," etc., to express the two aspects. Type IV is designated as an "Iniops," Type V as a "Synote." In Type VI one face is wholly suppressed, at least externally, and appears like a normal head to which two bodies are attached laterally.

of one side is complete, while the features that appear upon the other are (1) a large nasal proboscis, consisting of a stalk and a larger terminal bulb; (2) a minute palpebral opening, but with externally no

trace of an eye-ball; and (3) the two external ears, meeting each other in the median line, whence the name *Synote*.

For convenience in description and in order to emphasize the compound nature of many of the structures, it will be convenient to designate the two components as A and B, A being the one on the left when the specimen is held with the more perfect side towards the observer. This rule, which can be readily understood by the help of the illustrations to this article, which are designated in accordance with this system, is applicable in the case of almost every specimen belonging to this series, since cases in which the components are placed exactly opposite each other are extremely rare, and since the rule can be easily applied whenever there is the slightest lateral torsion. If now the right and left lateral aspects of each component, viewed by itself, be designated by the letters *r* and *l*, the composition of a given compound organ may be indicated as Ar+Bl or Al+Br, as the case may be. Thus the "perfect" face, in reality composed of half faces contributed by the two components, has the composition Ar+Bl, while that of the imperfect side, of which a few features alone appear, is composed of the two half faces Al+Br. This would indicate, for example, that the two external ears, which are situated together upon the imperfect side, consist of the left one of A and the right one of B, as a moment's inspection will prove.

As with all monsters of this type, the two components become more nearly opposite each other posteriorly, and at the level of the common umbilicus they are practically quite opposite, that is, their median sagittal planes coincide. This may well be shown by a comparison of the parts at different levels, beginning with that of the mouths. The mouth of the perfect side leads into a pharynx of normal appearance, furnished with a good tongue, while the imperfect side has a much narrowed pharynx, without external opening, and fitted with a narrow, tapering tongue. Tongues and pharynges thus correspond to the two apparent faces, the apparently normal ones for the perfect face and the narrow ones for the imperfect face. Each is thus not an organ belonging to a single component, but compound in the same way that the faces are. The same relationship obtains in the case of all organs that face the same way as these, namely, towards the sides of the components.

In the center of the transverse pharyngeal plane there lies a single common œsophagus, into which both pharynges open. Upon the apparent ventral side of each neck, lateral in respect to the components, there is placed a larynx, one upon either side of the œsophagus. Each

is apparently a single organ, but that of the imperfect side is narrower than normal, yet not incomplete, while that of the perfect side is apparently a normal one. From each larynx a trachea leads down into a pair of lungs, the pair upon the perfect side being in reality Ar+Bl and that of the imperfect side, Br+Al, reading in each case from left to right, as is natural.

In the chest region the imperfect side is being gradually rolled out and is thus becoming more nearly the equal of the other. This may be readily shown by ascertaining the degree of inrolling at two levels, for example, (1) at the acromia and (2) at the nipples, and comparing the two. The distance between the acromion processes of the perfect side is 71 mm., and between those of the imperfect 48 mm. In the case of the nipples, which are situated at a lower level, the distance between them on the two sides is 36.5 mm. and 29.5 mm., respectively. If in each case we consider the measurement for the perfect side as 100, that for the imperfect side at the level of the acromia is but 67.6 per cent of it, while at the nipple level the measurement of the imperfect side is 80.8 per cent of that of the perfect one. The sternum of the imperfect side shows this change throughout its length, as it is somewhat narrowed anteriorly and a little rolled in, as if by the close approximation of the shoulders, but posteriorly it is practically like that of the other side.

The alimentary canal well illustrates the principle of the secondary modification of an organ through embryonic functional activity, since for some weeks previous to birth the intestine has been made the receptacle for the meconium and has had more or less to do with the function of nutrition. The common œsophagus leads into a common stomach, though evidently one formed of two components, since it presents two cardiac enlargements, one on either side of the œsophagus. The outline of the stomach is thus heart-shaped, but is not quite symmetrical, since the cardiac lobe of component A is a little larger than that of B. The stomach leads through a single pylorus into a common intestine, which continues single throughout about three-quarters of its length (80.9 cm.) and then divides into two, which extend to the two colons located in the separate components, the connecting piece of A being 29.3 cm., and that of B 25 cm. in length. Beyond these extend the cæca, appendices, and colons of each individual, that of A being 21.6 cm. in length, and that of B 27 cm. As the intestinal canal is a common one from the united pharynges to the bifurcation at the lower fourth of the small intestine, the decision as to physiological function comes at this latter

point, and, owing undoubtedly to the chance of gravitation or of some temporary mechanical condition, such as a fold of the gut, the first of the fecal matter selected the branch belonging to component B as its functional outlet. B's intestine and colon therefore became filled and distended from this point on, while those of A, although perfectly normal, remained empty. In one feature there is a secondary deformation, and

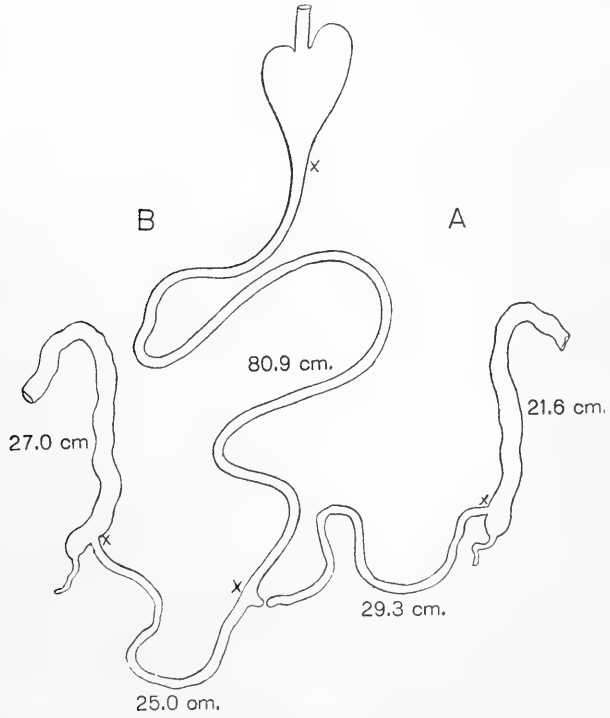


Fig. 4. Alimentary canal of the Baldwin Synote, Teras III. The measurements given were taken between the points designated with an X.

that is, the entire intestine of A, beyond the bifurcation, has pinched itself off from the rest, leaving a short stub at the place where the intestines have become individual. It seems probable that this cutting off occurred subsequent to the adoption of B's canal for functional activity, although there was probably some direct connection between the two events. Perhaps the pinching off occurred as the result of inactivity, or perhaps, which is more likely, it was the final result of a restriction

or some other slight cause responsible for the original decision. It would be of much interest to examine the intestines of other Jani and see whether one side is preferred for the meconium, whether, if this be the case, the unused side becomes separated from the other, and whether the same side is always preferred. This latter point could of course be determinable only in cases with some lateral torsion, and in view of the varying relation of the aortic arches in different specimens, as described below, it is most unlikely. The cutting off of A's intestine, in view of its perfect development otherwise, appears to have been a late event, due to some mechanical cause, and in no way the result of a primary inequality in the two components.

It has been claimed for certain cases of duplicate twins that, in some particulars at least, they are the symmetrical equivalents of each other, but in this case, at all events, the two components are not thus related, but each is perfectly normal in this respect. Thus the appendix of A lies superficially upon the perfect side, and that of B upon the imperfect, the right side of each component, and the same thing is shown by the spleens, which lie diagonally with reference to the double stomach, but each upon the left side of the component to which it plainly belongs, and therefore normal in its relations. The double liver is an enormous organ, and upon each aspect covers the entire width of the visceral cavity. The face of this mass seen upon the perfect side consists of the right lobe of A, with the gall bladder of that component, and the left lobe of B, without a bladder; the opposite face, that of the imperfect side, which at this level is nearly as wide as the other, is composed of the right lobe of B, with its gall bladder, and the left lobe of A, without one. In these organs, then, except for the continuity of the liver masses belonging to the separate components, the relations are the normal ones which would be found in two separate individuals that stand facing each other, and show no trace of looking-glass symmetry. At this level, also, the other organs are mainly individual, and not shared by the two components.

As a detailed study of all the parts of this specimen is not possible here, we may select two, the details of which seem to present especially good material for discussion: (1) the middle ear of the synotic side, with its included ossicles, and (2) the heart and the larger blood-vessels. The first of these is a part that has not yet become functional, and would thus naturally be expected to show the primary and unmodified symmetry characteristic of a typical Cosmobion; the second is one that shows the

modifications due to functional activity from almost the beginning of development, and thus exhibits the solution of what may be considered a new physiological problem, a study in Experimental Zoölogy made by Nature herself.

C. *The Compound Middle ear of the Synotic side.* This region may be taken as an especially good example of one which, in part through lack of function during embryonic life, has retained its primary symmetry. The parts are at the same time sufficient in number and complexity to express this symmetry in a high degree, and the complete correspondence, even of the smallest details, is highly suggestive in the present argument.

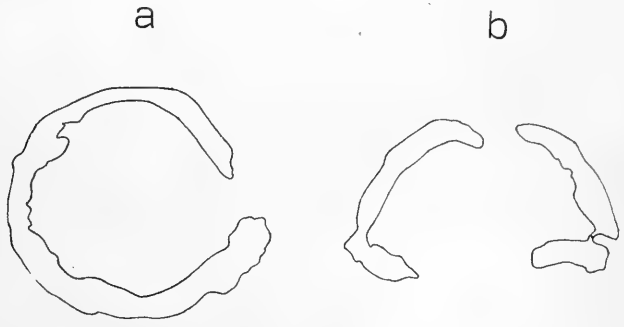


Fig. 5. Baldwin *Synote*, Teras III.
(a) Normal os tympanicum of the right ear of component A.
(b) The two reduced ossa tympanica surrounding the synotic ossicles. These consist of the right one of B and the left one of A.
All are drawn to the same scale.

Within the single external meatus lay the middle ear chamber, its entrance framed in by a pair of tympanic bones, symmetrical in respect to each other but each somewhat smaller than the normal ones of the perfect side [Fig. 5]. Normally each forms a nearly complete circle, the frame for the outer tympanic membrane, but on the synotic side the two together framed in an oval space, its greatest diameter lying transversely; of this each tympanic bone formed a little less than half the circumference. Undoubtedly there was also here a tympanic membrane, but as the parts had been subjected to maceration in caustic potash before examination this point cannot be determined.

Lying within the oval tympanic frame there appeared the auditory ossicles, a doubled malleus upon a doubled incus, and two distinct stapedes

diverging right and left from the longer crura of the two latter. [Fig. 6.] The details of the separate ossicles are best learned from Figs. 7-9, which represent the synotic ossicles, in most cases accompanied by a

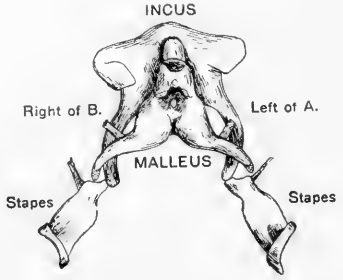


FIG. 6. BALDWIN Synote, Teras III. General view of the double ossicles of the synotic side; external aspect. This complex was situated within the oval frame formed by the two tympanic bones of this side, Fig. 5 (b).

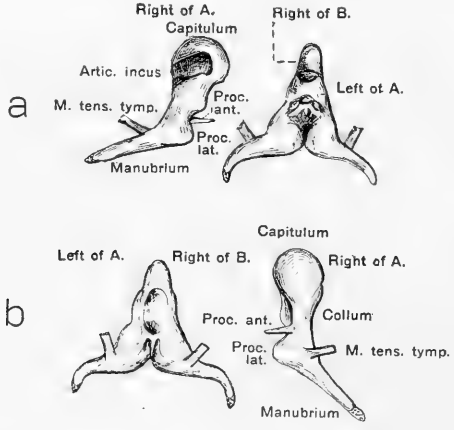


FIG. 7. BALDWIN Synote, Teras III.

(a) Double malleus; external aspect. The normal malleus, taken from the right ear of the perfect face (= A, r) is placed beside it for comparison.

(b) The same ossicles; internal aspect. Upon the double malleus note the slender median processus anterior [Folii], directed downwards and suggesting the former location in the embryo of a double median Meckel's cartilage.

Both bones are drawn to the same scale.

corresponding one from the perfect side, which appears in the case of each bone perfectly normal. In the macerated specimen it was of course impossible to demonstrate the associated soft structures, but by the

existence of tendons, processes, and other features, each occurring so far as possible in the normal position, and showing always a complete bilateral symmetry, we may feel sure that the soft parts were as regular and symmetrical as are the osseous features.

In the synotic malleus [Fig. 7] there is present upon either side the tendon of M. tensor tympani, also a median processus anterior [Folii]. This latter is well developed and suggests the presence in the earlier embryo of a median rudiment of Meckel's cartilage, the equivalent of both halves of the mandible. The double capitulum is small and narrow in proportion to that of the normal one of a single side, but it is per-

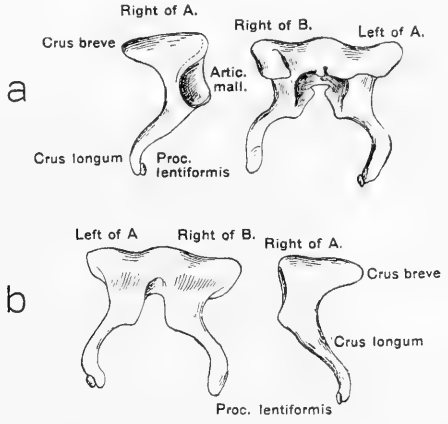


Fig. 8. Baldwin Synote, Teras III.

(a) Double incus; external aspect. The normal incus, taken from the right ear of the perfect face (= A, r.), is placed beside it for comparison.

(b) The same ossicles; internal aspect.

Both bones are drawn to the same scale.

fectly symmetrical and obviously similar to more familiar reduced median parts that occur in Cyclops and Siren monsters. The conspicuous foramen in the median line appears to correspond to nothing in the normal malleus, but is suggestive of the double nature of the piece, and reminds one of the old explanation of a "fusion" of two originally separate components, a theory which has in its favor only such appearances and which is entirely inadequate to explain the phenomena.

Like the malleus, the double incus [Fig. 8] exhibits upon either side the features characteristic of the normal bone, save that the processus lentiformis appears to be present upon one side only. This part is, how-

ever, extremely small and easily detachable, and it may easily have been lost in the preparation.

The two stapedes [Fig. 9] differ from the normal in one noticeable feature, and that is the lack of the characteristic foramen. As its presence is due to the formation of a stapedial artery, which is transient and embryonic in Man, but persistent in certain other mammals, its lack here suggests the failure of this artery in the earlier embryo, just the sort of disturbance in the course of the developing carotid that might be expected.

Perhaps nowhere in my study of Cosmobia have I found the problem expressed so simply as here; reduced to its lowest terms, as it were. Instead of a complicated organism, with, perhaps, some degree of secondary deformation, we have here, taking either one of the compound auditory ossicles, a simple bone, median in position, perfectly bilateral, fur-

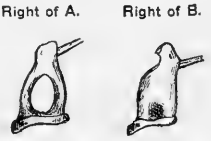


Fig. 9. Baldwin Synote, Teras III.
(a) Normal stapes from the "perfect" side.
(b) Stapes from the synotic complex; lacking the perforation.
Both bones are drawn to the same scale.

nished with accessory structures, and without a trace of pathological tissue. If we can explain this, we shall probably hold the key to the solution of all other abnormal Cosmobia, both less and more than a normal being; perhaps, also, that of the latter as well. Modern biology, in attacking the problem of development, has wisely directed its attention mainly upon the germ cells, and the first cell generations that proceed from them. To the earlier investigations in this field, which, observational in their nature and conducted under the microscope, were applied directly to the germ cells, has been recently added a line of investigation by means of experiment upon early embryos, with careful observations of the results. In Cosmobia we have such results, and we have reason to believe that the initial causes, which are at the present time unknown, lie in the early germ, perhaps even in the unfertilized ovum. It is even permissible to suggest that the cause may lie in a doubling or a deficiency of the primi-

tive granules, by whatever name they may be known, and if so it would seem impossible to produce true Cosmobia as the result of experiment, except by the application of means that would modify the developing germ. On the other hand, if this can be done. the cause would not seem to be so fundamental. In the former case the only way in which the matter can be investigated is by studying the results as they are produced by nature, and it may thus be that these unusual beings, which are at the same time orderly and definite in development and structure, may prove a most important factor in the solution of the great biological problems.[9]

D. *The hearts and the main blood-vessels.* As characteristic of this entire series there are two hearts, each composed of a half from each component, and placed so that they correspond to the two apparent faces and not to the two components. With each of these hearts is associated a pair of lungs, which bear apparently normal relations to the two apparently normal hearts, but which are also made up of a lung from each individual. There thus lies back of each double sternum a set of thoracic viscera which, except for some slight and evidently secondary deformation, look like those of a single individual, yet, by their relationship to the two bodies lower down, are seen to be composites, each part the property of two individuals.

To analyze this in greater detail, the thoracic viscera facing the perfect side consist of a heart, made up of A's right and B's left half, to which are attached A's right and B's left lung. The trachea and larynx, which are in their usual place with reference to this composite set of organs considered as a unit, are single in appearance but formed of halves contributed by each of the two component bodies. In the same way, upon the imperfect side, there lies a set of viscera that consists of A's left and B's right lung, the two associated with a heart composed of A's left and B's right half. Between these two sets of viscera, each of which is, as it were, backed up against it, lies the œsophagus, a single tube common to both individuals. The vertebral columns with the spinal cords, as will be remembered, are never compound in this type of Cos-

[9]It is hardly necessary to state that the above was written before the results of the recent experiments of Stockard became known. Since, however, the entire paragraph was intended to awaken speculation, and not to assert a dogmatic position, I have thought it best to allow it to stand as originally written. The discussion of Stockard's work is given below, mainly under the review of the recent literature.

mobion, but belong to the separate individuals and lie upon the sides of the two sets of thoracic viscera, their ventral aspects facing the median œsophagus. An aorta and a posterior vena cava, each individual, run down the ventral aspect of each.

The two sets of thoracic viscera are separated from one another by a partition of pleura, forming two thoracic cavities, the larger one associated with the perfect, the smaller with the synotic side. The partition is, however, placed obliquely with reference to the compound thorax, so that the large chamber occupies not only the space immediately behind the sternum of the perfect side, but also that framed in by the vertebral column and ribs of component B; the smaller thoracic cavity is similarly related to the synotic side and component A. The results of the dis-

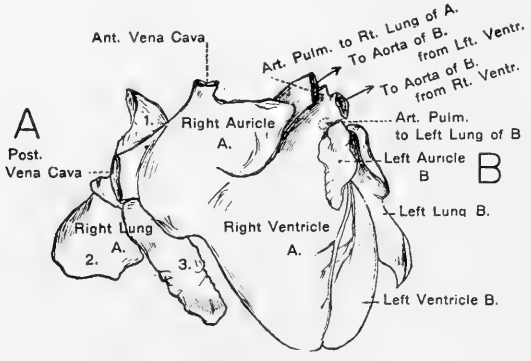


Fig. 10. Baldwin Synote, Teras III. Heart of perfect side, with lungs attached.

sections of these chambers and their organs may be treated separately, bearing in mind the composition of each set of viscera.

The heart and lungs of the larger chamber, that of the perfect side, are exposed by laying back the sternum and costal cartilages of this side [Fig. 10]. They appear nearly normal, so much so in fact that it seems probable that the slight deformation they display has been due to development in too cramped surroundings, and that they must have been entirely normal at an earlier stage of development. The heart is large, with well defined auricles and ventricles in normal relation. Upon the sides of this organ, and partly adherent to it, lie the lungs, rather incomplete in their development, but normal in respect to the number of lobes, the right (A's) with three, the left (B's) with two. The large

blood-vessels are somewhat abnormal in their relations, and may be made out by the comparison of Figs. 10-12. Each ventricle possesses an aortic arch, both of which pass to the ventral aspect of the vertebral column of component B, where they meet an arch from the right ventricle

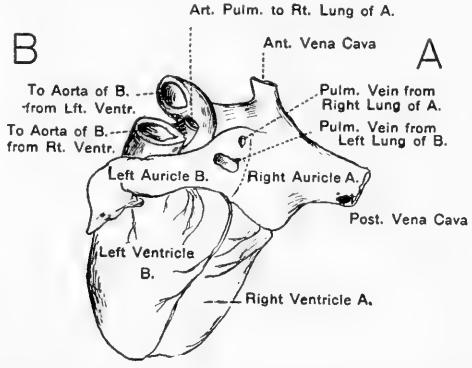


FIG. 11. BALDWIN Synote, Teras III. Heart of perfect side; inner aspect. The dotted line across the auricular region marks the position of the incomplete partition separating the two auricles. The lungs and trachea have been removed.

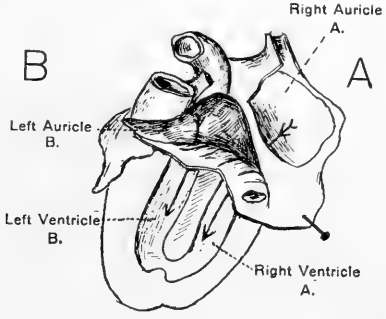


FIG. 12. BALDWIN Synote, Teras III. Heart of perfect side; inner aspect, cut open to show the interior chambers. The auriculo-ventricular openings are marked by arrows.

of the heart of the synotic side and together form B's dorsal aorta. Since, in Cosmobia belonging to this series, the dorsal aorta of each component is usually made up of the union of two arches, one from each of the ventricles that belonged originally to the side in question, the only departure from the type lies in the fact that the arch that arises

from the right ventricle of the heart on the perfect side (A's) crosses over to the aorta of B and does not turn the other way and join the dorsal aorta that belongs to A's vertebral column. The fact that the arch from the right ventricle of the synotic heart comes over to B's aorta is the usual thing in such Cosmobia, since this heart moiety belongs originally to the B component. An innominate trunk arises from the arch that comes from the left ventricle and branches to form the carotids for the perfect aspect. Thus both a B half and an A half are supplied from an aortic arch that belongs to B.

There are separate pulmonary arteries for the two lungs, and they both arise from the pulmonary arch that comes from the right ventricle, *i. e.,* A's. The artery to the right lung (A's) is large and easily seen,

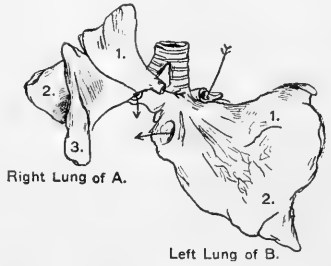


FIG. 13. BALDWIN Synote, Teras III. **Lungs of perfect side, the right of A and the left of B; outer aspect, with heart removed. The arrows denote the points of entrance of the arteries and of exit of the veins. The numbers designate the lobes; those of the left lung are not well separated. Compare** with Figs. 10 and 11.

but that to the left (B's) enters the lung at a point where this latter organ is adherent to the side of the arch. This is indicated in Fig. 10 by a dotted ring; and the point where it enters the lung is shown in Fig. 13. The pulmonary veins likewise, owing to the close adhesion of the lungs to the heart, can be seen only by cutting the two organs apart, when they appear as openings [Fig. 13]. There seems to be but one such vessel for each lung, and they enter the left atrium on the anatomical dorsal aspect. The two venæ cavæ are normally related to the right atrium.

The heart and lungs of the smaller chamber, that of the synotic side, are more reduced than are those of the perfect side, and are crowded into a considerably smaller space, lying rather more in the territory belonging to the A component. [Figs. 14-17.] The lungs are quite closely

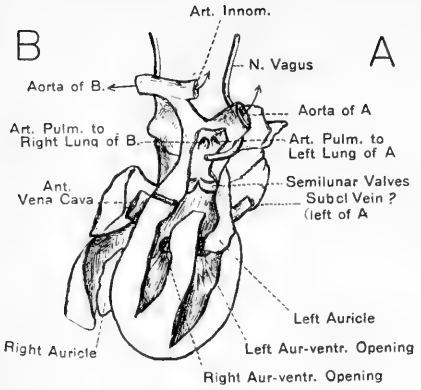


Fig. 14

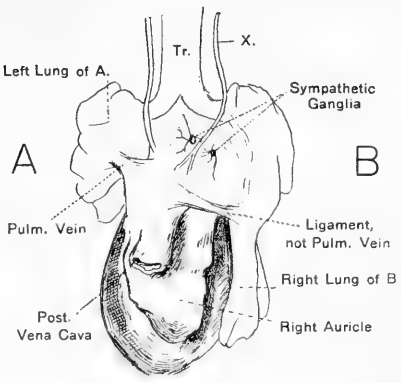


Fig. 15

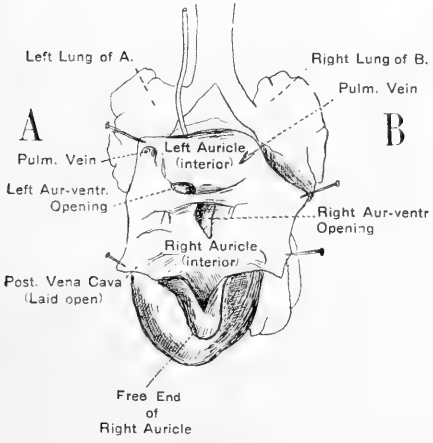


Fig. 16

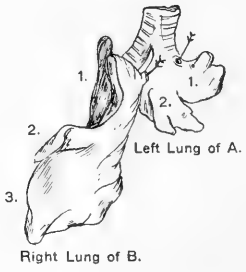


Fig. 17

FIG. 14. BALDWIN Synote, Teras III. Heart of imperfect side; outer aspect, sectioned longitudinally to show the interior of the chambers. Component A is on the right of the figure, B on the left. The small lung on the side of A, confined to the region of the auricles and the larger vessels, is the left lung of A; the one on the opposite side, represented by three lobes, is the right lung of B. Compare with Fig. 17.

FIG. 15. BALDWIN Synote, Teras III. Heart of imperfect side; inner aspect.

Tr., trachea; X, pneumogastric nerve.

FIG. 16. BALDWIN Synote, Teras III. Heart of imperfect side; inner aspect, with the auricular region laid open.

FIG. 17. BALDWIN Synote, Teras III. Lungs of imperfect side, the left of A and the right of B; outer aspect, with heart removed. The two arrows denote the entrance of the pulmonary arteries. The numbers designate the lobes. Compare with Fig. 14.

adherent to the heart, and the left one is especially reduced, yet both possess the normal number of lobes [Fig. 17]. From each ventricle an aortic arch proceeds to the dorsal aorta of the component to which the ventricle belongs, that from the right ventricle passing to the aorta of B, and that from the left to the aorta of A. The first of these has been described before in connection with the heart of the other side. From the arch that arises from the right ventricle (B's), anatomically a pulmonary arch, there arises an innominate artery that divides into the carotids of the synotic side, and as this supplies an A moiety it balances the condition upon the other side where a carotid from the A component supplies a moiety belonging to B. The two aortic arches in question, although each is plainly given off from the ventricle indicated, yet possess a common trunk along the region of the semilunar valves, and it is from this that the two pulmonary arteries are given off. The pulmonary veins are represented, much as in the other heart, by two openings into the left atrium, as seen in Fig. 16, in which this chamber is represented as cut open. The two venæ cavæ open into the right atrium as normally.

A general idea of the relations of both hearts and the main blood-vessels may be learned from an inspection of the accompanying diagram [Fig. 18]. In this the view is taken a little obliquely, with the hearts at slightly different levels, in order to show the parts better. This brings the vessels on the two sides of the common neck at an unnatural distance from each other, and necessitates a lengthening of the aortic arch that runs between the lesser heart and the aorta of component B. Otherwise the proportions are not far from actuality.

The data shown in this diagram may be put into synoptical form as follows:

1. *Four aortic arches, one from each ventricle.* Of these the most abnormal is that from the right ventricle of A. Had that arch gone in the opposite direction and entered A's main aortic trunk we would have a symmetrical condition, probably the typical one for such monsters, in which each aorta would be formed by the union of arches from the two ventricles originally belonging to its respective component. Of these arches those from the right ventricles are naturally the pulmonary arches and give rise to the pulmonary arteries. Their connection with the other arch is of course through the ductus Botalli.

2. *Four pulmonary arteries, two from each heart.* In the greater heart these proceed from the aberrant aortic arch, contributed by the right

ventricle of component A. This is the proper pulmonary arch of this component, but the pulmonary arteries are distributed to the two lungs of the perfect side and thus the right ventricle of A supplies its own right lung and B's left one.

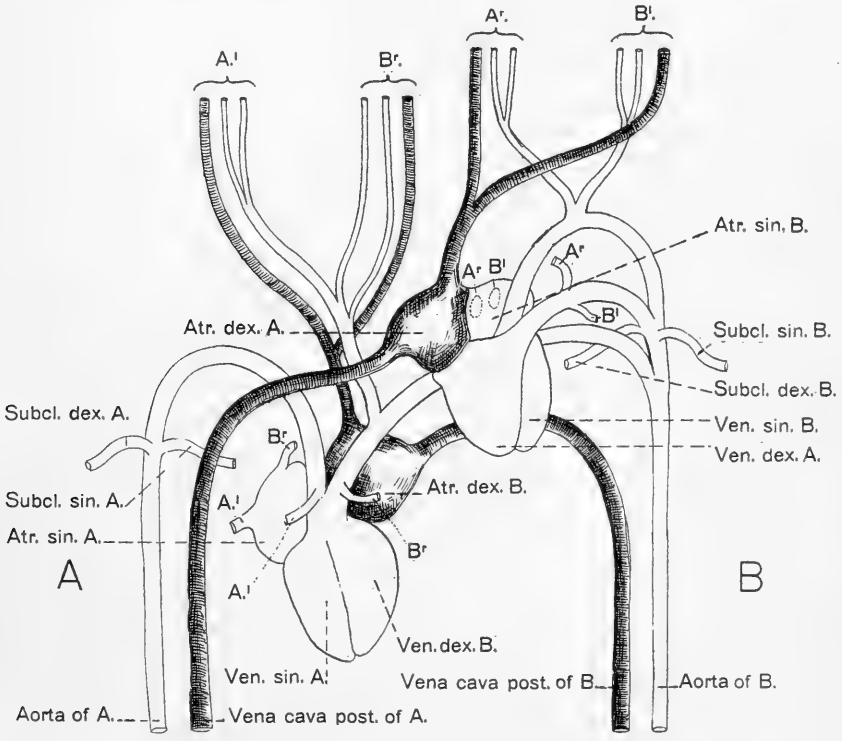


FIG. 18. Diagram of the main organs of circulation in the BALDWIN Synote, as shown by dissection. The right auricles and the systemic veins are shaded, the other parts are outlined. The view is taken a little obliquely, and with the hearts at slightly different levels, in order to show the parts better. This brings the vessels of the common neck, which are in reality closely associated, at an unnatural distance from one another. It also produces an abnormal lengthening of the aortic arch which extends from the lesser heart to the aorta of B. Otherwise the proportions are not far from the natural ones.

In the lesser heart the pulmonary arteries proceed from a trunk common to both arches, but may be considered as coming from that part that belongs to the right ventricle, which belongs to component B. This would make them normal in origin. They are distributed in a manner

exactly comparable to those of the perfect side, that is, to the right lung of B and the left one of A.

3. *Four pulmonary veins, two for each heart.* These communicate with the left atrium of each heart and enter at points where the lungs are adherent to the atrial wall. The vessels thus have no length except that which is within the lungs, and appear merely as foramina in the walls of the atria. Their relations are thus normal with reference to the lungs, but it is to be noticed that the left lung in each case belongs to the other component from that to which the atrium belongs.

4. *Two carotid trunks, one from each heart.* The trunk of the perfect side is given off from the arch that arises from the left ventricle, and thus primarily belongs to component B; that of the synotic side arises from the arch that apparently arises from the right ventricle, and thus belongs to B also. Upon the perfect side the carotid trunk divides into two laterally placed common carotids, one for the right side of A, the other for the left side of B; these soon divide again into external and internal carotids, as normally. Upon the synotic side there is a common carotid for the left side of A, but upon B's right side the external and internal carotids are separated down to the main trunk.

5. *The subclavian arteries.* These proceed from the aortæ posterior to the separation of the carotids, and at a point where the two components have become nearly distinct. A pair is given off from each aorta and these supply the two arms of the component to which the aorta belongs.

6. *The anterior and posterior venæ cavæ.* Each right atrium receives an anterior and posterior vena cava, as in the case of a normal individual, but while the posterior cava comes from a single body and empties into the atrium belonging to it, the anterior cavæ are related to aspects instead of components and the two sides from which each comes are those of two components. This relationship is like that of the carotids, except in the matter of final connection with the heart.

E. *Comparison of the circulation here with that of other reported cases of the same general type.* The best proof of the statement that an abnormal Cosmobion represents a distinct physiological problem to be solved anew in each case comes from the comparison of functional parts in several different specimens of the same general type. Fortunately for the investigator Janus monsters are not rare in the human species and, although not able to survive the period of birth, they live and develop up to this epoch without suffering any special deformation save, perhaps, a limited growth of such parts as the lungs, which are cramped

by lack of space for a full development. These specimens are therefore obtainable of a size large enough for convenient dissection and thus the circulatory system has been well described in a number of cases. The conditions of the heart and the larger blood-vessels in six cases, including the present one, are for convenient comparison reduced to diagrams of similar construction [Fig. 19]. These have been taken from the original description in each case. In some cases the description was verbal only, in others the text was accompanied by one or more figures; usually, however, those latter were drawn as if viewed from the side, thus requiring translation into the diagrammatic form here adopted. MAYOR, however, makes use of a sectional diagram similar to mine, but includes rather more parts than are here necessary. In all cases excepting one (VI), pulmonary as well as aortic arches are employed in forming the aortæ, *which, if all developed, would form in such a diagram a perfectly symmetrical figure with arches in the form of a rhomboid.* The actual cases show, however, that one out of the four always fails to form a complete connecting arch, and persists only at its cardiac end, as a variously used adjunct to the rest, while the remaining portion, which would naturally span the interval between a heart and an aorta, disappears. Since in the diagram each monster is shown with the imperfect and perfect sides and the A and B components in the same relative positions, an exact comparison of the cases is easily made; and in this way it may be seen that the missing arch may be any one of the four. Thus in the first four of the diagrams, taken from as many different authors, each of the four possibilities is shown; No. V is much like No. III; No. VI shows a quite different result from any of the others.

The relations of pulmonary arteries, and of the carotid and subclavian trunks, show also some variation, depending on the identity of the persisting arches. For instance, the pulmonary arteries seem always to arise, as is natural, from a right ventricle through the pulmonary arch, and in cases where this vessel fails as a complete arch (as on the perfect side of Nos. I and IV, or on the imperfect side of Nos. II and V) a stump still persists which gives rise to the vessels, after which it usually anastomoses with the arch that persists. No pulmonary system is given in No. VI, since the paper is silent concerning these vessels. In the case of the carotids the most typical arrangement is undoubtedly that shown in No. I, where a pair comes from each aortic arch; yet, while the arch itself passes over into the dorsal aorta of a single component, the two carotids that proceed from it supply the two sides of a neck that faces either

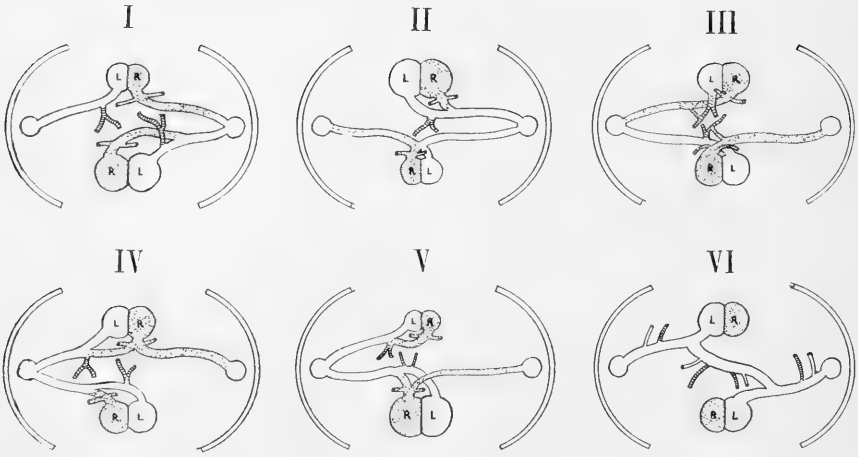


Fig. 19. Comparison of the main blood-vessels in six cases belonging to the Janus-Omphalopagus series (Monomphaliens). In all of these the more reduced aspect (often called "posterior") is above, the more perfect below. When placed in this position, as elsewhere in the paper, the component on the left is designated as A, the one on the right as B. The upper heart in each of these cases is thus Al + Br, the lower, Ar + Bl. The right ventricles and the arches proceeding from them, primarily the pulmonary, and the separate pulmonary arteries to single lungs, are dotted, the carotids are striped. Left ventricles and the arches proceeding from them are simply outlined. The small outlined trunks in VI are the subclavians, which in the other cases proceed from the aortæ of their respective components.

The cases in detail are as follows:

I. Baldwin Synote; Teras III of the present paper.

II. Calori, 1883. A synotic pig. In this, although there was no face on the imperfect side, the corresponding heart was larger than the other, and from its aortic arch arose the only carotids, supplying the face of the perfect side. No carotids arose from either arch of the heart of the perfect side.

III. Mayor, 1881. A nearly symmetrical human Janus. Note the connection between the carotid trunk and the pulmonary arch of the perfect side.

IV. Debierre and Dutilleul, 1890. A human synote.

V. Calori, 1883. A human iniops.

VI. Williamson, 1895. A human prosopothoracopagus (= gnathopagus of the present paper).

Of these six diagrams I-IV represent the four possibilities presented by the failure in turn of each of the four arches of the typical rhomboid, although the four sides of the rhomboid are not always constant in the identity of the arches forming them. No. V is like No. II reversed. No. VI is the most aberrant, and comes from that monster in which the components are the most separate, *i. e.*, the most aberrant monster.

the perfect or the imperfect side, and thus belong to both components. In No. III, where there is no aortic arch on the imperfect side, the two carotids of that side arise directly from the left ventricle, but an anastomosis between the left carotid and the pulmonary arch is perhaps a ductus Botalli, and suggests that morphologically this apparent left carotid includes as well a rudimentary aortic arch.

This comparison of the circulatory system of several monsters of the same type is suggestive of a series of secondary modifications of a primary symmetrical plan exhibited by each at an earlier period. What this original plan may have been in the case of his own specimen is figured by MAYOR, side by side with his instructive diagram of the existing relations (the equivalent of my No. III.) In this diagram MAYOR suggests, as I have done, an earlier persistence of both the pulmonary and aortic arches of each compound heart, forming a circle, broken at two opposite points by the hearts of the perfect and imperfect sides, and at points 90° from this by the two aortæ, each of which is thus formed by the union of the pulmonary and aortic arches of the two adjacent half-hearts; *i. e.,* the two arches belong primarily to that individual whose aorta they form. This ideal arrangement is, however, not borne out by MAYOR's own specimen (No. III), even with the replacement of the aortic arch of the imperfect side, since here (and in the majority of the cases) the arches cross over each other and supply, not the component to which their ventricle of origin belongs, but the opposite side. Serious discussion, however, concerning the exact form of the primary relation of these parts is, in the absence of definite data, hardly worth while; we may well wait until the lucky find of an early embryo of this type of monster gives us exact knowledge on this point. The important point to assert is that evidently there is primary symmetry in the organs of circulation as well as in other less active parts, that in the early embryonic stages they exhibit this primary symmetry, and that during later development they become modified in accordance with their physiological needs.

PART II. DOUBLE EYES.

General Principle. By a "double eye" is here meant a bilaterally symmetrical eyeball formed of two components. Such double eyes occur among Cosmobia in three different ways, as follows:—

Type 1. In a *Cyclops;* in this form the two eye components are the right and left ones of a single individual.

Type 2. In an *Iniops* or *Synote, i. e.,* on the imperfect side of a Janus monster; in this form the two eye components are those of different individuals, the right of one and the left of the other.

Type 3. In an incomplete *Diprosopus,* in which the two head components are distinct about as far as the eye region, bringing the two inner eyes of the two components into close contact, or so as to form a compound organ.

As for the relative position of the two eyes in the different types, the components involved are always a right and a left. In types 1 and 2 they are normally related to each other, that is, the right and left components are placed on their respective sides, but in type 3, they are reversed so that the anatomically right eye is placed on the left and vice versa. This follows in each case from the relation of the components to each other, and may be easily proven by a study of the structure, the best guides to the original position of the eye components being the Trochlearis and Abducens nerves, through which a component, although much reduced, may be definitely oriented.

The relation of the eye components in Type 1 is the normal one for the two eyes of a single individual. The median eyeball is strictly bilateral and its lateral aspects are like those of separate eyeballs furnished with normal external recti. In cases in which the two components are very deficient, the internal recti may be entirely wanting, although the typical parts generally manage to appear by means of certain displacements and accommodations.

Type 2 is the most anomalous of the three, but may be easily understood by a glance at the diagram that shows different degrees of torsion in monsters of the Janus type, especially stages III and IV. [Fig. 3, p. 374.] Here again the relation is normal so far as the eyes themselves are concerned, but the two components belong, not to a single individual, but to two, the left eye of component A being fused with the right one of component B. In spite, however, of this radical difference between Cases 1 and 2, the results are extremely similar, and so far as I have had opportunity to judge, the stages in the reduction of one parallel the cases in the other, so that from the study of the eye alone, without tracing out the cranial nerves to their origin it would be difficult or even impossible to say from which type a given double eyeball had been taken.

Type 3 is, in the position of the components, the exact opposite of the first two, for here the sides of the two eyeball components that are in contact with each other are the anatomically outer ones. As in Type 2

there are involved two head components from which the eye components have been derived. In cases in which the two eyeballs are distinct and possess a short interval between them (and these cases also should be included in the study of double eyes), the two external recti, or a single bilateral muscle to represent them both, may be expected in the interval between them, while the internal recti will be found upon the apparent outer sides, thus corroborating the fact of the reversed position of such components.

Furthermore it will be noticed that Types 1 and 3, placed in series, with the condition found in normal individuals interposed between them, correspond exactly with the series shown in Fig. 1, as may be seen by a comparison of this diagram with the accompanying Fig.20, although no attempt has been made to make the individual stages correspond. This last diagram represents the eyes of the former series, and shows them as if the heads were cut in cross-section at the level of the eyes, and the investigator were looking down upon the cut surface. Of the stages represented, Nos. I-VI are cyclopean, VII and VIII show the different degrees of eye separation in a normal individual, and the remaining stages, IX to XIV, form the series leading to dicephaly. These latter thus represent the cases designated here as Type 3, and the cyclopean stages, I and VI, Type 1.

The study of these three types of double eyes, aside from their differences in the relationship of the eyeball elements and in the number of component individuals involved, possesses another distinct advantage in the present connection, that of being a passive system, without function during embryonic life, and hence not subject to the secondary malformations due to functional activity under abnormal conditions, as in the case of the circulatory system. Allowing for possible mechanical hindrances, due mainly to insufficient room for complete development, and which become more manifest as development proceeds, these parts ought to show with especial clearness the characteristics of typical cosmobia, perfect bilateral symmetry and normal tissues. Owing to this importance in point of theory I have thought best to publish all the cases that have come to my hand. These represent all three of the types and are as follows:—

Of the first type I have two specimens, Terata VI and VII, the one a Cyclops child at term, the other an advanced pig fetus. Type 2 is represented by the double eye of the imperfect side of the Baldwin Synote, situated just above the double ear described above, and for Type

3, I am fortunate to have two partly diprosopic pigs, the one being the remarkable LAMBERT embryo, Teras I, the other a new-born pig, Teras XII, that represents a stage with less separation than the other.

Type 1. Cyclops eyes.

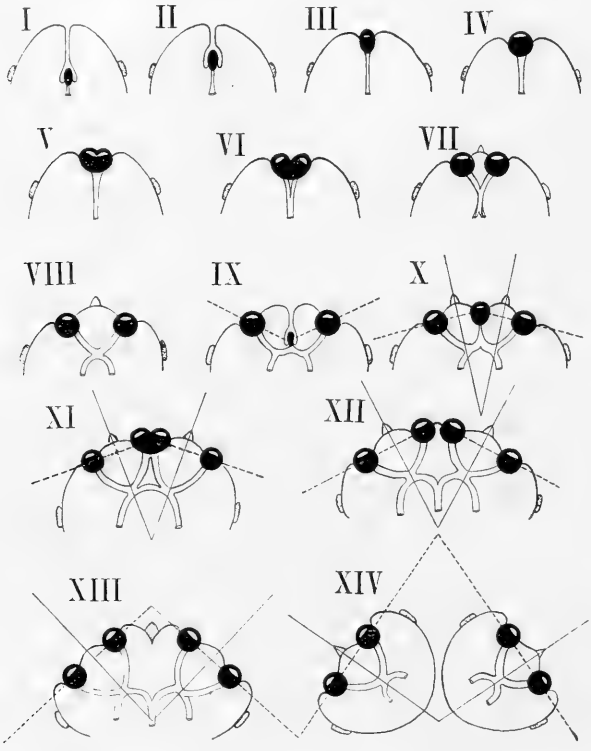


FIG. 20. Diagram of the cosmobiotic series leading from extreme Cyclopia, through the normal, to complete Dicephaly. This diagram represents the same series as that given in Fig. 1, although the separate stages are not always the same. In this diagram, as in Fig. 3, the separate figures represent cross-section taken through the heads at the level of the eyes and viewed from above. Stage VIII represents a normal being; those before it are cyclopic, those following it dicephalic.

Case 1 (Teras VII). The eye of this monster, a cyclops pig fetus, is considered first because it is more double than that of the other case studied, and the parts are consequently easier to identify. The specimen is No. 2913 of the Wistar Institute Collection, and the head is

shown in profile in Fig. 21. If in a human cyclops one should be disposed to doubt that the characteristic supra-orbital process is really a nose, the fact is corroborated by this specimen, for here this process has taken on the unmistakable character of a pig's snout. This snout is covered dorsally and proximally by a single median nasal bone, accompanied at its outer proximal angles by a pair of small lacrimals. The palpebral opening, placed immediately beneath this snout, is prolonged laterally into angles, the outer canthi, and discloses an oval eyeball.

The dissection of this eyeball and its associated parts was accomplished in the usual way by first removing the skull-cap, then the brain, and lastly the bony roof of the single orbit. The accompanying sketches

Fig. 21. Cyclops pig; Teras VII.

will illustrate the most important of the relationships found. The large round nasal fossa of normal pigs is here much reduced, yet still transmits a pair of branches from the Trigeminus, the anterior nasal nerves. Behind this is a single median optic foramen, and behind this again a pair of supra-orbital fissures [sphenoidal]. The single pair of foramina behind these latter, which represent a confluence of the foramina rotundum and ovale, is the normal condition in the pig, and in general from this point posteriorly there is nothing unusual about the specimen. The superficial portion of the orbito-sphenoid, which separates the optic foramen from the supra-orbital fissure, also serves as a point of origin for certain muscles of the eyeball, which may be seen in part through the large optic foramen. After the removal of this Y-shaped piece the three openings involved become confluent and appear as a single opening in the form of an inverted heart, framed in by the præ- and orbito-sphenoids, and by the orbital plates of the frontal. A

small but conspicuous spine, of unknown value, is seen extending along the middle line forwards from the præ-sphenoid. This furnishes origin for the remaining muscles of the eyeball.

Of the relations of the cranial nerves it may be said that the Optic nerve was single and median, and entered the single eyeball in the middle; the Third arose as a pair in the normal way, but the two united after

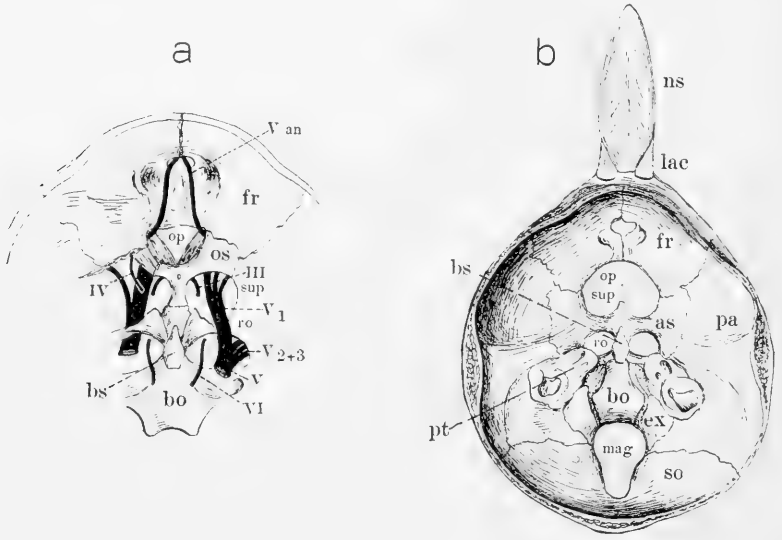


Fig. 22. Two views of the cranial floor of the monster shown in Fig. 21. In (a) the bones are shown entire, except on the left side, where a portion of the orbito-sphenoid has been removed; in (b) the entire orbito-sphenoid has been taken away, thus rendering the optic and supra-orbital foramina confluent.

ns, nasal; *lac*, lacrimal; *fr*, frontal; *pa*, parietal; *os*, orbito-sphenoid; *as*, ali-sphenoid; *bs*, basi-sphenoid; *bo*, basi-occipital; *ex*, ex-occipital; *so*, supra-occipital; *pt*, petrosal; *op*, optic foramen; *sup*, supra-orbital foramen; *ro*, foramina rotundum et ovale, always confluent in the pig; *mag*, foramen magnum. The Roman numerals designate the cranial nerves.

passing through the superior orbital fissure into the orbit; and that from the Fourth nerve on the two lateral elements of each pair remained distinct. It may be of some significance in this connection that the anterior nasal nerves, previously noted, although they ramify a part in which the reduction is marked and situated anterior to the compound Second and Third nerves, yet remain distinct, as do the other parts of the Fifth nerve, to which they belong.

The relations of the eyeball and its associated parts, as revealed by the further removal of the bony roof of the orbit, are shown in Plate II, Figs. 1 and 2. The muscles that arise from the Y-shaped portion of the orbito-sphenoid, as well as the most superficial of these attached to the spine, are shown with cut ends; the remainder are shown in their origin in Fig. 1, and with cut ends in Fig. 2. In the dorsal view there may be first made out the superior oblique, detached from its origin, and the external rectus, arising as the deepest of the three that are attached to the median spine. These two muscles are positively identified from their innervation, and are of great assistance in locating and determining the rest. The remaining detached muscles, of which one is heavy and muscular, the other thin and tendinous, undoubtedly represent the elements of the levator palpebræ. They do not, however, insert directly into the eyeball rudiment, but into a firm membrane (conjunctiva?) that covers the front of the eyeball, a condition that appears to be more or less usual in such monsters. The two other muscles seen from this aspect take their origin from the median spine, and evidently represent, beginning with the more superficial, the rectus superior and the rectractor bulbi. The first of these is in nearly its normal relationship to both the superior oblique and the external rectus, and the latter, forming with its fellow a broad sheet that covers the eyeball and forms a partial sheath about the median optic nerve, indicates its identity by these characters.

Upon the ventral aspect, aside from the muscles already identified, there occur two more, fitted into a triangular space that is formed by the two external recti. These are more or less clearly differentiated into two bundles, a more distal one, the fibers of which arise mainly from without, and a more proximal one that extends from one side of the eyeball to the other. These are probably the inferior oblique and the inferior rectus respectively, the elements of the two sides being united into single median elements. The first of these has preserved an origin for each lateral component, and an insertion for a part of it, while the other shows the insertions of the two components, but no origins.

Adopting the above scheme for the identification of the eyeball muscles, there is but one left unaccounted for, the internal rectus, and this is the very one that would naturally fail to develop owing to the complete suppression of the region to which it belongs. It is also to be noted that the positions and the points of insertion of certain of the muscles, especially such as the external rectus and the superior oblique, which

mark off the quadrants of the eyeball, are not quite normal, but as these are the very muscles which are positively identified by their innervation there can be no mistake, and it is rather to be assumed that the eyeball components have suffered some slight dislocation, as, for example, a rotation outward over 30-40°.

The examination of the interior of the eyeball shows that it is much less double than one would expect from the arrangement of the muscles. There is a single pupil, a single iris and a single lens, each slightly broader than long. The eyeball itself measures 15 mm. in height and 20 mm. in lateral width. The proportions of the iris and the other associated parts are also similar.

Case 2. (*Teras VI.*) This monster is No. 6956 of the Wistar Institute Collection, and is a typical human Cyclops, identical in general appearance with the specimen photographed by Hirst and Piersol, Vol. III, Plate XXI. In the muscular parts the eye components seem nearer together, and hence more reduced, than in the preceding case, but in the eyeball itself this specimen is decidedly more double. The palpebral opening is evident and oval in shape. At the exact center of the lower margin there is a single median caruncula, with a punctum lacrimale upon either side of it, one for each lower lid component.

Corresponding to the shape of the palpebral opening the eyeball is a flattened piriform organ. The relationships and position of irides and pupils could not be made out, but they seem to have been turned upwards, so that the optical axes would strike above the palpebral opening. Within, the eyeball is incompeletely divided into two compartments by a median partition that reaches from the front wall half way back. Each compartment is furnished with a well-developed lens, but that of the right side is slightly smaller than the other and not quite perfect in shape. Back of the lens each compartment is nearly filled with a large mass of firm connective tissue, of almost the consistency of cartilage, which bears the lens in an anterior cup-shaped depression. This is undoubtedly the vitreous humor, which, owing to the unnatural relationships occasioned by the narrowed space, has formed another type of connective tissue instead of the usual one. In view of the close relationship of the various forms of connective tissue to one another, and the ease with which one form may be transformed into another, this would seem to be a modification easily explained.

There are several well-developed eye muscles, which exhibit a perfect bilaterality, but as I did not wish to mutilate the specimen sufficiently

to study the cranial nerves, the determination of these muscles is largely conjectural. A comparison with the previous case is therefore the only guide we have, but as the components are here much nearer together, the reduction of parts is greater and the comparison is rendered difficult. It seems likely that if an investigator should study a large number of cyclops eyes, representing different degrees of reduction, he would become able to identify the muscles in a given case with some degree of certainty, even without the help of the innervation, but with two cases only, and these far apart in the series, my interpretation can be no more than conjectural.

As a starting point we may take the ventral aspect of the previous case (Plate II, Fig. 2), and try to imagine what would be the result of crowding the two eyeball components still nearer together. The muscle first to suffer by this treatment would naturally be the double inferior oblique, since it has but a precarious footing at best, and has already lost its attachment to the eyeball. The double rectus inferior, however, has two good insertions, and a farther crowding would probably do no more than push these two insertions together and bring the two muscles in contact in the form of a double band. In like manner the two recti externi would become also approximated and form a second median double band, probably lying above the other. This would bring the conditions on the ventral side precisely as they are found in the case in question, and would suggest a rational identification for the two muscular bands thus situated (Plate II, Figs. 4 and 5). The next muscles in order, proceeding outwards, would then be the obliqui superiores and the recti superiores, perhaps the two muscles that are here placed laterally, upon the outer sides of the double eyeball. Lastly comes the most superficial muscle upon the dorsal side, which readily suggests the levator palpebræ. As in the other case, and very likely in all cyclops eyes, the recti interni are entirely wanting, and thus all the muscular elements are accounted for.

This comparison of two different cases of Cyclops eye, in which as many different grades of separation are represented, suggests the value of the comparative study of definite cosmobiotic features, as they present themselves in different cases. This study of Comparative Teratology rests upon principles similar to those of Onto- and Phylogenesis; in all three the varying degrees of development in a part furnish a clue to its identity under the various forms in which it presents itself. A series of stages as presented by different cosmobiotic monsters does not differ in re-

gard to the methods of investigation from a series obtained from the different members of a phylogenetic series, although it must be borne in mind that a deformity in either case must seriously vitiate the conclusions and must never be used so long as an undeformed specimen is available. Of course, as explained in the introduction, deformation is far more frequent in the abnormal than in the normal, and to avoid this it may be necessary in a given case to select embryonic stages, which increases enormously the difficulty in obtaining material, yet any one who has the pleasure of investigating undeformed cosmobiotic monsters will constantly forget that he is dealing with the abnormal, and be as eager for the interpretation derived from comparison as any comparative anatomist when he turns to a new animal species that represents another stage in phylogenetic development.

Although the anatomy of monsters, especially the osteology, has been studied more or less for a long time, and although in some few cases a comparison of internal parts has been done, the recognition of the study of the comparative teratology of cosmobiotic monsters as a legitimate part of biological investigation seems not to have been previously emphasized, and, like other new branches of inquiry, would be greatly benefited by a distinctive name. To emphasize the value of studying these forms in series, that is, the similarity of this line of research to comparative anatomy and embryology, I would like to call it the study of *Teratogenesis,* and speak of the different stages as represented by the different cases as *teratogenetic,* but these terms seem to have been already employed with reference to the causes which may have produced monsters, or even as the science of the artificial production of monsters. The phrase "comparative teratology" cannot be used, since it is ambiguous, and may refer to all sorts of monsters. It is also occasionally used in the sense of the study of monsters among the other animals, as distinct from human monsters.[10] This leaves us no words to express either the study as confined to Cosmobia, the series formed by related Cosmobia, or the separate stages of such a related series, and thus with some hesitation and because the need is great I may suggest for the study of Cosmobia in general (*i. e.,* the comparative study of both normal and abnormal forms) the word Cosmobiology, and for the series formed by related Cosmobia the word Cosmobiogenesis, with the adjective form Cosmo-

[10]Cf. the review of Mall's paper in the section on the literature at the end of this paper.

BIOGENETIC, to refer either to the stages in such a series, or to other phenomena associated with Cosmobiogenesis.

Type 2. Double Janus Eyes. (*Teras III.*)

The only case of this type that has come under my inspection is the Baldwin Synote (Teras III), but as this has both a perfect and an im-

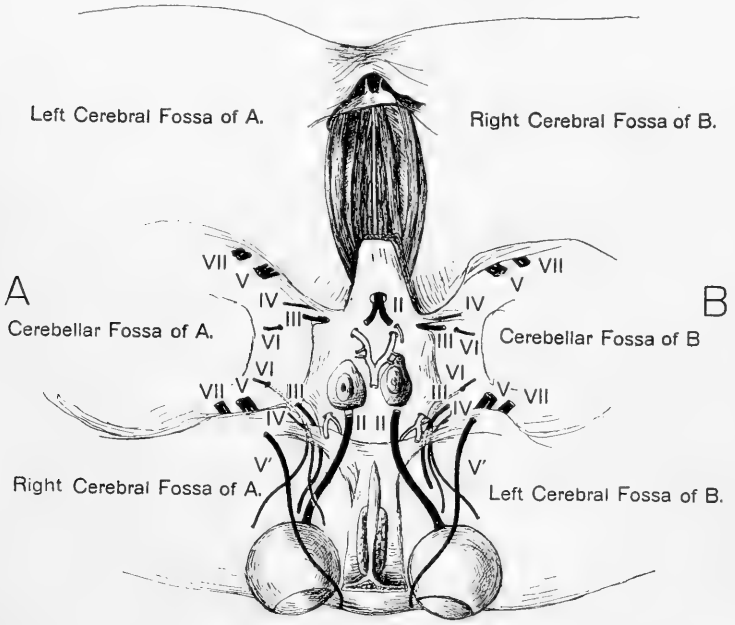


FIG. 23. Cranial floor of the BALDWIN Synote. The synotic eyeball has been exposed by the removal of the orbital roof; the eyes of the perfect side, with the associated nerves, are represented somewhat diagrammatically, to show as many relationships as possible. The Roman numerals designate the cranial nerves; the two hypophyses are shown near the center of the figure. The outlined vessels are arteries. The muscles of the synotic eyeball may be easily determined by comparison with Text Fig. 25 and with Plate III, Fig. 6.

perfect face it is of especial value here, since the two faces represent two different degrees of approximation of the eyeball components.

For the study of the muscles and nerves of the eyeballs it was necessary to remove, first, the double skull-cap, then the double brain, and finally to cut through the bony roof of the orbits formed by the frontals. The final preparation, in diagrammatic form, appeared as is shown in Fig. 23. In this, which in extent of torsion corresponds nearly to Stage V

of the diagram (Fig. 3), the supraorbital region of the perfect side is practically normal, and beneath the bony roof formed by the orbital plates of the frontals the two eyeballs (Ar+Bl) are related as those of one person, save that they have a tendency to turn their optical axes inwards towards each other, that is, the "perfect" face is a little cross-eyed. Upon the imperfect side there is, of course, a considerable narrowing of the supra-orbital region, and on chiseling off a portion of the roof the double eyeball of this side becomes visible, covered by a double set of band-like muscles. This organ, which in its composition is Al+Br, is narrower and more elongated than a single normal eyeball, but is perfectly bilateral in all its details.

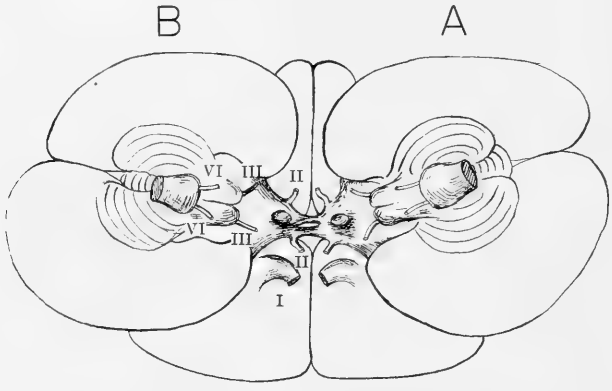


Fig. 24. Under side of the double brain of the Baldwin Synote. The Roman numerals designate the cranial nerves. Note the commissure between the two components (optic?), also the two hypophyses.

Upon studying both the cranial floor and the base of the double brain the origins of the cranial nerves and their exits from the cranial chamber may be readily determined. They have, however, a two-fold relationship, the one to the brain from which they arise, the other to the apparent face to which they are distributed. This is exceedingly difficult to describe, but may be readily seen by comparing Figs. 23 and 24. At their origin they arise in pairs from each brain, quite normally with the exception of the first two, Olfactorius and Opticus, which arise the most anteriorly and in that region of the brain adjacent to the plane of contact, and consequently modified. In this region the two brains are connected by a narrow connective of white matter, which

is probably a modified double optic commissure, since from the sides of this the two pairs of Optici take their origin. The Olfactorii, which arise from the under side of the hemispheres, have nothing to do with this connective, and appear upon the perfect side quite as in a normal individual, although upon the imperfect side they appear to be entirely wanting.

Behind the second pair the remaining cranial nerves are quite normal in respect to origin, but their relation to the two apparent faces is such that each face is supplied by corresponding nerves from the two brains, which proceed from the sides adjacent to each face and become related exactly as though they were an original pair of cranial nerves. The result of this is that the two corresponding nerves that supply a given face come from a very divergent origin, and in their course need to turn outwards nearly at right angles from their initial course.

In this manner the eyeballs of both faces are supplied with the associated cranial pairs, II, III, IV, and VI. Upon the perfect side the two Optic nerves are distinct, each with its own foramen of exit, but upon the imperfect side the two nerves approach each other, run in contact through a single median optic foramen, and finally enter the median eyeball as a single nerve. The other nerves of the orbit are distinct while within the cranial cavity, but upon the imperfect side there are certain abnormal relationships between them, to be described later.

The two hypophyses have been already mentioned, but it may be noted here that, unlike the two heads or the two livers, which are formed each of two components, they belong wholly to the component of the side upon which they are situated. Both still retain the fetal connection with the pharyngeal cavity, and the two openings are plainly visible in the roof of this latter cavity, appearing as two small pores, situated close together, opening from a small recess and not directly from the pharynx. They are almost at the exact center of the monster as in the case of the œsophagus, but the two openings are placed laterally, and thus each belongs to a single component.

The eyes upon the perfect side, since they consist of A's right and B's left, are related to each other as are the two eyes in a normal face, and thus the orbital nerves, although proceeding from different brains, are nearly normal in respect to position and relationships. The external rectus muscle, with the VIth nerve, appears upon the outer side of each eyeball and the superior oblique, with its pulley and the IVth nerve, is upon the inner. The ophthalmic branch of the Trigeminus crosses

between the roof of each orbit and the eyeball, and issues forth to supply its half of the forehead as though both the latter and the nerve pair were those of a single normal individual. A special interest must attach to median parts, especially when thin, like the nasal septum; but this, as well as the crista galli and the two olfactory fossæ lateral to it, appear precisely as in the head of a normal fetus of the same age. In the same way the suture between the two frontals is in no respect different from that which

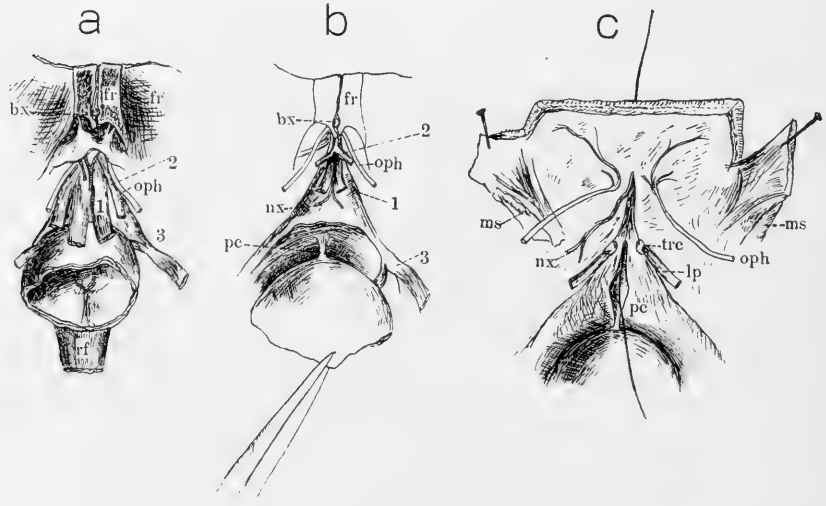


Fig. 25. Dissection of the double eyeball of the Baldwin Synote. The three views represent progressive stages in the dissection.

fr, frontal; *oph*, ophthalmic branch of the Trigeminus; *trc*, rudimentary tarsal cartilage; *pc*, "palpebral canal"; *ms*, median suture between the two frontals; *1*, *2*, and *3*, muscles explained in the text; *lp*, levator palepebræ; *nx*, an unknown nerve; *bx*, an unknown bulbous organ.

in normal cases separates the two frontal bones which belong to the two halves of a single body.

Upon the imperfect side the double median eyeball lies immediately beneath a bony bridge that is evidently composed of the orbital plate of the double frontal, here united into a single bone without a trace of double origin. The eyeball is covered by a series of narrow band-like muscles, arranged in perfect bilateral symmetry, those of the two sides separated by a median artery. As seen from above, these muscles are four in number upon each side. Of these the innermost pair is innerved by the

Trochlearis and is thus positively identified as the superior oblique. The other three pass over and beyond the eyeball, and hence suggest the levator palpebræ, although they are too numerous to correspond with the normal condition of this muscle. The outermost of these three pairs of slips converges in front of the eyeball, and after giving a small slip to the surface of the latter, inserts into a conical sheath of connective tissue, which passes forwards and inserts into the frontal bone. The two inner slips upon either side are closely associated together and run forwards and inwards above the conical sheath just referred to, and in such a manner that the outer ones become dorsal to the other pair. These latter join to form a median tendon, that inserts into a slight projection of the conjoined frontal bone, at a point where a minute canal traverses it. The inner pair, now ventral to the other, passes into a small triangular opening in the connective tissue sheath and becomes inserted into a pair of minute cartilages that for reasons to be considered farther on must be the vestigial tarsal cartilages of the upper eyelid. This latter element then, the innermost of the three extrinsic bands, is without doubt the levator palpebræ, but whether the two other pairs, the one expanding into the sheath, the other inserting into the frontal bone, represent also certain elements of this muscle cannot be definitely decided. It is above all things necessary to determine with certainty the exact meaning of the conical sheath which seems here so important, and for this we must wait for the investigation of another specimen in which the involution of parts has not gone so far, an investigation that must interpret to a certainty the parts that here in their reduced state are unrecognizable.

Beneath the layer of palpebral muscles lie the intrinsic muscles of the eyeball, of which the superior obliques have already been noted. [Cf. Plate III, Fig. 6.] The strips that lie upon the outer side are innerved by the Abducens, and are thus definitely shown to be the external recti. Of the rest, which are placed in perfect bilateral symmetry, the superior recti are easily identified by their position. Below the eyeball there are two muscular elements, the one a band, the other a sheet, and these, as well as the superior rectus, are innerved by the Motor oculi. Of these, following the analogy of the eyes of the Cyclops type, it is probable that the band is the inferior rectus and the sheet the inferior oblique. This accounts for all the muscles normally associated with a pair of eyes with the exception of the internal recti, and these, which would naturally come between the two eyeball components, would have no place for development.

Certain peculiarities of the nerves demand attention. The two Motores oculi, coming from the two brains, become continuous with one another and form a common trunk stretched transversely across the middle line back of the eyeball. From this small twigs arise and supply the muscles, and a similar one, lateral to the others, forms a communicating branch with the Abducens of each side. The two ophthalmic branches of the Fifth nerve, having no chance to reach the exterior, ramify the inner surface of the frontal bone; but a small median nerve, the connection of which I was unable to find (Fig. 25 b), passes between the two vestigial tarsal cartilages and is probably distributed to the proboscis, and possibly also to the infolded skin lining the palpebral canal next to be described. This branch is probably derived from the ophthalmic nerve, although this was not proven.

The eyeball, which was situated far in the interior of the head, was attached to the center of a blind front wall by means of a membraneous stalk that proved upon examination to be hollow and to constitute a part of the wall of a canal that ran forwards in the middle line and came to the exterior immediately beneath the base of the proboscis. The laying open of this canal proved its nature, for its walls contained all of the antorbital structures, even including a small portion of the face. Beyond the membraneous tube, which undoubtedly represents the conjunctiva, lies a pair of carunculæ lacrimales, followed by a double ridge composed of Meibomian glands, and just beyond these a well defined row of eyelash rudiments. This region, still within the canal, is followed by normal integument, furnished with delicate hairs. Outside of this canal, at about the outer limit of the conjunctival membrane and placed dorsolaterally, is a pair of minute nodules of cartilage, each somewhat in the form of a capital D, and into these are inserted the pair of muscles identified above as the levator palpebræ; farther down on the sides of the canal is a pair of large glandular masses. These structures are plainly the tarsal cartilages and the lacrimal glands, and from these and the other features we can see that the entire canal is formed by a turning in of the normal external parts accessory to the eyeball. The matter becomes at once clear if one imagines a normal pair of eyeballs first fused into a single symmetrical one and then drawn back into the interior of the head, taking with it the parts that are attached to it. The conjunctiva, turned wrong side out, save the part covering the front of the eyeball itself, would form the innermost part of the canal, then would come the margins of the lids, and lastly the external skin in the

vicinity. This canal may thus be conveniently termed the *palpebral canal,* although in the present case the turning in has proceeded so far that not only palpebral parts but the external skin as well are included within it.

The rudiment of the external nose, in such monsters commonly referred to as the proboscis, is placed as usual above the median eye, thus develop-

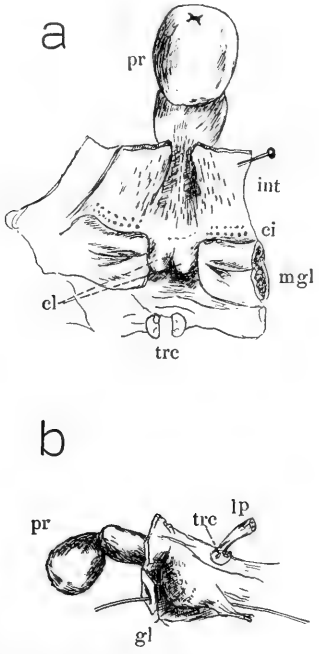


FIG. 26. Proboscis, *i. e.*, rudimetary nose, of the BALDWIN Synote.
(a) From below, with the palpebral canal laid open.
(b) From the side; palpebral canal entire, but traversed by a bristle.
pr, proboscis; *int,* integument of the face, included in the palpebral canal; *ci,* eyelashes; *mgl,* meibomian glands; *cl,* carunculæ lacrimales; *trc,* rudimentary tarsal cartilages; *lp,* levator palpebræ; *gl,* lacrimal gland.

ing in its primary position, its descent being prohibited by the position of the double eye immediately beneath it. Its form and its division into a stalk and a terminal bulb are sufficiently indicated by the figures. A terminal orifice, seen at the end of the bulb, ends blindly a little distance within, and undoubtedly represents a median nostril. The internal nasal

parts are but slightly indicated and some of these rudiments can be interpreted only through the dissection of such a specimen as Calori's Iniops, in which these parts are better developed. For example, the two halves into which the frontal bone becomes divided at the level of the proboscis include between them a membraneous septum, which expands at one point into a swollen nodule, Fig. 25 (a). This nodule is lodged in a special cavity formed by the two frontal elements, as though it were an important organ, but although its significance may be evident to some of my readers, it seems to me wholly problematic. There is no trace of olfactory fossæ, crista galli, nasal septum or nasal conchæ.

Type 3. The Inner Eyes of Incomplete Diprosopi.

I have been fortunate enough to secure two cases that illustrate this type, representing different degrees of divergence. One of these is the small pig embryo of Dr. Lambert (Teras I), the other is a pig at term with two snouts (Teras XII), sent me by Dr. B. G. Wilder. In the first of these the degree of separation is such that the two inner eyeballs of the monster are in contact along their respective outer sides, yet entirely distinct from each other; in the second the components of these inner eyeballs form a single ball of abnormal width, which shows many traces of its compound nature and, with its associated organs, exhibits a perfect bilateral symmetry. For ease in interpretation the first of these, the one with the separate eyeballs, is considered first.

Case 1. (Teras I.) This specimen, undoubtedly the most valuable in my entire collection, was received from Dr. Lambert perfectly preserved for microscopic study and, after a brief preliminary inspection, was cut into a series of cross-sections. Its general appearance may be learned from the accompanying sketch [Fig. 27 a], and, as I have no sketch of the facial details of this double pig embryo, I add at the last moment a sketch of the face of the double kitten embryo, just received from Prof. B. G. Wilder. [Fig. 27 b.] This is a little more mature than the pig embryo, as may be seen by the closed eyelids, but it represents about the same degree of duplicity and angle of divergence of the two components. The mouths of the pig, however, were entirely distinct externally, but are confluent in the kitten specimen. If, in viewing this sketch of the double kitten, the reader will cover alternately, first one half and then the other, with a sheet of paper, he will have before him two nearly normal embryonic faces, exactly alike.

The total length of Teras I, the pig embryo, was 18-19 mm., and the degree of development was the same as that shown by normal pig embryos

of the same length. It was perfect in symmetry and exhibited none of the pathological characters, such as everted viscera, exencephalus, or ectromelus, which are often found in monstrous embryos. The duplicity, which was externally confined to the head region, was the most pronounced anteriorly and diminished so rapidly that at the level of the shoulders the embryo appeared like that of a normal pig of the same length, although the sections revealed evidences of two components to a greater distance posteriorly. Thus, in the bodies of the vertebræ, there

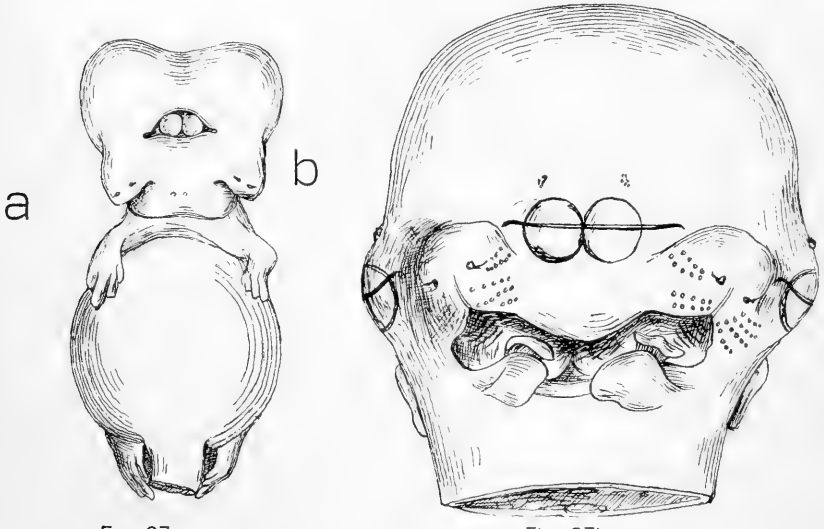


Fig. 27a Fig. 27b

FIG. 27. (a) Diprosopic pig embryo; Teras I.
(b) Face of diprosopic kitten embryo, Teras XXX, almost the counterpart of (a), received too late for further investigation in the present paper. To obtain the full value of the components cover each half alternately with a sheet of paper, taking care to place the edge along the median line.

are found the vestiges of two notochords, side by side, as far back as section 674, which is situated at about the middle of the abdomen. At this point they unite in the form of a transversely placed figure-8, and one or two sections beyond this the notochord is single.

There were two distinct snouts, divaricating from each other and forming the same angle with the median sagittal plane of the entire monster. Above and between these were two separate eyeballs in a single large palpebral opening, plainly the left eye of component A and the right

one of B. The outer eyes of the components were normally placed and the entire outer side of each head, with its associated snout, was normally proportioned and appeared precisely like the corresponding side of a perfectly normal embryo.

For ease in imbedding and sectioning the embryo was divided transversely at about the middle of the belly into an anterior and a posterior half. The sections were each 20 microns in thickness and the entire series filled 43 slides of large size, and included 920 sections. From these, aside from general study, I have already constructed three wax models, one of the brain, together with the eyes and some of the more obvious cranial nerves, one of the skeletal elements of the head, and one of the two inner eyes with their associated nerves and muscles. Of these the two first were on a rather small scale ($\times$ 12), and the third was constructed of twice this size ($\times$ 25). All three of these, down to the smallest details, are fully as symmetrical as the corresponding parts of a normal head, and the one or two slight deviations are of the same nature as those found in the two sides of any individual.

Every section in this series, allowing for the mechanical defects present in all series, is a symmetrical one, and nowhere is there a suggestion of tissue that is in any sense pathological or abnormal. There is not even an area of dense connective tissue due to the crowding of parts, such as almost always occurs in places along the median line of double monsters when more fully grown, and to one looking over the series the impression given is that of normally developing parts, in perfect harmony with one another, as in any other organism. In working over this series, with nothing to suggest the abnormal, one comes to forget that it is even unusual, until finally it seems as natural to see in a given section two brains or two sets of nasal cartilages, symmetrically placed, as it is to find two eyes or two ears. To give the reader some suggestion of this impression as well as to form an introduction to the description of the monster in question, I present here drawings of two sections of the series, taken from the double region, the one through the median eyes, the other at the level of the two lateral eyes and cutting across the two snouts. The several slight departures from perfect symmetry are due, as in any series, to slight variations in the level of the two sides and to obliquity in the plane of section.

In the first of these sections are seen the two median eyes, the two fore-brains and a single hind-brain of abnormal width, partly double ventrally. Both fore-brains are cut a little obliquely, owing to the

divarication of the two axes in the doubled region. This gives the double and single axes a relation like that of the three elements of the letter Y, and the relation of the plane of the section to these can be readily seen if we imagine this letter crossed by numerous parallel lines perpendicular to the stem. The arms will be cut obliquely and, in the case of

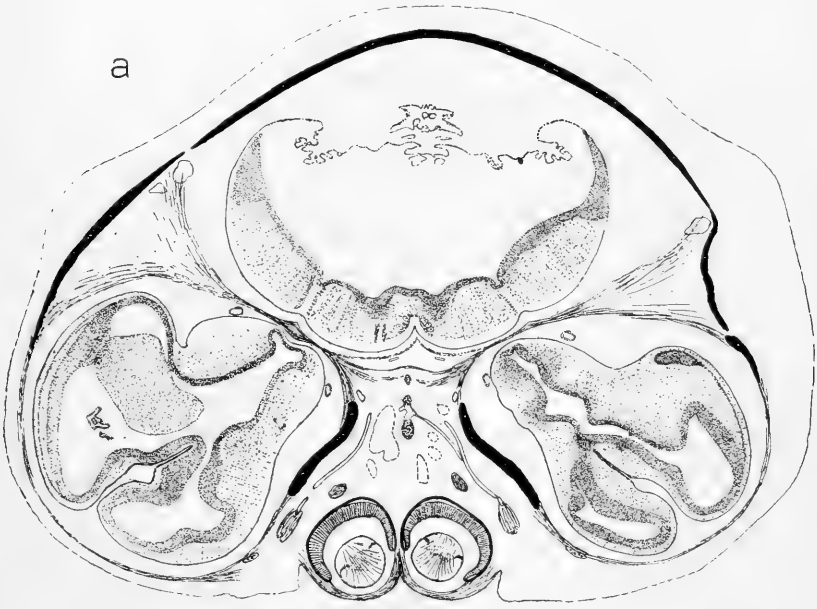


Fig. 28a

Fig. 28. Two sections from the cross-series made from Teras I.

(a) Section 180. At the level of the two inner eyes. The nerve cut longitudinally and placed the most lateral is the Trochlearis; its supply to the superior oblique is also seen. Behind this is the Motor oculi, cut transversely. The median ganglion, with a nerve branching from one side, is the median Trigeminus, with the ophthalmic branch, and the smaller median nerve, directly behind it is the Abducens.

paired organs placed directly opposite each other with reference to either of these, the inner one will be cut first. This is why in this series the two median eyes appear on more anterior sections than those which show the lateral ones, and it explains also why in the first of the two sections given each fore-brain is cut obliquely with its inner side considerably in advance of the outer. Between these two fore-brains lies the region of

especial importance for the present paper, the two inner eyes and their accompanying muscles and nerves. It was from this region that the model referred to was constructed and the description given here is based upon this, although constantly checked by reference to the sections themselves. In section 180, here given, oblique sections of two of the eye muscles appear, the two superior obliques with their nerve supply,

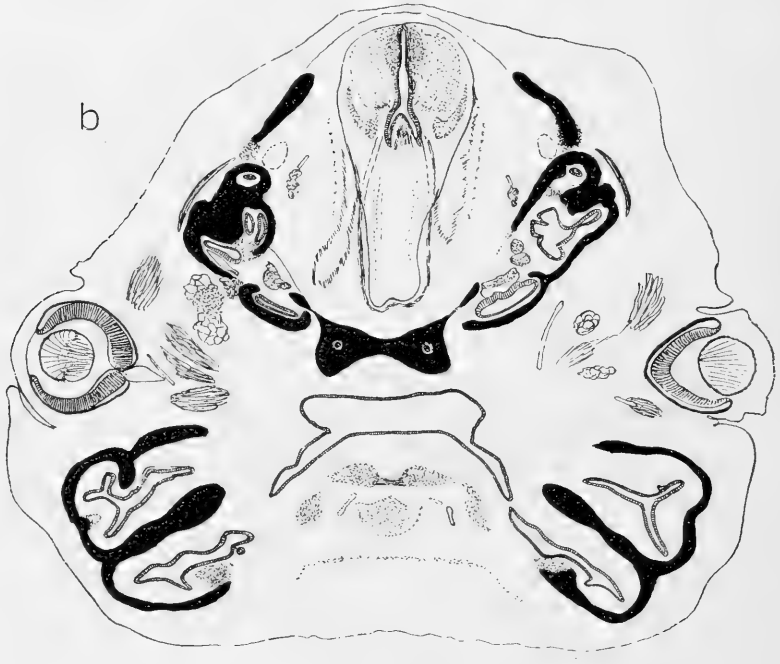


Fig. 28b

(b) Section 250. At the level of the two outer eyes. There are also to be noted two noses and the two lateral ears, encased in the os petrosum. Note also the double centrum of the vertebra, with the two notochords.

the Trochlearis, and the two superior recti. The first of these appear in this section ventral to the others, and lie upon that side of the eyeballs which is external with reference to the entire section but internal with reference to each component, *i. e.*, between the eyeball of a given side and its own median axis. They are thus perfectly normal in position. The third nerve, Motor oculi, which in another section is seen to innerve the superior rectus, appears here in cross-section, one upon each

side, immediately dorsal to the end of the cranial cartilage. The ganglionic mass which lies exactly in the middle, and from one side of which a nerve issues that runs along the side of the Trochlearis, has nothing directly to do with the eyeballs but represents a median componental Trigeminus, which becomes much larger a little posterior to this section (Gasserian ganglion), and sends out a stout nerve to each side. From their relation to the adjacent parts these lateral branches prove to be the Nasal branches of the Ophthalmic, which supply the inner sides of the two components. The small median nerve, dorsal to this and seen in cross-section, is the componental Abducens, which, like the Trigeminus, arises too far back to possess two separate roots. It supplies the external sides of the two retractores bulbi, and the small external recti, which lie naturally in the middle between the two eyeballs and are fused at their origins.

The second section figured here, No. 250, is cut along the level of the lateral eyes and involves the two snouts as well. In the dorsal part of the section lies the medulla, showing certain indications of doubling, in particular a ventral forking of the central canal. In front of this lies the doubled median cartilage of the basis cranii, probably in the basi-occipital region, containing two notochords, some distance apart. Upon the sides of the skull are normally formed petrosal cartilages enclosing sections through the labyrinth, but there is no indication, here or elsewhere, of median ear components. Ventral to the basicranial cartilage is placed the pharyngeal cavity, with portions of the recesses which, in other sections, are seen to lead into the inner nasal cavities of each snout. The obliquity of section through these latter organs corresponds to that which appears in the other section in the case of the fore-brains, and arises from the same cause, the oblique position of the axes of the laterally placed components. The various anlagen ventral to the pharynx have not yet been identified.

The details of the two inner eyeballs and their associated parts are shown in Plate III, Fig. 7, and Plate IV, Fig. 8, which were drawn almost directly from the model of the region. Aside from these the accompanying figure [Fig. 29] is of use to show the relationship between the eyeballs, the associated cranial nerves, and the brain. In this the telencephalic lobes (hemispheres) of component B, the one nearest the reader, are represented as partly rmoved, thus rendering visible the median eyes and other median parts.

The two eyeballs consist of the left one of component A and the right one of component B, so placed that the former is on the right and the

latter on the left with reference to each other. The two are thus in contact by their lateral or external sides, a position which will readily explain the relationships of the associated parts. The optical axes of the two converge towards the mid-line of the monster taken as a whole, a

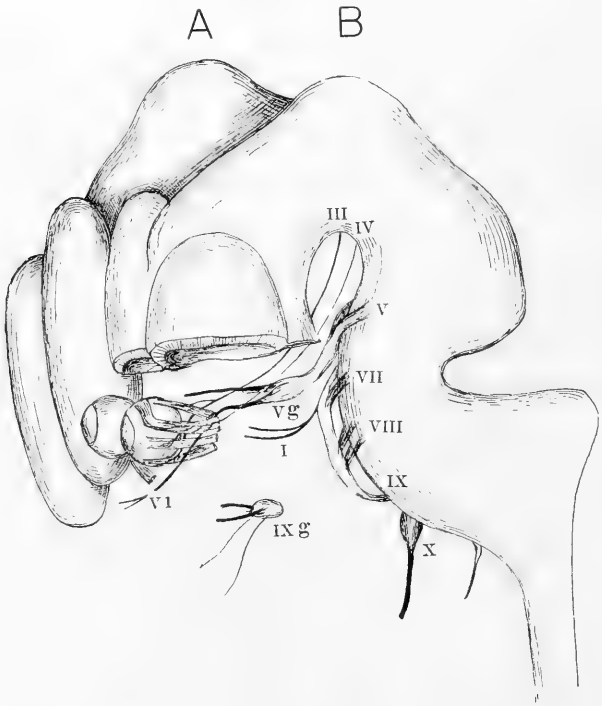


Fig. 29. Diagram of the double brain and the inner eyes, seen from the side. The median cranial nerves are also shown, but the lateral ones, which are located as in the normal embryo, are left out. The two hemispheres of the nearest component (B) are in part removed, in order to show the median parts.

This sketch was drawn in part from the model of the brain, but is also in part the result of the interpretation of the sections, without modeling.

condition noted also in the imperfect face of Janus monsters and in the compound double eye of the next monster to be described (Teras XII).

Each eyeball is supplied with a full set of intrinsic muscles, which include the four recti, the two obliqui, and the retractor bulbi, but there is as yet no levator palpebræ, a condition found also in the more normally

related lateral eyes, and probably to be accounted for in all by the immaturity of the embryo. For the same cause none of the four has as yet a tarsal cartilage, nor either a lacrimal nor a Harderian gland. In the identification of the muscles *the relative position of the two eyeballs must be constantly kept in mind, that is, that their anatomical external aspects are adjacent to each other, and that they are thus not related as a normal pair of eyes, but just the reverse.*

Three of the eye muscles may be at once identified by their innervation; the superior oblique, innerved by the Trochlearis; the external rectus, innerved by the Abducens; and the retractor bulbi, which is innerved upon its external side by the Abducens and upon its internal by a branch of the Motor oculi. Aside from the innervation the shape and other relations of these muscles is also characteristic and assists in the identification; the superior oblique shows already the bend for the pulley along the inner side of the eyeball, the retractor partially encloses the optic nerve from the external side, and the two external recti lie upon the external sides of the eyeballs, although the close proximity of the two to each other crowds them together into a pair of closely associated slips, united at their origin and somewhat reduced in size.

The three other recti, superior, internus, and inferior, are sufficiently distinguished by their relative position and by their innervation from the Motor oculi; their relations are quite normal and they are equally developed in both components. At the lower (posterior) aspect of each eyeball is found the little obliquus inferior, arising from the side of the nose of the same component, and running laterally to the eyeball. The nerve supply to this muscle was not easy to determine from the sections, but seems to be by means of small twigs that arise from the branch to the inferior rectus and run along the anatomical outer side of the latter muscle, that is, the relationship is normal. In the case of the lateral eyes, which, owing to the slight lateral obliquity of the components, is cut at a little different plane, the nerve supply to this muscle is easily seen, and is also the normal one.

In Fig. 32, where the relations of the eye muscles in this and the following Teras (XII) are compared, the conditions just described are given in the form of a diagram. In this may be seen at a glance the fact that the muscles of each eyeball are wholly normal and that the two are perfectly symmetrical.

The nerves that supply these muscles are as normal in origin and course as the case will allow. The two Third and Fourth nerves come

from the inner side of the two brain components in the normal place, the first from the ventral side, at about the highest point in the bend of the neural axis, the other from the dorsal side of this curve and a little further back. From these points of origin they run parallel to each other obliquely downward and forward, as shown in the profile view, much as in the case of a perfectly normal embryo or as upon the outer sides of the same components, where the corresponding nerves come down to the two lateral eyes. At the level of section 180 the Trochlearis makes a sudden bend and runs horizonally to its insertion into the superior oblique muscle. The Motor oculi continues its straight course a little farther and is eventually distributed to its usual muscles.

The Sixth nerve, the Abducens, is peculiar at its source, although in perfect accord with the conception of such a cosmobion as presented in this paper. Since the separation of the two components is widest at the anterior end of the body and becomes gradually less posteriorly, *i. e.*, more like a normal single individual, there must come a point, proceeding from before backward, at which the cranial nerves of the inner sides of the two components must be represented by apparently single, median trunks, which are, nevertheless, potentially double. In this monster this point is reached between the Fourth and Fifth nerves and while the inner components of the former are separate and distinct, those of the latter develop a single median Gasserian ganglion formed by the coalescence of the two lateral roots. From this ganglion a strong branch passes out to either component and runs across the back of the orbit between the separate eye muscles. The relations of this nerve to the various muscles and to the optic nerve identify it with the nasal branch of the Ophthalmic. Behind this a much reduced pair of little branches undoubtedly represents the vestiges of the inner Maxillary nerves, the parts controlled by which never develop. Since the Fifth nerve thus lies posterior to the region that exhibits two separate trunks for its cranial nerves the Sixth must be also median and apparently single. This is indeed the case, and this nerve is found in contact with the posterior surface of the Gasserian ganglion from which point it runs somewhat farther back along the median line. When on a level with the external recti muscles it makes a sharp turn to a horizontal position, and divides into two lateral branches which supply the external recti and a part of the retractores bulbi.

While on the subject of cranial nerves it may be proper to add that, although the components converge more and more posteriorly, there yet

appear fairly well-developed median rudiments of several nerves beyond the Sixth, probably representing not only all of the remaining cranial nerves, but a few of the most anterior spinal nerves as well. Thus, a little posterior to the Sixth nerve a long ganglionic ridge extends longitudinally in the mid-ventral line. At least two pairs of nerve roots run into it from the sides of the medulla and it is attached also at its posterior terminus, presumably by a pair of roots that arise so close together as to form a median mass. Posterior to this and still in the median line are two farther nerves which may be regarded as cranial, the first smaller and the second larger. These arise as median roots and run as single fibers in a straight course, keeping in the median plane. About opposite these ventrally lies a large median ganglion, entirely detached from them and from the cord, yet from this proceed two pairs of nerves, the anterior ones very fine and short, the posterior ones larger and longer. These nerves seem soon to lose themselves in the surrounding tissues.

The interpretation of the above structures, although not capable of exact proof, is suggested by beginning at the Gasserian ganglion, the last point of certainty, and following the roots posteriorly [cf. Fig. 29]. In this way it seems as though the long median mass composed of several pairs of roots may be the Facialis-Acusticus complex, and the two median roots posterior to this the Glosso-pharyngeus and Vagus. The detached ganglion is less certain, at least until after a careful determination of the rudimentary structures to which its nerves are distributed, but it is probably either the ganglion petrosum of the Ninth or the ganglion nodosum of the Tenth, or possibly both together.

For some distance beyond these median cranial nerves a median row of nerve roots is continued, so that for each body segment the cord has three roots, the two normal ones upon the sides and a mid-ventral one, the latter composed of two elements. Posteriorly these latter grow constantly smaller and narrower and the former come nearer together until the median row is wholly lost and the relations become normal.

Case 2. (*Teras XII.*) This specimen, also a pig, gives a suggestion of what the monster just described would have looked like, had it been allowed to develop to maturity, since it also is a single individual with a double snout [Fig. 30]. Here, however, the divergence and separation of the two components is not quite so great, and the two inner eyes, instead of being separate, form a single median organ of abnormal width, though containing two separate lenses. This amalgamation, or rather

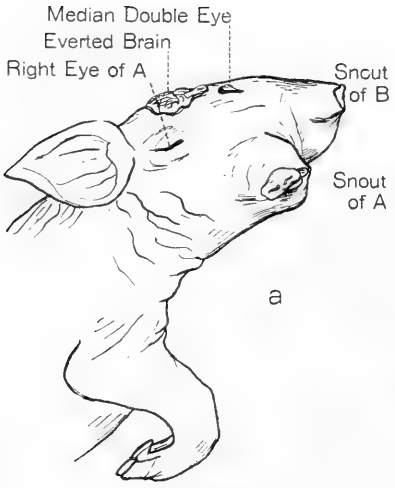


Fig. 30a

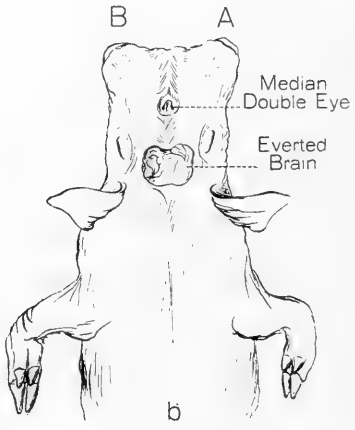


Fig. 30b

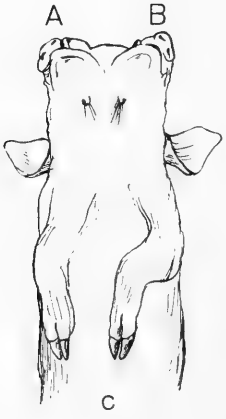


Fig. 30c

Fig. 30. Sketches of Teras XII, the double snouted pig. Note especially the everted brain, the median eye, the two throat bells, and the angle of divergence of the two snouts.

(a) Half-side view.

(b) Dorsal view.

(c) Ventral view.

incomplete separation, of anlagen extends also to the eye-muscles, so that this case represents another stage in the same cosmobiotic series with the previous one, thus making the comparison one of extreme interest.

In one particular the specimen was deformed; the brain was everted and the cranial cavity was very small. This, or some similar defect of the brain, as is well known, is quite common in certain types of abnormal cosmobia, and may be either primarily or secondarily connected with the same cause that produced the cosmobiotic abnormality, but the fact that these defects are by no means constantly associated with the latter is strongly indicative that they result rather from a secondary, probably mechanical, cause than from anything inherent in the germ and thus predetermined from the beginning. It would thus be likely that the early embryo in such cases would be free from these defects and that their appearance would date only from the point at which some mechanical barrier to normal development would be formed. For example, the double pig embryo just described shows no defect, and the sections appear as in normal animals, but it is easy to conceive that at a little later date, when the parts became more complex, the development would not have continued so harmoniously and that thus deformation of parts would be inaugurated. Since also the mechanical problems of normal development differ in different animal groups, it is likely that an abnormal, though cosmobiotic, form, which in the case of one animal usually develops as far as birth without deformation, may, in the case of another species, meet some difficulty in the mechanical adjustment of parts which may modify or even prohibit development beyond a given stage. This would furnish an explanation of the well-known fact that certain types of cosmobiotic monsters are characteristic of certain groups of animals; and in this connection it is worthy of remark that in birds, the one group in which we do happen to know a little about embryos of cosmobia, the types most frequently observed during early embryonic life are not the ones characteristic of this class of animals after hatching. Thus varying grades of Janus monsters are often found in embryos of the first two or three days, but records of this type among birds after hatching must be extremely rare, and I cannot recall a single instance, either in literature or in my own experience.

From the study of such embryos it would seem that the mechanical moment which here introduces a complexity that proves disastrous is the turning of the head to the right, characteristic of early bird embryos,

since before that event such embryos are usually symmetrical and undeformed, while the turning of each of the two components causes a mechanical interference of parts and components that utterly destroys the natural symmetry [KAESTNER].

With the exception of the everted brain and the correlated changes in the adjacent parts, Teras XII, the monster in question, is symmetrical and perfect, that is, it is cosmobion. Each component has both outer and inner eyes, but the axial divergence of the two components is so much less than in the previous case, Teras I, that there is no longer room for the independent expression of the two inner eyeballs, and they therefore develop in the form of a double organ, of abnormal width but perfectly symmetrical in all details. The palpebral opening is single, but bent in the form of a U, suggesting its compound nature.

In other points this specimen is very much like the preceding. There are two snouts, diverging laterally from the median plane of the monster at an equal angle, and the two lateral sides, with their eyes, are normal in every respect. Upon the ventral side of the head each component is seen to be possessed of the characteristic sub-mental wart with its tuft of bristles; these plainly mark the mid-ventral line of each, and thus their distance from each other shows the amount of the divergence of the two components at this level. There is also a cylindrical papilla of unknown significance, which projects from the inner angle of each mouth. Its external surface is covered with hair-bearing integument, giving the suggestion that it is a detached piece of the lower lip, but it takes its origin, not merely from the edge of the gum, but from the surface of the hard palate nearly to the median line.

In describing the compound median eyeball, it seems best to consider first the eyeball itself, both externally and internally, with its associated parts other than the muscles, and then these latter, the determination of which must rest in part upon the relations of the eyeball.

The compound eyeball, which consists of the left one of A and the right one of B, is of a flattened pyriform shape, and in its lateral diameter is nearly double the normal width. Along the dorsal and ventral middle lines it is slightly grooved, suggesting its double nature. It is supplied with two optic nerves, which converge from the two sides and enter the eyeball normally and quite near together. Beneath each eyeball component, and lying a little to the inner side, is a large glandular mass, which is evidently the Harderian gland, an organ always large in the pig.

The eyeball was dissected by dividing it in two horizontally and then lifting up the dorsal half. The condition thus found is shown in diagrammatic form in Fig. 31. Here the key to the situation is found in the iris, or rather irides, which by their position express the general relationships. There are two of these, each forming a complete ring as normally, but they are united along their inner edges for about half their circumference, leaving the remainder free and divergent. It will thus be seen that there are two distinct pupils, as indicated by the two arrows, and that these look forwards and towards one another and open into a common aqueous chamber which is covered in front by a common cornea of an oval shape. Each iris ring contains a crystalline lens, which is considerably larger than the diagram, so that in reality the two lenses

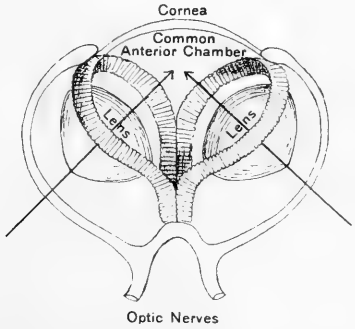


Fig. 31. Diagrammatic view of the median double eye of Teras XII. The two pupils are formed by the apertures through which pass the two arrows, and thus open into a common anterior chamber.

were in close contact with each other and nearly filled the pupillar orifices. At the point of contact each lens originally displayed a small flat facet, formed by the pressure of the other lens, but there was absolutely no organic connection between the two. The two lenses were of exactly the same size, and were set at exactly the same angle relative to the median plane of the whole monster.

Since this specimen was being used for the study of other systems it was thought best to remove the compound eyeball as a whole and thus the nerve relationships and the innervation to the separate eye muscles were rendered uncertain. The determination of these latter must therefore rest upon their general shape and position and especially upon a comparison with the previous specimen, in which the two inner eyeballs

and their associated parts were farther apart and therefore more nearly normal. This form of comparison, the cosmobiogenetic, is precisely that advocated in the introduction and has yielded excellent results. In this form of comparison the most effective method consists in drawing separate and complete diagrams of each of the components involved in

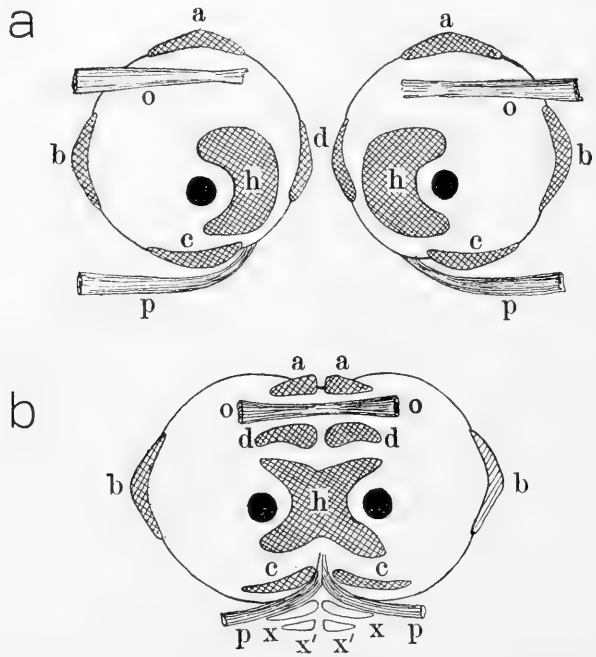


Fig. 32. Diagrams representing the relations of the eye muscles in the inner eyes of monsters of the diprosopic group.

(a) Condition shown by Teras I, in which the two eye components are close to one another, but distinct.

(b) Condition shown by Teras XII, in which the components are more closely approximated.

a, rectus superior; *b*, rectus internus; *c*, rectus inferior; *d*, rectus externus; *o*, obliquus superior; *p*, obliquus inferior; *h*, retractor bulbi; *x* and *x'*, muscles of unknown significance occurring in Teras XII.

their usual form upon two pieces of thin paper, and then superimposing the one over the other at exactly the degree of proximity and at the angle of divergence suggested by the entire monster. The diagram thus formed suggests, often in detail, the relationships to be expected and serves as a key to their interpretation.

In the present case the first of the two diagrams in Fig. 32, which represents the actual conditions of the two inner eyes of Teras I, with their muscles, gives us the two pictures to be superimposed, and the second the result of an approximation equal to that shown by the monster in question. Here, however, aside from simple superposition one must consider an hypothetical force which tends to push to one side, either dorsally or ventrally, parts that come in so close contact that they endanger each other's existence.

Thus the two muscles in the first diagram which would suffer the first and the most by a gradual approximation of the two eyeballs are the external recti and the retractores bulbi; of these, the first, which lies a little above the other, would be the one pushed out from the region of contact, while the two components of the other pair would simply fuse. Above the two external recti the two superior obliques would come together by their insertions, which run directly across the eyeballs and point outwards, in this case towards one another, and the resulting organ would be a transverse band with a tendon in the middle and a muscular belly at either end. This band would lie in contact with the surface of the eyeball but would at no point be inserted into it. Still above this would be found the two superior recti, closely approximated.

Upon the ventral side of the united retractores we would expect to find the two inferior obliques, united at their insertion and separating the two inferior recti. The two former might, in accordance with the degree of approximation of the two eyeballs, either unite to form a transverse median tendon, as in the case of the obliquus superior, or might find themselves, as represented here, running into a groove between the two eyeball components. The two internal recti would occupy the side of the eyeballs farthest removed from the region of approximation and would consequently remain in their normal position upon the anatomical inner sides of the two components.

Thus far the second diagram of Fig. 32 has been treated as though it were a purely hypothetical diagram, constructed, as suggested above, for the purpose of furnishing a key to the interpretation of the actual conditions, but it is at the same time much more than this, for it actually represents, not merely a possible stage in a cosmobiotic series, but the real relationships found in the monster in question (Teras XII). These conditions are shown in Plate IV, Figs. 9-12, drawn directly from the dissections before any attempts at interpretation were made.

In one point, however, the reasoning is not complete, and that is in reference to certain extra muscular slips found in Teras XII, for which

I can find as yet no satisfactory interpretation. These are the ones lettered x and x^1 in Figs. 11 and 12. Each consists of two narrow slips, the one inserted into the eyeball at the margin of the cornea, the other passing beyond to an unknown insertion farther forward. The free ending of this latter suggests the levator palpebræ superioris, but its position below the eyeball and at a distance from the superior rectus with which it is genetically connected, renders this practically impossible. For any satisfactory study of this muscle its relation to adjacent parts is an absolute necessity and considering the present condition of this specimen, we must wait for the examination of some similar specimen in the future.

Aside from this the comparison between the two cosmobiotic stages represented by Terata I and XII seems wholly satisfactory and is corroborative of the relationship between the stages of a cosmobiotic series, the investigation into which has been the purpose of this paper.

Conclusions.

The word "Conclusions" is almost too ambitious a one to be placed at the head of this paragraph, for it seems to me that we are hardly ready for the formulation of such in the still mysterious realm of Teratology. If, however, I were to attempt any statement that might appear under this heading it would be to place a final emphasis upon the type of being designated here as a Cosmobion, and to assert the mutual relationship of the various examples in the form of several related series. This theory may be stated here in tabular form to serve as a working hypothesis:—

1. Bilaterally symmetrical beings of both usual and unusual types are not deformities, but are developed in respect to their architecture, by means of a mechanism of control inherent in the germ. Such beings, developing in obedience to definite laws, may be termed Cosmobia, or *orderly living beings.*

2. In respect to frequency of occurrence Cosmobia may be considered as "normal" and "abnormal", the former being the usual type, the the latter the unusual. Of the latter some may be, in respect to parts, less, and others more than the normal, the "monstra in defectu" and the "monstra in excessu" of the earlier teratologists.

3. All forms of Cosmobia, both normal and abnormal, may become deformed and misshapen, so that the bilaterality is incomplete, and

the physiological processes hindered. Such deformity, which may be considered as secondary, is very much more frequent in the abnormal than in the normal Cosmobia since both the surroundings during development and the anatomical mechanism are fitted for the usual type. It may even happen that certain abnormal types, which are theoretically possible, cannot come to full development, being always and inevitably stopped at a definite period by some mechanical difficulty which it is impossible to overcome. These difficulties are different in different animals, since the anatomical structure and the mode of development is different, and this may account for the frequency of certain types of monsters and the non-appearance of others in certain animals or animal groups.

4. As in normal, so in abnormal Cosmobia, the ultimate cause of the development of the organism and its architectural details lies in the germ, and is probably determined by the time of the first cleavage. There is thus neither a "fusion" of parts already formed nor a gradual development from the normal towards the abnormal during embryonic life, but the parts appear doubled or reduced from their first appearance and their development is controlled in the same way as are the bilateral structure and other architectural characteristics of normal beings.

5. If this latter be true, and it is the most hypothetical part of these conclusions, it naturally follows that true excessive or defective Cosmobia can be produced experimentally only through a cause which is applied early enough to lead to the formation of a germ that differs as much from the normal type of germ as the resulting organism differs from the normal adult. This would lead us to question the value as true Cosmobia of such experimentally produced organisms as the double embryos that result from the partial separation of the early blastomeres; and as a matter of fact the results of such experiments, when critically examined, are hardly symmetrical enough to be called Cosmobia, and although extremely suggestive, give the impression of *monsters produced, not by the same cause as that employed by Nature, but by a similar one, which secondarily duplicates that part of the mechanism of control which in the germ of a true Diplopage is double from the start.* In the more recent experiments with Teleost eggs (Stockard's) in which defective monsters have been produced by the introduction into the water of

a trace of magnesium chloride it may be that here also the germ is secondarily modified and that the greater precision in the results is due to the substitution of a chemical rather than a mechanical force, that is, a molecular rather than a molar one. Since this force is an extremely subtile and delicate one it is also possible that the forming germ may be thus induced to alter its structure from the beginning, and in this case the resulting organism would be a true Cosmobion.

Again, even though the monsters resulting from present or future experiments, in which the cause is applied after the formation of the germ and is therefore secondary, be found upon careful examination to be definite Cosmobia, it will prove only that such monsters *can* be thus produced and not that Nature *does* produce them in the same way.

6. This last paragraph may, perhaps, be added here, although it is not so much a conclusion as a statement of position. I may first emphasize that while I hold that the conception of Cosmobia, as given in paragraphs 1 to 3, is an established fact, and that in the determination of anatomical parts of undeformed though abnormal Cosmobia no greater difficulty is experienced than in the study of normal beings, I wish to consider all that I have said concerning causes (Paragraphs 4 and 5) to be in the form of an hypothesis, about which I have no wish to be dogmatic. Secondly I wish to urge farther experimentation, especially with external causes that may affect the formation of the germ before and after fertilization, since it is my strong belief that the natural causes of abnormal Cosmobia are applied during this period. Finally it must be remembered that results similar to those produced naturally may be formed by means other than the ones Nature habitually uses, and that even a definite experimentally produced monster may not in itself furnish a proof that we have found the natural cause of such an organism. A fairly good double (or doubled) monster may be produced by grafting, but such a result is far from substantiating the assertion that double monsters are produced by Nature in that way.

Literature.

Although, with such comprehensive and modern text-books on Teratology at hand as that of E. Schwalbe, there is no longer any need of accompanying individual papers on the subject with extensive biblio-

graphical lists, I wish in this place to briefly review certain of the most recent works which are of especial interest in the present connection. Of these I may select for especial mention the exhaustive text-book of E. Schwalbe, the recent descriptive papers of Mall and Kaestner, and the experimental ones of Spemann and Stockard. I will also mention the work of two authors with similar views, Tornier and Tarnani, as representing a vigorous opposition to the opinions expressed in this paper.

The great work of Schwalbe,[11] of which two parts have already appeared, with a third promised, will form the standard text-book on the subject for many years to come. In this connection I may especially mention his full treatment of Janus monsters in the second volume, with a good discussion of the anatomy and the various geometrical relationships. Following the traditions he makes no distinction between orderly and deformed beings and is consequently somewhat embarrassed in framing a definition of a monster, since he endeavors to include in one conception things which were never intended to be considered together. His definition is as follows:—"Missbildung ist eine während der fötalen Entwickelung zu Stande gekommene, also angeborene, Veränderung der Morphologie eines oder mehrerer Organe oder Organsysteme oder des ganzen Körpers, welche ausserhalb der Variationsbreite der Species gelegen ist."

This is an excellent definition and defines exactly the usual idea of a monstrosity. It is a departure from the usual order of things, but there is no suggestion of a distinction between a monster that develops from the beginning in an orderly though unusual way and one that becomes secondarily misshapen and distorted through a defect in some system of functional importance or through a mechanical hindrance or direct injury; in other words between a Cosmobion and a deformity. On the other hand great weight is laid upon the event of birth as a point absolutely separating a monster from other forms of deformation. "Eine Missbildung muss angeboren sein." This he illustrates by a fetal amputation as compared with one performed by the surgeon after birth; the one is a monster, the other not.

In these two points, the classing together of all congenital abnormalities and the making of a sharp distinction between intra-uterine

[11]Schwalbe, E. Die Morphologie der Missbildungen des Menschen und der Tiere. 1te Teil, Allgemeine Missbildungslehre, 230 pp., 1906. 2te Teil, Die Doppelbildungen, 410 pp., 1907. 3te Teil, Die Einzelmissbildungen (has not yet appeared). Published by Fisher, Jena.

and post-uterine life, he, as well as others, emphasizes a point of little importance and ignores one that is fundamental. The time of birth is relative, and is merely an incident in the life of the young organism. A similar mechanical injury happening to a marsupial and to a placental mammal in precisely the same stage of development might cause the latter to be classed as a monster, the former as a cripple! The other fault, that of placing in one category diplopagi and fetal amputations has already been sufficiently commented upon.

Following this definition comes a concise and valuable review of the previous work on teratology, and a discussion of the principles underlying the formation of monsters, a discussion in which the author is hampered by his attempt to class all monsters together under a single term. In his discussion of causes he leaves the Diplopagi for later treatment in the second part of the work, and considers here the following as possible causes of monstrosity: mechanical causes, psychic causes, changes of temperature, lack of oxygen, chemical influences (mainly poisons), changes in osmosis, fetal disease, and deformities due to the amnion. Psychic causes, *i. e.,* maternal impressions, he naturally dismisses as improbable, and lays great stress on causes due to mechanical derangement of amniotic elements. In all this part of the work the author shows the interest of a trained pathologist and the cases referred to are mainly pathological. As the discussion of double monsters is postponed until later, the only cosmobia to be considered here are those that are less than a single individual, and of these Cyclopia is the only type treated. This he is disposed to view as the result of abnormal pressure exerted upon the very young embryo (*i. e.,* a secondary and mechanical cause), but he is especially careful to point out the fact that this cause does not make the separate lateral parts grow together, but prevents them from developing at all; "eine anscheinende Verwachsung ist sehr häufig eine unvollkommene Trennung."

Schwalbe's second part, which appeared in 1907, is wholly devoted to the discussion of Diplopagi and will long be of the utmost importance to students of that branch of teratology. In this, aside from a voluminous descriptive part, he discusses the causes of double formations, and includes in this a treatment of the various theories that have been suggested in the past. His own opinion, which is cautiously stated, may be tabulated as follows:—

(*a*) In the case of most double monsters the time for the action of the cause closes with gastrulation.

(*b*) The primary cause is a subdivision of the egg material, which develops two formative centers (Bildungszentren).

(*c*) The cause may lie in a displacement of the early blastomeres with respect to the norm. Granting, with DRIESCH, that "the prospective significance of a cell is a function of its position," a disturbance of the normal position, and hence the relationships, of a cell may cause it to develop differently.

(*d*) All that may be postulated in general, to cover all cases, is that the cause is a division of the egg material. Special cases must be considered by themselves.

The third and last part of the work, which has not yet appeared, is to have the title "Die Einzelmissbildungen." Here, it is evident, we will find the defective cosmobia in the same bad company to which they have long been assigned: schistosoma, exencephalus, fetal amputations, *et hoc genus omne*. If, however, as we have every reason to expect, they are treated with the same thoroughness as is shown in the rest of the work, the description will be extremely satisfactory, and of the greatest value to teratologists.

In a series of papers dealing with certain types of double chicks KAESTNER[12] has sought to ascertain the causes underlying the doubling and has arrived at results which, although not final, are yet of extreme importance. Of especial interest in connection with the present paper are his investigations of cases of two and three day chicks in which the two components are placed with the heads united and the bodies diverging at a greater or less angle to each other, even to a position in which they form a straight line, these he refers to the series of Cephalothoracopagi. In his fifth paper, which is unfortunately the only one that has thus far come into my hand, he gives a thorough descriptive treatment of six early avian cephalothoracopagi. All of these he has sectioned, and of two he has prepared wax models, many details of which are reproduced in his plates. To my mind one of the most satisfactory points of his paper is the emphasis which he places upon this method of treatment, especially since I had already, before the appearance of his work, sectioned a chick embryo quite similar to his No. 5, and pre-

[12]KAESTNER, S. Doppelbildungen an Vogelkeimscheiben. 5te Mitteilung. Zugleich ein Beitrag zur Kenntnis der Doppelbildungen bei Amnioten im allgemeinen, besonders der Janusbildungen und der ihnen verwandten. Archiv. für Anat. und Physiol, 1907. (Four earlier papers on the same general subject in the same periodical for 1898, 1899, 1901, and 1902.)

pared a series of embryograph drawings for the construction of a wax model. The excellent work of KAESTNER upon this very subject will render any work of mine on the same subject superfluous, especially as I have become so much interested in the investigation of later mammalian embryos by the use of the same methods. That such methods, applied to teratology, are quite new is indicated by his confession that he kept his first double embryo for two years in Canada balsam, to serve as a "Schaustück" before it occurred to him to section it, and here again comes a parallel from the other side of the Atlantic, for my preparations were handed me in precisely this form and I had first to dissolve them out of the balsam before sectioning.

Aside from the descriptive part there is a little general discussion, although the author feels that we are hardly ready for it as yet. At the outset he states that as yet no "Doppelbildungen" have been experimentally produced in the case of Amniotes, although it has been accomplished in the case of certain Anamnia and invertebrates. The claims of former investigators that they have produced such monsters in artificially treated hens' eggs (by varnish, shaking, high temperature, etc.), cannot be acknowledged, since a fairly large proportion of these normally occurs in eggs, at least those artificially incubated, and it has not been shown that the proportion is any larger in eggs that are specially treated.

I am, of course, in full accord with this view, and may go still farther and suggest that the double formations produced artificially in Anamnia and invertebrates may perhaps differ essentially from those that are produced by Nature, at least in the ultimate cause. In natural cases it is probable that the cause which is later to produce a double monster lies in the germ-cell previous to the first cleavage, and that the more or less complete loss of continuity between the early blastomeres which undoubtedly takes place, is the first of the visible results of the germinal condition. This, in its turn, helps to condition the whole later development and when induced artificially, naturally produces similar results. A germinal cause is, however, much more delicate and precise than a mechanical one can be, and thus the results of the latter cause are not as symmetrical and perfect as are those produced by the former. The experiments are of extreme value in suggesting one of the early mechanical steps employed by Nature during the genesis of a double monster, but that the ultimate cause lies in merely a separation of the blastomeres does not appear probable.

At the end of the paper KAESTNER discusses numerous cases of multiple embryonal areas upon a single yolk, a field which is of the utmost importance, especially with reference to the formation of unequal diplopagi (autosite and parasite). He accords with several other writers in emphasizing the presence of multiple cleavage centers, "mehrfache Furchungszentren," as the earliest stages of multiple formations. These may differ widely in their distance from and their geometrical relation to one another, ranging from those placed at diametrically opposite poles to those that are so near that the two cleavage systems interlock, "dass die beiden Systeme von Furchen jetzt schon ineinander greifen." When these two cleavage centers are far apart they lead to the development of two separate germinal discs, but whether in later development their edges remain separate or become united we do not know. From a preparation of MITRAPHANOW, in which, in a six-hour chick, there are two areæ pellucidæ upon a single "biskuitförmige" germinal disc, the impression is given that here two originally separate germinal discs have fused, although the sections show that ectoderm and endoderm pass in direct continuation across the dividing line from the one to the other. This latter observation strongly suggests that no secondary fusion has taken place and that the material of the two has been continuous from the first, "also scheint das Material von Anfang an zusammengehangen zu haben." In either case, whether there was a secondary fusion or not, KAESTNER concludes that there must have been originally two cleavage centers, although rather nearer together than in cases in which there are two separate germinal discs. From this, cases like his Fig. 15, with two closely adjacent areæ pellucidæ, can be readily explained, and a still closer approximation of the cleavage centers would result in a form in which the areæ pellucidæ would be themselves confluent. From this KAESTNER draws the conclusion that cleavage centers placed far apart lead to two independent embryonal anlagen, while, if we imagine them as gradually approximating each other, there comes a point beyond which they are so influenced by each other that they form a symmetrical double formation.

Finally he cites several well-known multiple embryos and suggests what they might have become, judging from the relations of the separate anlagen. WETZEL'S case, with four centers, is of special interest. The centers are associated in pairs, A+B and C+D, of which A and B are nearer together than are C and D. KAESTNER thinks that the former have already come into collision, and that they would lead to two

incompletely separated embryonal anlagen, in short, a symmetrical double monster. A similar fate would later overtake the two other centers, although the resulting double monster would differ in degree from the other, owing to the varying distance of their centers, and finally the two double embryos thus formed, true diplopagi, would fuse with each other, although unsymmetrically. In RAUBER'S embryo, with three centers, two of them would later form a symmetrical double formation, the third would be independent of this, but would probably still later fuse with it, although unsymmetrically. These last two cases have a special interest in connection with the several known cases of human double monsters produced at the same birth with a normal and separate twin (cf. introduction, p. 357, note 1).

The last few pages of the paper suggest that the author considers fusion as an important factor in the production of double formations, a view that of late has been treated with much suspicion, and seems to me rather unlikely. Still he refers the cause in all cases back to a very early stage, and suggests the need of studying also in this connection the holoblastic eggs of mammals, although there is for this as yet but a single available specimen, the early sheep's egg of ASSHETON. He thinks it unsafe to apply to the mammal the conclusions obtained from the egg of the Amphibian, although technically both are holoblastic.

Experimental teratology, although, perhaps, more than a century old, has but recently begun to yield definite results. Of special bearing upon this paper I may mention the work of two recent experimenters, SPEMANN and STOCKARD.

The first of these authors[13] has experimented with the eggs of the Urodele, Triton, and, by ligating them, generally in the two-celled stage, produces at will double-headed monsters, representing different degrees of duplicity, combined or not with cyclopic defects, according to the treatment. If, for example, he ligates the two-celled stage in such a way that the plane of the ligature coincides with that of the first cleavage plane, a monster is produced with two equal heads; but if the ligature is obliquely placed with reference to this same cleavage plane, one of the componental heads exhibits a greater or less degree of cyclopia. More than this, SPEMANN has established a definite geometrical rule by which he can predict which of the two heads will be thus defective, for the

[13]SPEMANN, H. Ueber experimentell erzeugte Doppelbildungen mit cyclopischem Defekt. Zool. Jahrbücher, Suppl. VII, 1904, Festschrift für Weismann, pp. 429-470, 2 pls., 24 Figs.

defective half develops "auf derjenigen Hälfte des Keims, von welcher das Vorderende der Hauptsymmetrieebene abgewandt ist." This result he attributes to the definite loss through this procedure of the anlagen of certain median parts, which consequently never even begin to develop, and thus the parts lateral to these develop in contact from the start. This explanation is quite a different thing from a "fusion," although the results are similar, as indeed they are. The different degrees of cyclopy which he obtains, and which can be arranged in a natural series "die vom normalen Zustand durch Uebergänge zum höchsten Grad des Defects führt," thus receive a natural explanation as due to a varying amount of these Anlagen cut off by the ligature. With this basis for the explanation of cyclopy he naturally rejects the older hypothesis of DARESTE, that cyclopy is induced by a premature closing of the medullary tube, and points out the fact that we cannot know whether the cyclopy is caused by this premature closing, or whether the premature closing is the result (perhaps the earliest that is visible to the observer), of a cyclopic condition of the germ. In the medullary tube of an anterior half that afterwards develops cyclopy there is less material than in a normal one, and it would therefore naturally close earlier, since it has less material to control.

The monsters produced by SPEMANN are hard to classify, and are occasionally quite unlike those thus far known to develop in nature. They seem never to be Jani, of either the symmetrical or unsymmetrical types, although he calls them such, for a Janus must have two bodies placed opposite each other, suggesting the true composition of the faces, and the SPEMANN monsters are always single bodied, with a more or less doubled head and suggest rather the various grades of dicephaly, like my Terata I and XII. He figures one absolutely unique case (l. c. Taf. 24, Figs. 1-6 and Text-figures W, X and Y), in which there are four eye components, symmetrically placed, and all united into a single piece or complex, which the author, and creator, calls "das grosse Viererauge." From the figures, both of the entire monster and of several sections, it passes all the criteria of a typical cosmobion, and the sections are as symmetrical, and as free from all suggestion of the pathological, as are those of the series of my Teras I.

The author finally discusses the relation between artificially produced monsters and those that arise spontaneously in a state of nature, and states it as his belief that it is yet too early to herald such results as his as the definite explanation of monsters of the spontaneous class, although

he points out that the correspondence, even in anatomical detail, is often very great. "Also Beziehungen sind jetzt schon vorhanden; aber wir wissen noch nicht, wie weit wir die Kette der Ursachen zurück verfolgen müssen, um das Tertium comparationis zwischen der spontan entstandenen und der experimentell erzeugten Cyclopie zu finden."

A recent paper of STOCKARD,[14] which is in bulk merely a matter of nine pages, is one of the most remarkable of recent teratological papers, as he obtains results similar to those of SPEMANN by a radically different method. By treating the artificially fertilized eggs of the Teleost *Fundulus* with a trace of magnesium chloride the author has been able to produce, not once only, but again and again, cyclopean monsters that pass all the standards of true Cosmobia. Individual specimens show this peculiarity in different degrees, and the microscopic sections which the author shows are as symmetrical and free from pathological suggestion as are those of my incompletely dicephalous pig (Teras I) described in the body of this work.

These experiments are of the utmost importance in connection with the present paper, and quite forbid me from taking the strong view concerning a germinal variation as always the necessary cause which I might otherwise have done. I am here very willing to say that DR. STOCKARD'S work has been of the greatest value to me, and that this author has in every way been extremely kind, both in writing me from time to time concerning his experiments, and especially in placing in my hands the first proof of a paper now in press, the results of which I am thus able to take cognizance of as my last proof is leaving my hands. Lest, however, someone may be led astray as to STOCKARD'S present views by reading his early paper alone (1907) it may be permitted me to point out here that his first assumption that the cyclops monsters were produced by a gradual approximation and subsequent fusion of two lateral eyes was found by him to be incorrect, and that, in his newest paper, he has corrected this, and now affirms, quite in accordance with my position, that "the cyclopian defect . . . is present from the first in the same condition that it will continue throughout development."

Furthermore, if this claim of fusion be not true, and if such a process does not take place during each individual development, it invalidates

[14]STOCKARD, C. R. The influence of external factors, chemical and physical, on the development of Fundulus heteroclitus. Journ. of Exper. Zool, Vol. IV, No. 2, 1907.

Stockard, C. R. Archiv für Entwick.-Mech., Vol. XXIII, 2 Heft, 1907.

another early conclusion, namely, that the "lens is formed from ectoderm different in position from that of the normal lens-forming region" for in each of the specimens figured each lens component is perfectly normal with reference to the associated elements of the optic cup, and it is more likely that the ectoderm from which these were formed was that which belonged in front of the eye-anlage from the start, and that the parts missing, which normally appear between the eyes, consist as well of integument as of the other tissues. In the mammalian Cyclops monsters which I have described in the body of the text it will be remembered that this interocular integument is rolled in as the lining of a median canal, while the other parts appear either in the walls of this canal or above the componental eyeball. It would then seem that the assumption that the ectoderm which here develops into the lens components, was originally inter- or præ-ocular, rests upon no definite basis.

The dependence of this theory of a shifting lens-anlage upon that of a migrating eye-ball was also seen by Dr. Stockard during the progress of his work and in a recent number of *Science* (Oct. 2, 1908) he corrects this early position by means of the following results. It seems that in a large number of the monsters produced the defect is not cyclopy but the reduction or loss of one of the normal lateral eyes, the other being normal in all respects. In many of the monsters of this type a lens develops on the eyeless side, showing that a lens may develop quite independently of the stimulus presumably afforded by the presence of an optic cup; *i. e.*, the lens is "self-differentiating." This standpoint is quite the opposite of his earlier one, which claims that a lens develops wherever a migrating optic cup comes to rest, but is a necessary consequence of a change of position with respect to the fusion question.

Aside from the theoretical side, however, there remains the fact that the author, in a series of brilliant experiments, has been able to produce experimentally what appear to be genuine Cyclopean monsters, and that, since his method is a chemical rather than a mechanical one, and therefore more subtle in its action upon minute parts, his results have been similarly more perfect than those usually employed for the production of double monsters. Since, however, the chemical medium seems to have been applied not later than the four-celled stage, at which time the blastomeres may not have become differentiated, its action may have affected the germinal mechanism itself rather than the developing embryo, and thus farther investigation will be necessary before we can point out the true factor in the development of defective

Cosmobia, although a very hopeful line of research has been indicated by these experiments.

The voluminous paper of MALL,[15] is one of the most recent contributions to teratology, and consists of two parts, a general one, in which he discusses principles and conclusions, and gives a summary of his specimens, arranged chronologically; and, secondly, a special part, in which he describes 163 abnormal human embryos. The author's center of interest is clearly pathological rather than biological, and among this large number of abnormalities there is not a single one that is an undoubted Cosmobion. In his introduction he draws a distinction, indeed, between two groups of monsters, "those which are hereditary and germinal, and those which are not hereditary but due to mechanical injury or disease," but a farther reading shows this distinction has nothing to do with that between Cosmobia and all other kinds of monsters, as defined here. To the "germinal" group he ascribes such cases as "polydactylism" [hyperdactylism] and hare-lip, and expresses his opinion that they "cannot be produced experimentally." In the "mechanical" group he places such cases as spina bifida, anencephaly, and a few others, including cyclopia. The first group he calls "abnormal," the second "pathological." The fact that he does not mention in this connection any form of diplopage, while he includes cyclopia in the pathological group shows clearly that his classification is quite a different one from that emphasized here, and that his "germinal" group does not have any relation to the conception of Cosmobia. His insistence that the cases included in this group can never be produced as the result of an experiment is of interest here. "We must divide monsters into two groups, those in which the proper conditions to produce them are already in the germ (are therefore inherited), and those due to certain external influences which act upon the egg after it is fertilized. It is obvious that only the second group can be considered in any experiments made upon the embryo."

Although in this place he says nothing concerning double ("polysomatous") monsters, he treats them later as monsters which can be produced experimentally, thus showing that he places them, together with Cyclopia, in the mechanical or pathological class. It is also to be noted that he uses the phrase "comparative teratology" (p. 21) in a sense similar to that of comparative anatomy, *i. e.*, the study of monsters of

[15] MALL, F. P. A study of the causes underlying the origin of Human Monsters. Journal of Morphology, Vol. XIX, No. 1, February, 1908.

the lower animals in distinction from those of man. Since in the present paper, I have emphasized quite a different sort of comparison, that between monsters that represent different grades in the same cosmobiotic series, a phase of the subject to which I have given the name Cosmobiogenesis, the distinction between the two must be kept in mind.

Finally in this review of recent literature, which makes no pretense at being complete, I may mention a school whose ideas concerning the genesis of double monsters are definite, and decidedly different from those promulgated in this paper. This is the school which looks upon most or all forms of double monsters as caused by an attempt at regeneration following a fetal trauma.

Thus TORNIER[16] speaks of the "Stammindividuum" and the "Ueberzähliges Individuum," a set of terms that receive their best application in the case of those forms of double monsters in which one component is considerably smaller than the other, and it is precisely such cases that this author seems to emphasize. In the cases of equal components, especially in a typical case of duplicate twins, this theory does not prove satisfactory, and this author is careful not to make his claims for "superregeneration" too sweeping. Thus in SCHWALBE'S Jahresbericht for 1902, in referring to a paper which I have unfortunately not been able to obtain, the referant says of him, "mindestens einen Teil der Doppelbildungen will T. ebenso auf Superregeneration zurückführen", a statement which suggests a probable difficulty with symmetrical and equal diplopagi. TARNANI,[17] whose conclusions rest upon the anatomical study of 21 double monsters, 5 being mammalian, the others birds, proposes a form of the theory which gets around this difficulty, but only by assuming a theory for which there is no support in observed fact, namely, that double monsters are produced by a trauma which splits the vertebral column longitudinally and medially. After this assumed splitting, which may involve either end to any degree, or both ends, there is a regeneration of the parts lacking to either half. If, for example, such a splitting involves a girdle the separated right

[16]TORNIER, G. [Numerous articles upon experimentally produced hyperdactylism, hypermelism, double tails, etc., mainly in Zool. Anzeiger from 1897 to the present time. Of these cf. especially "Neues über die natürliche Entstehung und experimentelle Erzeugung überzähliger und Zwillingsbildungen" in Zool. Anzeiger, 19 Aug., 1901, pp. 468-504. See also his paper in the Berichte des 5ten Zool. Kongresses, Berlin, 1901.]

[17]TARNANI, I. K. Yrodstva shivotniech; (3) K'morphologie dvoiniech yrodstv. Zool. Cabinet of the agricultural and forestry institute of Novo-Alexandria, 1906.

half will regenerate a left girdle-half with the associated limb, and the separated left half will regenerate a right. In the case of duplicate twins the splitting divides the entire body into its two bilateral halves and each half regenerates the lacking half. This theory, he claims, is not at variance with any of my investigations concerning such twins, and he even finds that he can employ my diagram showing the series of double monsters leading to duplicate twins[18] to explain the theory he presents.

If one wished to seriously oppose this school of superregenerationists he could do it most properly by pointing out, first, that no instance of these frightful fetal injuries has ever been observed, and, second, that, on the other hand many embryonic stages of genuine double monsters are known, including such very early ones as those of KAESTNER, and yet, even in these, there is no trace of any fetal calamity. Surely, if such monsters were formed by any regenerative process an embryo would occasionally be found in which the process is still incomplete, but as a matter of fact, the earlier the embryo so much the more symmetrical and typical are the two components, while inequalities in the components make their appearance later on in development. This final argument shows the great need of the study of teratembryology, especially that of types belonging to the various cosmobiotic series.

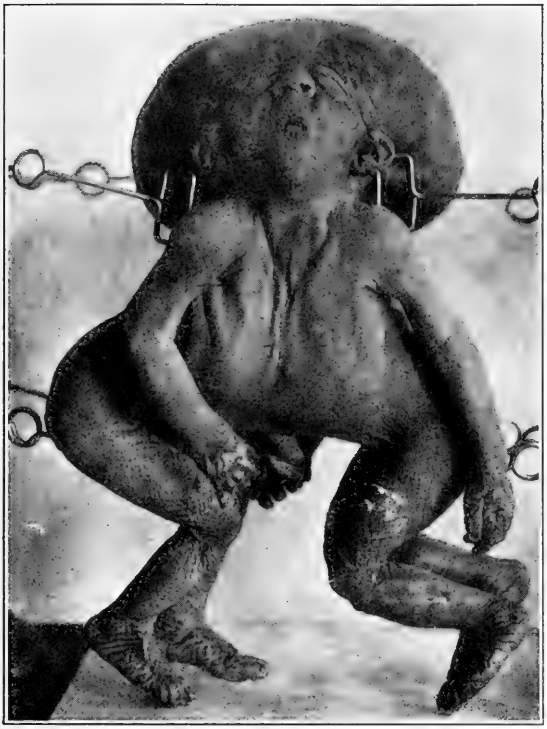
[18]Duplicate twins and Double Monsters, Amer. Journal of Anatomy, Vol. III, No. 4, 1904, Pl. A.

EXPLANATION OF ABBREVIATIONS.

a, rectus superior.
b, rectus internus.
c, rectus inferior.
d, rectus externus.
o, obliquus superior.
p, obliquus inferior.
h, retractor bulbi.
t, levator palpebræ.
s, elements associated with the levator palpebræ, perhaps parts of it.
x, *x'*, muscular elements of unknown significance.
The cranial nerves are designated by Roman numerals.

PLATE I.

FIG. 1. Photograph of the BALDWIN synote, perfect side.
FIG. 2. The same as Fig. 1, imperfect side.



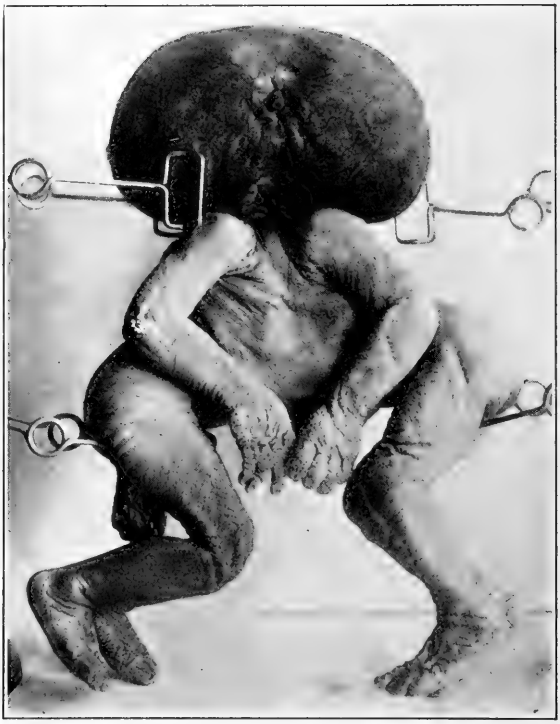


Plate II.

Fig. 1. Eye of Cyclops pig, Teras VII; from above.
Fig. 2. Same, from below; superficial.
Fig. 3. Eye of human Cyclops, Teras VI; from above.
Fig. 4. Same, from below; superficial aspect.
Fig. 5. Same, from below; deeper aspect.

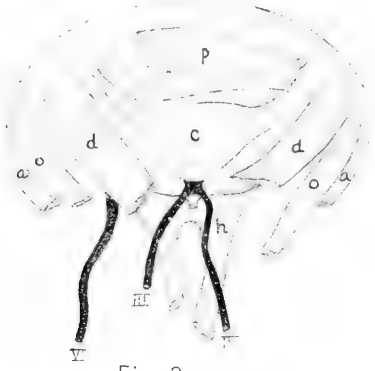


Fig. 2

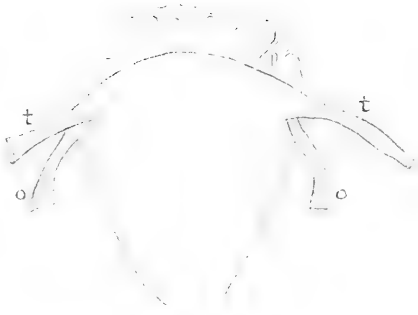


Fig. 3

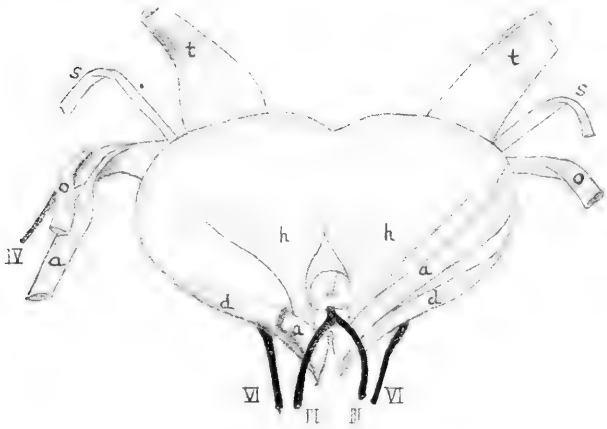


Fig. 1

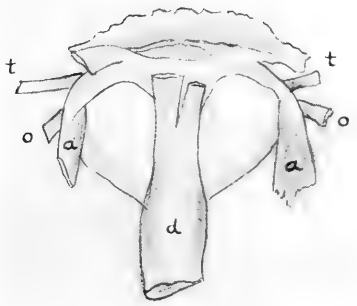


Fig. 4

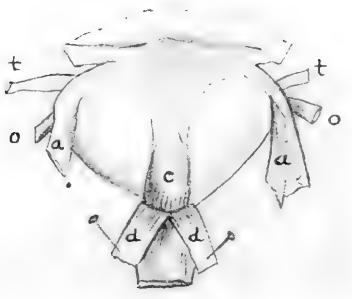


Fig. 5

PLATE III.

FIG. 6. Double eye of imperfect face of the BALDWIN synote, Teras III; from above.

FIG. 7. Double eye of diprosopic pig embryo, Teras I; from above.

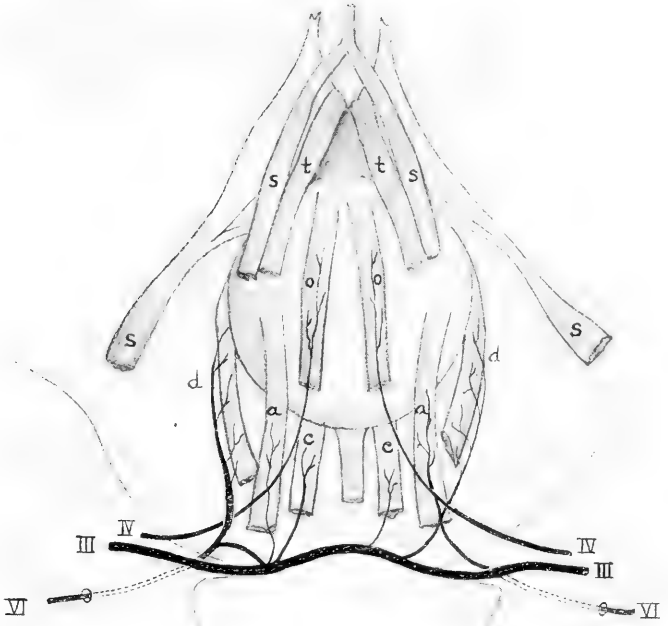


Fig 6

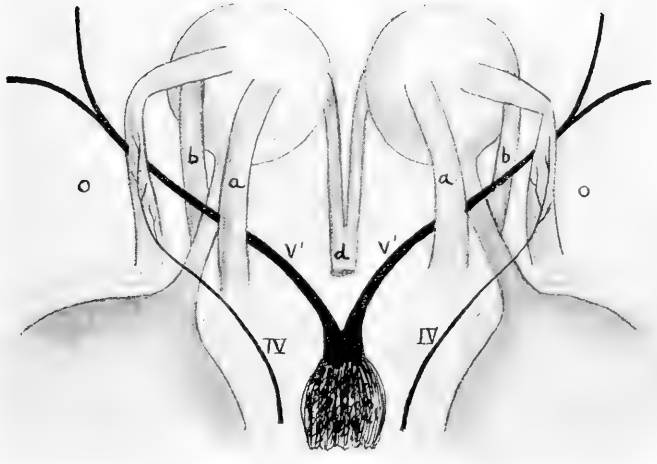


Fig. 7

PLATE IV.

FIG. 8. Same, from below.

FIG. 9. Double eye of older diprosopic pig fetus, Teras XII, from above; superficial aspect.

FIG. 10. Same, from above, deeper aspect.

FIG. 11. Same, from below; superficial aspect.

FIG. 12. Same, from below; deeper aspect.

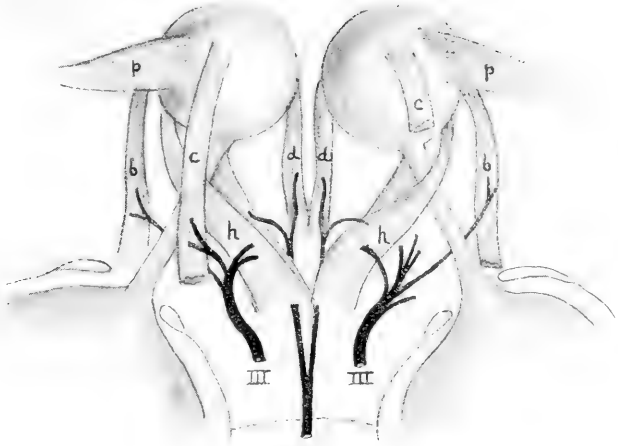


Fig. 8

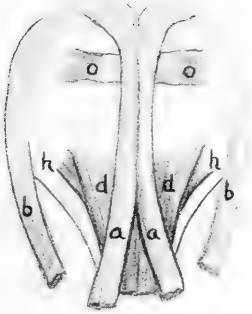


Fig. 9

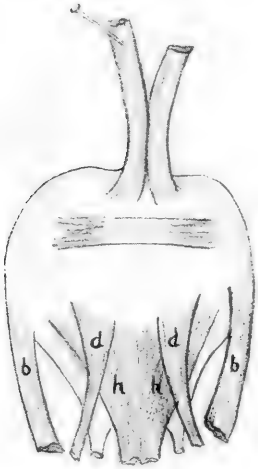


Fig. 10

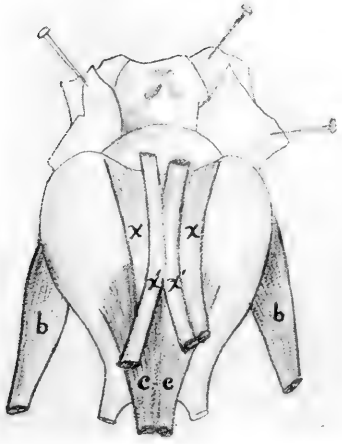


Fig. 11

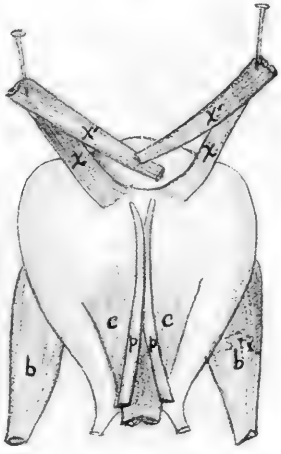


Fig. 12

HEART AND ANTERIOR ARTERIES IN MONSTERS OF THE DICEPHALUS GROUP; A COMPARATIVE STUDY OF COSMOBIA.[1]

BY

MABEL BISHOP,

Fellow in Zoölogy, Smith College, 1907-1908.

With 7 Plates and 5 Text Figures.

Outline.

I. Introduction.

Investigation of monsters, hitherto descriptive.
Comparisons now needed.
Definition of "Cosmobia."
Purpose of the present investigation.

II. Material studied.

A. Young normal pig, lamb, and turtle.
B. The following terata:—
(*a*) Pig fœtus at term, Teras XII.
(*b*) Pig embryo, 22 mm., Teras I.
(*c*) Dicephalous lamb, 3 to 4 weeks old, Teras XV.
(*d*) Two-headed turtle, just hatched, Teras XX.

III. General description of each Teras, including comparison with human monsters of similar type as represented in well-known atlases.

IV. Detailed description of the Heart and Anterior Arteries in each Teras.

[1]A thesis submitted to the Faculty of Smith College in partial fulfillment of the requirement for the degree of Master of Arts, May 20, 1908.

(1) In Teras XII.
  (*a*) Heart—Comparison with normal.
  (*b*) Anterior Arteries—Comparison with normal.
    x—Arteries of the outer sides of the two components.
    xx—Arteries of the inner (median) sides of the two components.
(2) In Teras I—Reserved for separate investigation.
(3) In Teras XV.
  (*a*) Heart—Comparison with normal.
  (*b*) Anterior Arteries—Comparison with normal.
    x—Arteries of the outer sides of the two heads.
    xx—Arteries of the inner (median) sides of the two heads.
(4) In Teras XX.
  (*a*) Heart—Comparison with normal.
  (*b*) Anterior Arteries—Comparison with normal.
    x—Arteries of the outer sides of the two heads.
    xx—Arteries of the inner (median) sides of the two heads.

V. Comparisons of the Heart and Anterior Arteries of the Cosmobia.
  (*a*) Teras XV with XII.
  (*b*) Teras XX with XV.

VI. Speculations concerning the formation of the actual conditions in the Cosmobia.

VII. The establishment of a single cosmobiotic series between normal individuals and duplicate twins.

Teratological literature is prolific with descriptive investigations of individual monsters, but prior to the present study very little has been recorded of COMPARISONS of monsters.[2] While a record of single cases

[2]Wenzel Gruber in 1815 cited certain differences of internal anatomy in two cases of "Thoracogastrodidymus," but his comparisons were few in number and very general. In 1901 R. H. Johnson compared "Axial Bifurcation" in thirteen or more two-headed snakes. These and certain obvious comparisons of skeletons, such as illustrated in well-known atlases, seem to be about all the work that has been done in this line.

is obviously essential it means the accumulation of a mass of unrelated facts, each fact interesting in itself, but valuable only as it contributes to a fuller understanding of the subject as a whole.

H. H. Wilder[3] has pointed out that a certain class of monsters may pass through a development as natural, orderly, and symmetrical as a normal individual "in accordance with the laws of growth inherent in the organism." He has granted that the monsters in this class are unusual, "abnormal" in the root meaning of the word, but they are neither deformities nor malformations, and should be carefully distinguished from deformed or pathological anomalies. This distinction Wilder has made, and he has shown that the class includes "forms with less and those with more than the normal number of parts," and that it suggests an almost complete single series of symmetrical anomalies lying upon either side of and including normal beings. If this be true, it further suggests a progressive relationship between defective and dicephalous monsters.

This separation of unusual from deformed or pathological monsters necessitates a distinct term for the former, one which is broad enough to include also normal beings. Wilder has proposed the name Cosmobion (plural Cosmobia) meaning "an orderly living being," and since he has explained the term in full I shall adopt its use without further consideration.

The verity of his assumption that there is, "First, a distinction between the symmetrical anomalies on either side of a normal being and the various sorts of deformed and misshapen monsters resulting from abnormal conditions during development, and, second, the possibility of considering in a single series both those forms with less and those with more than the normal number of parts, including also normal beings," can be proved only by the investigation of the structure of all kinds of cosmobia, and by careful comparisons of those that belong in the same series. Hence, what are needed now more than descriptive investigations are comparative investigations of material already at hand.

This paper is presented, therefore, as the first comparative study of cosmobia with the hope that it may stimulate further research in this field. I shall endeavor to show that the four cases of monsters, studied in the details of their internal anatomy, represent four progressive stages between normal creatures and complete, symmetrical duplicity,

[3]Wilder, H. H., Morphology of Cosmobia, this Journal, 1908, p. 355.

or, in other words, they represent four successive stages in the cosmobiotic series which leads through dicephali to the Tocci group, and thence through ischiopagy to duplicate twins [Wilder, 1904, series A and D].[4]

The material studied consists of:—

1. A normal pig, very young, umbilical cord still attached. [Obtained from F. D. Lambert.]
2. A normal lamb, and a normal turtle (Chrysemmys picta).
3. Pig fœtus, probably at term, diprosopus triophthalmus; Teras XII of H. H. Wilder's collection. [Obtained from B. G. Wilder.]
4. Pig embryo 22 mm. long, diprosopus tetrophthalmus; Teras I of H. H. Wilder's collection. [Obtained from F. D. Lambert.]
5. Dicephalous lamb, three to four weeks old, born at Ludlowville, New York; Teras XV of H. H. Wilder's collection. [Obtained from B. G. Wilder.]
6. Two-headed turtle, Chrysemmys picta, just hatched; Teras XX of H. H. Wilder's collection. [Obtained from A. D. Mead.]

The last four specimens are listed in the order of their sequence in the cosmobiotic series, the simplest stage first. For the sake of convenience I shall hereafter refer to these according to the number in Professor Wilder's list, as given above.

I am directly indebted to Professor Wilder for this material, and indirectly to the gentlemen whose names are bracketed. To all of them I desire to express my thanks for their contributions of material, which have made the present investigation possible.

Teras XII is a pig fœtus delivered at term, perfectly normal in appearance, except in the head region. The length of the animal from the tip of either snout along the mid-dorsal line to root of tail is 36.5 cm. (tail — 7.5 cm.). The condition in the head region places the creature at once in that class of anomalies which is more than one but less than two individuals (monstra in excessu), and represents the first stage beyond the normal in the cosmobiotic series already defined.

For simplicity in this and in the other terata, I shall designate the right head, or portion of head, as "Component A," and the left as "Component B."

Teras XII resembles closely in external doubling the human diprosopi triophthalmi of Förster [Tafel I, Fig. 1], Ahlfeld [Tafel IX, Fig. 1],

[4]Wilder, H. H., Duplicate Twins and Double Monsters, Amer. Jour. of Anat., Vol. III, 1904.

and Hirst and Piersol [page 147, Fig. 72]. The human face is so short as compared with the elongated faces of the monsters under consideration that at first sight, perhaps, the similarity is not striking, but a moment's consideration will verify the likeness. In my specimen the two snouts are quite separate, the distance between their tips being 85 mm. Both appear normal, well developed and of equal size. Two normal external ears are present, but there is no indication of a median pinna. Within the mouth cavity of each component is a fully developed tongue and several teeth. Protruding from the inner lateral side of the mouth of each component is a short papilla-like protuberance which curves slightly upward over the upper jaw [see Plate I, Fig. 1, c.].[5] This minor deformity is symmetrical, however, in each component with reference to the entire organism, being on the inner lateral side of each componental snout and growing from the same region of the roof of each mouth. The characteristic throat warts appear here as two about 18 mm. apart, and equidistant from the median axis of the body. The two outer eyes are also normal, the eyelids being perfectly formed, even to the presence of eyelashes. The median eye is made up of a double eyeball lying within a single socket. The eyelids are fringed with lashes and form an inverted heart-shaped opening, which with its associated parts is perfectly bilateral. The median eye socket is nearly spherical in shape, being 19 mm. in diameter measured transversely across the head, and 20 mm. in diameter measured in the direction of the median axis of the monster. Contiguous with the socket posteriorly and separated from it only by a thin septum of bone, is a curious heart-shaped cavity with the apex directed backward. This cavity lies between the two outer eye orbits and was filled with a protrusive mass of pathological brain tissue. Its bony floor and walls are perforated with foramina for the passage of nerves. It measures 23 mm. in diameter across its broadest part, and 25 mm. along its median axis. This is plainly a deformed cranial cavity, and the everted brain thus represents an actual deformation, which must have taken place in an early embryonic stage. It forms an exception, however, to the greater part of the organism, but is at the same time a deformity that is apt to be associated with such monsters; and all cosmobia are secondarily subject to deformities.

[5]The terms *inner lateral* and *outer lateral*, *inner side* and *outer side* are used with reference to the two sides of the components. *Median* and *lateral* refer to the whole organism treated as a single symmetrical solid.

The embryo designated as Teras I represents another progressive stage in the series under consideration. Aside from its value as a link in this series, it has a still greater value in that it records a chapter in the history of early embryonal development of a dicephalon and is, therefore, extremely important in examining the theory that cosmobia are at first perfectly orderly and symmetrical, and that the deviations found in them are due to a lack of balance in later physiological activities. Hence it has seemed best to reserve the study of this specimen for a separate paper, owing to the technical difficulties in studying an embryo of such size. I have noted it in the list of material, however, and describe it here in general in order to make the series as complete as possible.

Teras I was received by Professor Wilder in an excellent state of preservation so that he was able to make from it a set of beautiful serial sections, which have been loaned to me for study. In consequence, Plate II was made from sketches belonging to Professor Wilder, and the description of the creature in toto has been made from his notes.

Teras I corresponds to the specimen of human diprosopus tetrophthalmus represented by Förster [Tafel I, Fig. 4], Hirst and Piersol [page 148, Fig. 74], and Ahlfeld [Tafel IX, Fig. 5]. It measured 22 mm. in length, was bilaterally symmetrical and well developed. The median eye was composed of two eyeballs in one socket; no median ear was present. The two snouts were more separated than in the case of Teras XII, thus defining the embryo as representing a later stage in the cosmobiotic series—a stage between Teras XII and Teras XV.

Concerning the history of Teras XV, I know little, except that it is apparently a fully formed dicephalous lamb delivered at term, and that it lived to be from three to four weeks old. Behind the region of doubling, that is, the head region, the lamb presents externally a perfectly normal appearance. The two heads are identical in contour, and of practically the same size, their differences being extremely slight as the following measurements will show:—Length of a straight line from left ear of head A to extremity of muzzle is 10.5 cm.; from the right ear of B to same limit is 10 cm.; a similar line from the dorsal rim of the left eye orbit through middle of eye to angle of jaw measures 6 cm. in both heads. An inner lateral line across the muzzle posterior to the nostrils is 3.5 cm. long in A and 3.8 cm. in B. The distance between the tips of the muzzles is 17.3 cm.

The most noticeable difference between them is in the angle of attachment of the two heads. Certainly one head, at least, suckled

during the short life of this cosmobion, since the stomach was filled with curds. The appearance of the mouth cavity, together with the fact that the axis of head B makes almost a straight angle with the body axis, indicates strongly that this was probably the suckling head. Head A is turned at a somewhat broader angle from the median axis of the monster, and the snout is directed more ventrally than that of the other component, thus forming a more acute angle between head and chest [see Plate III]. If the mode of suckling in ruminants be recalled, it will be readily seen how very difficult it would be for this head (A) to suckle, since it would necessitate an awkward twisting and distortion of the whole dicephalous region. It seems only logical, therefore, to conclude that the head most nearly normal in position would usurp the feeding function from the beginning and be constantly favored at the expense of position of the other head, so that, although at the present stage the difference in position of the two components is not extremely great, it is quite possible to foresee that if the animal had lived longer, head A would have come to be thrust even further from the normal and to assume an almost parasitic position.[6] There is still another reason to support my conclusion, which I shall point out when speaking of the blood supply in the head region.

An approximate idea of the stage of doubling of Teras XV may be gained by comparing it with Förster's human diprosopus tetrotus [Tafel I, Fig. 7] and with Hirst and Piersol's [page 149, Fig. 77]. The two heads of Teras XV are united in the occipital region, the union involving the bones, thus resulting in a composite occipital. The ears on the inner lateral sides are separate, though the ear of head B is crowded a little above that of the other component. Behind them the heads appear at first sight to be superficially united, but closer examination shows that a union does not really exist, since hair is found growing between and behind the ears down to the composite occipital region. Both outer ears and all four eyes are normal. The brains of this dicephalus have been removed and preserved. These are also normal *per se* and conjoined only in the region of the medulla oblongata just

[6]This explains the case told me by Professor Wilder, which he recalls from memory, of an adult double-headed ox widely exhibited about twenty years ago, in which one head, although of practically the same size as the other, did not function in alimentation, but was borne habitually upon the side of the other head, which was held so as to continue the main axis of the body. In this monster the functional head was also the left.

before it continues backward as a single spinal cord. The larynges and œsophagi are separate down to the level of the shoulders (approximately).

The last stage in the cosmobiotic series under discussion that I have to present is represented by a two-headed turtle of the common variety Chrysemmys picta, just hatched, traces of the umbilicus still remaining. Its carapace is a trifle smaller than a twenty-five cent piece. Both carapace and plastron show a beginning tendency toward doubling [see Plate IV, Figs. 1 and 2, x and y]. Components A and B are disunited as far back as the shoulder girdles. Two distinct hearts are present. Upon removing the plastron and gently spreading the heads apart, a median papilla is conspicuous between the two necks at the level of the outer fore limbs, and immediately posterior to it in the mid-shoulder region on the ventral side is a tiny median nodule of cartilage with delicate muscles attached. The papilla is unquestionably the anlage of a median pair of fore limbs, and the nodule is probably the beginning of a median double shoulder girdle. Save for these peculiarities the specimen appears normal in general structure. It represents a stage between the dicephalus dibrachius and dicephalus tribrachius of the human species represented by Förster [Tafel I, Figs. 10 and 11]. Ahlfeld portrays a condition more nearly like that of Teras XX [Tafel X, Fig. 10], but Gruber depicts a stage practically identical with it [Tab. III, Fig. 2]—with this exception, that in Gruber's specimen the conical tuberosity is compressed somewhat from the front backward (page 34) while in Teras XX the compression is lateral.

It will suffice for the purposes of the present study to consider but one of the many systems of these organisms. I have selected, therefore, a system that is fundamental to the growth and development of every being, and one that appears very early in embryonal life, namely, the circulatory system. This is functional from its beginning and thus reflects the physiological needs of an organism in every stage of development. Only the arteries in the doubling region and the heart will be considered in the present paper. In each teras described I shall consider the heart and anterior arteries in detail and make comparisons with those in normal specimens of the same species and of approximately the same age. I shall then compare these vessels in the cosmobia themselves, and offer speculative explanations of the variations noted, and endeavor to permanently establish the cosmobia in the series already defined.

The heart and anterior arteries of Teras XII present a striking similarity to those of a normal pig of about the same age. With the exception of a difference in size the hearts are identical. As in the normal pig studied, the heart of XII lies within the mediastinum in ordinary relation to surrounding parts, and extends from about the 3d rib to the 7th. It is a little larger, but the Teras as a whole exceeds the normal animal somewhat in total length; the former, although a little younger, measures 36.5 cm. from tip of either snout along the mid-dorsal line to root of tail, the latter 34 cm. In bulk the bodies are about equal.

The longest lateral dimension of the heart, that is, from apex to dorsal margin of the left auricle, is 43 mm.; in the normal specimen it is only 35 mm. The diameter of the organ, measured on its anterior surface across the ventricular border of the auricles, is 30 mm. while the same diameter in the normal pig is but 25 mm. As would be expected, the cavities of the two hearts are in proportion to their external dimensions; otherwise they present no appreciable differences. In both, the foramen ovale and ductus Botalli are still present.

The great vessels that issue from the base of the heart are normal in relationship, and it is not until the origin of the external carotids is reached that any striking differences are observable [Plate V]. The right subclavian together with the right and left common carotids arise from the crest of the systemic aorta by an innominate a centimeter long. The left subclavian arises independently from the convexity of the arch about 2 mm. from the innominate. Near its beginning each subclavian gives off a vertebral artery and the other customary branches for this region. The common carotids pass in normal manner to the componental head, each giving off an inferior thyroid soon after leaving the innominate, and farther headward the superior thyroid. Slightly anterior to the superior thyroid, the common carotid gives rise to the internal carotid and the occipital by a common trunk from its dorsal wall. The continuation of the parent artery now becomes known as the external carotid. It is from this point anteriorly that variations from the normal arrangement of vessels are obvious. Topographically the arteries in this region have responded to the changed structural conditions, but physiologically they maintain a normal value to the tissues supplied by them, a statement which will be proved in a later paragraph.

For a full appreciation of the arterial condition in the dicephalous region a brief comparison of its bony structure with that of a normal

head is necessary. The double head is broader and flatter, and the snouts are shorter, so that it has a very blunt, almost square appearance in dorsal aspect. Either component measures 10 cm. from tip of snout to the inion; the head of the normal pig studied measures 14.5 cm. This additional length in the normal specimen is due largely to the rotundity in the frontal, parietal, and occipital regions, a quality totally lacking in the dicephalus. The zygomata of Teras XII are spread laterally, which, in addition to the flatness of the roof of the skull, gives the head a much broader aspect through this region, although by actual measurement the distance between the dorsal margins of the outer eye-orbits is less in the Teras than in the normal animal, the former measuring 33 mm., the latter 45 mm. Owing to this narrowness between the orbits and the spreading of the zygomata, the outer eyes of XII have a very dorsal position.

The mandibles on the inner sides of the two snouts are only half as long as the outer ones from symphysis menti to rami. Each of these inner mandibles, instead of articulating with the temporal bone of its respective component, turns its ramus at a sharp angle to the median axis of the body, and the coronoid and condyloid processes of one mandible interlock with those of the other so that an S-shaped appearance is given to the margins of the bones, and a narrow S-shaped interstice is left between them, for they are not united at this point, but merely overlap. On their inferior borders, however, at the angle of the jaws, they are united by a short symphysis. Lying superficial to, *i. e.*, ventral to the symphysis a mass of glandular tissue was removed. From its position it was undoubtedly a median parotid gland. The S-shaped passage just referred to lies posterior to the symphysis. The crowding toward the median line of the monster has forced the interlocked rami to turn outward, that is, anteriorly in the direction of least resistance, thus forming a noticeable median protuberance [Plate I, Fig. 2, f]. The maxillary bones of the inner lateral sides of the two components are spread dorso-laterally, that of A somewhat more than that of B. Between them at their posterior margins a small bone has developed which forms a shelf over the protruding rami. Posterior to this region the bones of the roof of the skull are closely knit. The median eye-socket and the adjoining brain cavity lie in the median axis of the monster and largely between the outer eye orbits.

I have already called attention to the fact that the common carotid takes the name external carotid immediately after giving off the internal

carotid and the occipital artery. Normally the external carotid turns abruptly dorso-laterally beneath the digastric muscle, crosses the caudal extremity of the anterior cornu of the hyoid bone between it and the ventral end of the par-occipital process, whence it turns again dorso-anteriorly and divides into its terminal branches, the internal maxillary and the superficial temporal.

Near its origin the external carotid gives off the lingual, which crosses the cranial portion of the anterior cornu of the hyoid and passes to the tip of the tongue imbedded in its tissue and gives off many collateral branches. Close to the lingual arises the facial (external maxillary), which at first lies deep beneath the digastric muscle and submaxillary gland, to which it sends small branches. It sometimes gives origin to the sublingual. The facial then emerges from beneath the gland, courses parallel to the jaw for a short distance, turns abruptly, and mounts the side of the face along the anterior margin of the masseter muscle, whence it divides at an obtuse angle into the inferior and superior labials, which supply the muscles of the lower and upper lips respectively. At the ventral extremity of the par-occipital process the external carotid dispatches a collateral branch, the posterior auricular, to supply the posterior region of the external ear and the muscles of the nape of the neck. Immediately anterior to the posterior auricular, the main artery makes a second turn at the angle of the jaw, laterally and anteriorly and bifurcates into its terminal branches, the larger one in the internal maxillary, the smaller, the superficial temporal. The latter vessel gives off the anterior auricular, and sometimes the masseteric. In my specimen of normal pig, the masseteric arose from the anterior auricular.

A comparison of the above description with Plate V will show that the same distribution is found in the neck and on the outer sides of the componental head of Teras XII, and that variations from this normal condition are confined to the cramped and altered region between the two inner sides of the components.

If attention is given to component B for a moment, it will be seen that at the point where the left common carotid gives off the left external carotid, the main artery is apparently continued anteriorly and medially by curving slightly across the anterior cornu of the hyoid to a position along the median axis of the body, whence it continues forward and passes between the two componental snouts, winding through the S-shaped passage between the overlapping rami and emerging upon the inner lateral and dorsal sides of the face. Opposite the cranial extremity of

the anterior cornu it gives off a large branch which distributes itself in the tongue of component B after the manner of a normal lingual artery, for such it is unquestionably. This lingual sends off a smaller but conspicuous branch to the symphysis menti, which branch enters the mandible through a foramen on its inner lateral side close to the symphysis. These foramina, one on each inner lateral side of the symphysis, are quite large and conspicuous in young pigs. A bristle passed through one of them emerged from the most anterior of the mental foramina. In three specimens examined a definite branch from the lingual passed into each of these foramina, yet I failed to find them named in any of the literature, or given particular mention. Therefore, in order to designate the conspicuous branch that passes into them, I shall refer to them as the sub-symphysial foramina. Both the lingual and the sub-symphysial branch give off many small twigs to the muscles of the tongue. About a centimeter farther forward the main artery gives rise to a pair of lateral branches; one, another lingual with its sub-symphysial branch to supply the inner side of the tongue of component B, the other suggests the corresponding artery to the inner side of the tongue of component A, of which only the sub-symphysial branch has been preserved. The hypothetical former condition is represented in the plate by a dashed line (x'). The parent artery sends off from its dorsal wall many small collateral branches in pairs, which supply the inner lateral borders of the two tongues. Immediately anterior to these a single branch is given off, which proceeds dorsally in the median plane and passes into the interior of the head just posterior to the angle of the united mandibles. This could not be followed beyond this point without spoiling the specimen for further investigation. In the Plate it is deflected to one side in order to render it visible. The distribution of the branches of the main artery thus far establishes it as a Median Compound External Carotid, fulfilling a normal function for component B and in addition partially supplying component A. The only striking deviation from the normal distribution in component B is that both linguals arise from the same external carotid, instead of one lingual from each. The remainder of the ventral surface of component A is supplied by collateral vessels from the right common and external carotids as would be expected normally. Note, however, that there is a reduction in the tongue supply. It is nourished by only one lingual artery, which has a normal origin but does not give off a sub-symphysial branch. It will thus be seen that the tongue of component A depends

solely upon its outer lingual artery for nourishment. After giving off the single dorsal branch which strikes into the interior of the head, the median compound external carotid continues forward through the S-shaped interstice and emerges upon the face as already described. At the first curve of the S it gives off two lateral branches, one turning to the right to course over the inner lateral and dorsal surfaces of the face of component A, the other turning to the left to a like distribution over component B.

The subsequent course of their lesser branches is strikingly identical. Each gives off near its origin a delicate branch which may be a pharyngeal (?), and just beyond a very short artery which almost immediately bifurcates into two terminal branches that break up in the muscles at the angle of the mouth. These branches are obviously superior and inferior labials, therefore their stem is a very much shortened facial, which is quite in keeping with the anatomical condition, for the shortness of the inner mandibles brings the ramus and the angle of the jaw in a perpendicular line to the angle of the mouth. Immediately beyond the facial a long slender artery passes dorsally and caudally over the roof of the cranium and loses itself in the tissues around the outer periphery of the median eye. These terminal twigs had not taken the injection mass, and it was difficult to trace them thus far, but there is no question in my mind but that the artery which gives them origin is a superficial temporal. Near its beginning this vessel gives off an insignificant branch which ramifies the tissues at random over the median dorsal region anterior to the median eye. This may be an anterior auricular which has no legitimate distribution, owing to the fact that there is no median ear to call it into normal physiological service. Beyond the root of the superficial temporal an attenuated branch from the external carotid mounts to the dorsal surface of the snout and unites with one of the two branches which ramify this region and terminate in a single stem issuing from a foramen. The position of this foramen together with the fact that from it also issue a few nerve fibers establish it as a greatly reduced infraorbital foramen. A similar foramen, exhibiting identical relationships, is also present upon the inner side of the other component. Obviously, then, the blood-vessel is an infraorbital artery with its terminal branches, and the attenuated communicating branch is merely an anastomosing branch from the facial.

Having given off the two lateral branches, whose lesser branches have just been followed over the face, the main artery continues its serpentine

path between the overlapping rami and emerges at its most dorsal part, only to turn abruptly at a sharp angle and disappear into the interior of the cranium between the projecting rami and the protruding shelf of bone above them. Again the value of the specimen for future study opposed further investigation and I did not open the cranium to follow the course of this artery. Yet I think no serious check has been placed upon its identification, for from the data at hand I feel that it may be safely interpreted as a MEDIAN COMPOUND INTERNAL MAXILLARY. Although the median eyeball had been removed with no special reference to the preservation of underlying parts, there are still present within the orbit traces of nerve fibers and other tissue. On the anterior surface of the orbit, on either side of the median axis, and close to the roof of the cranium are two minute foramina. Issuing from them are two black threads, so to speak, which I mistook at first for discolored nerve fibers, but which upon closer examination proved to be injected blood vessels. It takes but a slight stretch of the imagination to suppose them branches of an internal maxillary, which normally divides within the eye-orbit, and such a vessel is the one in question. If this be granted, it is not difficult to trace back to their parent artery the intercranial course of the infraorbitals, whose external ramifications have already been followed, and whose origin is known to be from an internal maxillary. These two suppositions seem to me to render valid the identification of the artery under discussion as a MEDIAN COMPOUND INTERNAL MAXILLARY. The hypothetical relations are indicated in the plate by dotted lines.

It remains to be demonstrated how the changes in the mid-region have come about, and their significance. In this cosmobiotic series of organisms leading through dicephali and ischiopagy to duplicate twins, Teras XII represents one of the earliest stages. This specimen is developed but a little beyond normal and the doubling ceases externally at about the level of the angle of the mouths. Naturally the blood vessels of this region, as well as the other parts, exhibit the doubling also. As a cosmobiotic head passes beyond a single individual in development it grows further and further away from that single stage, but nearer and nearer to two separate and distinct heads. It should be borne in mind that I do not mean that these progressive changes take place in a single individual. Each represents but one stage in the series, individual links in a chain, which may be made up of an infinite number of links of which the last two represent duplicate twins.

Since the arterial system supplies all parts of an organism, it forms by its distribution an outline of the entire anatomy of the individual,

and since the present study is designed especially to delineate a series of consecutive stages of a given cosmobiotic series, the arterial system will illustrate the theory emphasized in this paper that such a series may be conceived as a gradual separation of component halves beginning with normal individuals and ending with duplicate twins. Of such a series, which my specimens represent, the monster in question, Teras XII, comes first and represents an initial stage in the splitting of the organism, a process which here involves only the anterior part of the head. Therefore there is present in this creature the forepart of two separate heads, that is, two snouts and both sides of two faces, but owing to the lack of division of the remainder of the head the inner sides of the two faces are close together and all intervening tissues are greatly cramped. Nevertheless, such division as is present is responsible for the physiological necessity of a double blood supply to the divided region, and nature has responded to the call as best it could. The division has not yet extended far enough posteriorly to demand two separate external carotids to the inner sides of the two components, but one median vessel has been able to meet the emergency by giving off double the normal number of branches, one moiety of which supplies component A, the other component B. Thus the median external carotid is made up of elements of the inner external carotid of A and also of B (A's left and B's right), and for this reason I have called the main median artery "compound."

Normally a common carotid, external carotid, and internal maxillary form a single compound curve. If such vessels should develop in a space too crowded to permit them to assume their natural curve, they would become elongated into a straight tube. This is the condition in the median region of Teras XII; the median compound external carotid and internal maxillary have been forced to develop as a straight tube owing to the cramped condition in this region.

An examination of Plate V will demonstrate that in the neck region and on the outer sides of the componental head the amount of space and other conditions are normal, and here the arteries are distributed in normal manner. This is also true in the median region wherever the topographical changes leave room for normal behavior, as for example, the distribution of the branches of the median compound external carotid which supply the inner lateral and dorsal sides of the two components. Only a single hypothetical branch, or capillary connection between the median compound external carotid and the outer external carotid of

component A is necessary to complete the symmetrical condition that I believe existed at an earlier period in the development of this Teras. This branch is indicated in the plate by a dotted line [Plate V, x]. Some secondary variations are present, for example, the origin of both linguals of component B from one external carotid, instead of one lingual from each, and the loss of one lingual artery by component A, but these are of minor importance and are the results of continual solutions of physiological problems during the entire development of the organism.

While it cannot be denied that this creature is "unusual," it is obvious, nevertheless, that it is perfectly symmetrical, that with the exception of the everted brain it is in no sense pathological, but that on the contrary it has developed according to the laws of an orderly living being, and therefore has a right to the title "Cosmobion," and a definite place in the cosmobiotic series with which this investigation is concerned.

As the doubling in the dicephalus group increases, so also the divergence of the two components increases. This is well illustrated by the two-headed lamb (Teras XV), which represents the next stage in the series. In this specimen the heads are separate as far back as the occipital region. Each head has its normal parts and organs, *e. g.*, two eyes, two ears normally placed and normally developed. Obviously, then, the doubling has progressed more posteriorly than in Teras XII. The following description and comparison will show that the blood vessels have perfectly reflected these other anatomical changes.

The heart of the dicephalous lamb is single, and fully three times the size of that of the cosmobiotic pig, but is proportionate to the size of the lamb. Its size may be easily approximated by the following measurements taken along the same axes as in the double pig:—the longest lateral line measures 6 cm., its transverse diameter across the anterior surface is 5 cm.[7] In shape the heart of Teras XV is identical with that of a normal lamb, and may be said to be shaped like an inverted pear, but it differs from that of a pig, the heart of which is roughly acorn-shaped. It is more elongated and pointed than a pig's heart, its posterior face is slightly more concave, its right face is less bulging, and it has not the appearance of having two apices that is so conspicuous in a pig's heart. In both, the auricular appendages are rather flat. The heart of the double lamb extends from the first rib to the fifth, which by com-

[7]It should be mentioned here that in all the terata the measurements of the heart, and its position in the thoracic cavity, were taken with the specimen in a dorso-cumbent position and after long preservation in alcohol.

parison with that of Teras XII is more anterior in position. A perpendicular lateral line from apex to middle of the base of the organ passes through the second intercostal space. Thus it is seen that its longitudinal axis is nearly at right angles to the median axis of the body, while that of the double pig is directed antero-posteriorly. The apex of the heart lies a little to the left of the mid-line of the body against the sternal wall, which at this point presents externally a slight bulging.

The exterior of the heart appears in general quite normal, but its interior and the great vessels arising therefrom present some interesting variations, traceable to early embryonal conditions as will be shown later. The right ventricle is small in proportion to the size of the heart, occupying about a third of the ventricular mass. The left ventricle is correspondingly larger, occupying the remainder of the ventricular portion. It is a curious fact that the ventricles (and the auricles) of Teras XV have seemingly changed position with those of a normal heart, for in the Teras the right ventricle has the position and extent of a normal left ventricle, and vice versa for the left ventricle (and auricle). The right ventricle has a very thick wall, equal to that of the left ventricle. Possibly the greater extent, and therefore the greater capacity, of the right ventricle and the greater thickness of its walls are compensations for its lack of size. It has an extremely posterior position, so much so that in a median longitudinal section it is not visible at all, but shows only in cross section. The altered position of the ventricles suggests an unusual twisting during the early development of the organ, but the heart gives no other evidence of such a proceeding. The right auricle is proportionally smaller than the left, and each opens into its respective ventricle in normal manner. A partially obliterated foramen ovale is still present. So far as position and extent are concerned, it would be very easy to mistake the right ventricle for a normal left and the left for a normal right, but the auricles and the great blood vessels that communicate with them respectively leave no room for error in identification. In the following description I shall use Chauveau's nomenclature, since the origin of the arteries from the heart differs somewhat in lamb from that in pig, and a slightly different nomenclature is used. The differences are those characteristic of ruminant and non-ruminant animals.

In a normal lamb the first part of the systemic aorta is termed the aortic trunk. This arises from the basal portion of the left ventricle and very soon divides into an anterior and posterior aorta. The anterior aorta is short and terminates in the right and left brachial (sub-clavian) arteries. The right subclavian, near its divergence from the left, gives

off anteriorly a short trunk, the cephalic, which in turn divides into the right and left common carotids. The main difference to be noted in this condition and that found in normal pig (also in Teras XII) is that in the latter no anterior aorta exists, since the sub-clavians arise independently from the aortic arch. The common carotids pass to the head in normal manner, giving off en route the customary branches.

The systemic aorta of Teras XV arises as an aortic trunk from the basal portion of the left ventricle, and from the first is directed slightly dorsally and posteriorly, thus beginning immediately at its origin to arch gently backward. It curves over the root of the left lung and crosses the trachea and œsophagus diagonally to the right. About opposite the third rib the arch is completed, the aorta resumes a median position and continues backward as the posterior aorta, lying along the mid-ventral surface of the vertebral column deep within the dorsal mediastinum and giving off in its course the usual intercostals. The aortic trunk is conspicuously large (diameter 15 mm.), but tapers gradually as it is continued backward into the posterior aorta whose uniform diameter is 11 mm.

The pulmonary artery arises from the basal end of the right ventricle, but owing to the position of the latter, the origin of the pulmonary trunk is immediately posterior to that of the systemic aorta, and not anterior to it as it would be normally. Therefore the convexity of the heart between the anterior margins of the auricular appendages is pronounced in Teras XV by the systemic aorta, and not by the pulmonary artery. Also as a result of the position of the right ventricle, the pulmonary artery of Teras XV courses parallel to the aorta on its posterior side instead of accompanying it on its right side, and is covered in part by the right auricular appendage, normally by the left. About a centimeter and a half from its margin the pulmonary artery bifurcates into a right and left branch, each of which redivides into smaller branches at the root of the lung and enters it together with the bronchi. Near the crotch of the bifurcation each pulmonary branch gives off twigs to the bronchus. The trunk of the pulmonary still retains a well defined ductus Botalli, six millimeters in diameter, which unites with the posterior aorta a few millimeters posterior to the anterior aorta. Between the two the aortic arch presents a left lateral constriction, analogous to the "aortic isthmus" in human beings.[8] The aortic trunk is short and at its posterior ex-

[8]Quain, Elements of Anatomy, Vol. II, Part II, Angeiology, p. 384. The diameter of the aorta at the isthmus in Teras XV is 9½ mm., and immediately anterior and posterior to it 12 mm.

tremity divides into the anterior and posterior aortæ. The anterior aorta is likewise short and terminates in the left subclavian and a cephalic, which in turn bifurcates into right and left common carotids to supply HEAD B. The right subclavian, instead of arising from the anterior aorta at the origin of the left, has retained a dorsal origin, and arises from the dorso-lateral (right) wall of the posterior aorta at the extremity of the aortic arch. It crosses the dorsal surface of the trachea and œsophagus diagonally and to the right and arrives at a position opposite the origin of the left subclavian. It then arches over the first rib on the right side of the body and continues its course to the right forelimb in normal manner.

Head A is not supplied by any portion of the arterial system thus far described, but has an independent supply direct from the heart. Parallel to and close beside the aortic trunk there arises from the left ventricle another artery of lesser diameter (8 mm.), which is continued anteriorly and to the right of the trachea to a point a little posterior to the origin of the common carotids destined to supply head B. Here this new vessel also bifurcates into right and left common carotids to supply HEAD A. Upon making a longitudinal section of the heart a few millimeters to the normal right of the median axis, a small cavity was opened up which is in communication with the left ventricle by means of a semi-lunar valve. During normal development the semi-lunar valve marks the division between ventricle and aortic bulb, and thus the new cavity is shown to be a new bulbus arteriosus. Therefore the vessel arising from it is a second aorta, and since it is continuous with the cephalic trunk, it may be termed an *aorto-cephalic trunk*. It gives off no branches, since all that are needed are given off by the systemic aorta which supplies component B, but terminates in a right and left common carotid destined to supply head A. Just above the semi-lunar valve but posterior to the root of the aorta-cephalic trunk, there arises from the bulbus a small, short artery which crosses over to the other aortic trunk on the posterior side, and unites with it about 7 mm. from its root. This branch is probably the remnant of a primitive arterial arch, as will be shown presently.

The independent arterial supply to head A is of great importance to the cosmobiotic theory. After following the course of the arteries in the two heads, I shall offer hypothetical explanations of the conditions found in the roots of the great blood vessels, and point out their significance.

Since there are present in Teras XV two completely separated heads, each with its normal parts, the heart is called upon to furnish a double

blood supply, not by compromise as in Teras XII where a median compound vessel was sufficient to meet the emergency, but by providing two separate and distinct head supplies. Therefore, the course of the arteries from the origin of the four common carotids is almost identical in the two heads, and furthermore, the distribution is in general as normal as it would be in two separate lambs standing side by side [see Plate VI]. The distribution of the head arteries is also very similar to the condition in normal pig, the chief differences being changes characteristic of ruminant and non-ruminant arteries. It does not seem necessary, therefore, to describe in detail the course of these arteries, but only to call attention to salient differences. The first chief difference between pig and lamb, normal and cosmobiotic, is that in pig there is no anterior aorta. The subclavians arise independently from the aortic arch; the right subclavian gives rise to the common carotids by a short innominate trunk, which is practically the same as the cephalic trunk of the lamb, only shorter. Chauveau[9] claims the absence of an internal carotid artery in sheep, which is compensated by a branch from the occipital. Since the internal carotid frequently arises by a common trunk with the occipital, I am inclined to think that Chauveau's occipital branch and the internal carotid are one and the same vessel.

The difference in origin of the linguals and facials can scarcely be called a characteristic difference, for they arise by a common trunk from the external carotid quite as frequently as by separate origins. Aside from the rise of the great arteries from the heart, the differences between corresponding arteries of pig and lamb that have been pointed out, and others that have not, are of minor importance, since they apply only to origin and not to distribution, and occur quite as frequently in normal organisms as in monsters.[10] Between heads A and B of Teras XV only two differences are worthy of attention. The most striking is the absence of one lingual in head A; the one present courses along the middle of the tongue instead of to one side. This single artery to the tongue of head A is the point I had in mind when I stated earlier in the paper that there was a third reason for supposing that head A had not suckled during the life of the cosmobion. If this tongue had functioned very

[9]Chauveau, The Comparative Anat. of Domesticated Animals, p. 592.

[10]Chauveau. Ibid., p. 520. "In a purely anatomical and physiological point of view (however) these anomalies are of no moment, as it matters little whether the blood comes from one source rather than another . . . provided its relations are not altered, and the principle of immutability of connections is maintained."

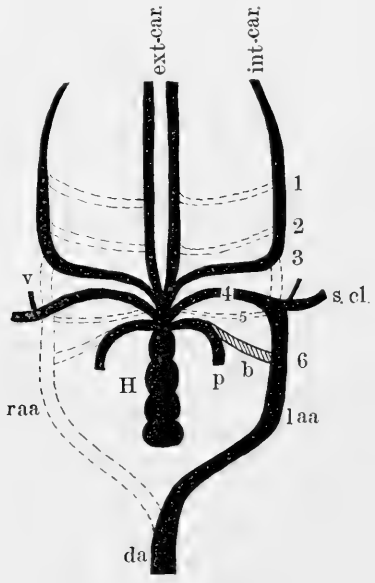
much it would have needed a normal blood supply to maintain it in a healthy, vigorous condition. The second difference referred to is the apparent absence of an independent occipital of its own to supply the dorsal neck region on the inner side of head A. It is apparently supplied by an occipital arising by a common trunk with the one supplying the inner side of head B. Both are greatly attenuated and insignificant.

The subclavians of the double lamb give off their normal branches, but since the right subclavian arises from the dorsal aorta, it does not give origin to its branches near its beginning as does the left, but from that portion of it which brings the branches in normal relation to the parts supplied by them [Plate VI].

How are the arterial conditions in Teras XV to be explained? The conditions in the head region have already been explained, so that all that remains to be accounted for here are the arteries that lie in the transverse zone between the heart and the region of the complete doubling. This consists mainly of an extra aortic trunk, the aorto-cephalic. It is readily seen that if in accordance with the theory set forth in this paper, the doubling of Teras XV had extended much farther posteriorly the heart as well as the anterior arteries would have been involved and thus there would have been ultimately two separate hearts, probably contained in two separate pericardial chambers. It is possible, however, to conceive of a degree of doubling which involves part, but not all of the heart, and it seems probable that this is the case in Teras XV. But in order to understand such a condition and interpret it correctly one must imagine this condition, not as in an adult heart, but as in the embryo.

Since the early formation of the heart is the same in all vertebrates, and since the arteries in all develop from six primitive arterial arches, it is possible to suggest the changes that have taken place in all the terata by diagrams representing the varying degrees of doubling and the changes that have taken place in the primitive arches, for all are capable of explanation by referring back to the normal vertebrate condition. The usual diagrammatic representation of the normal transformation of the six primitive arches is classic, and to compare with this I have reduced the actual condition in the terata studied to similar diagrams representing the way in which the primitive arches probably existed in these creatures. For the sake of easy comparison I insert here a text figure illustrating the normal mammalian changes in the primitive arterial arches (Text figure 1). The solid black lines in all the diagrams represent the permanent condition in the specimen, the dotted lines the

arches or parts of arches sacrificed. As text figure 1 represents the underlying condition in normal mammals, so also text figures 2 and 3 represent the underlying condition in Teras XII and XV respectively, for as soon as the arches began to appear in the Terata they were in the form represented in the diagrams. In other words, they did not make their appearance as in a normal mammal and later acquire duplication, but on the contrary, the doubling of the arches was present from their beginning.



Text Fig. 1. Diagram showing the transformations in the primitive arterial arches in normal mammals.

1, 2, 3, 4, 5, 6, The six primitive arterial arches; ext. car., External carotids; int. car., Internal carotids; H., heart; p., Pulmonary artery; b., Ductus Botalli; s. cl., Subclavian; V., Vertebral artery; raa., Right aortic arch; laa., Left aortic arch; da., Dorsal aorta; mcec., Median compound external carotid (Teras XII); ab., Aortic bulb divided (Teras XV); x., communicating branch between components A and B (Teras XX).

At the stage which the diagrams represent the heart is still a median straight tube, its most posterior portion being the sinus venosus, the next anteriorly the common atrium which communicates freely with the common ventricle, and most anteriorly the aortic bulb which is continued into the aortic trunk. The aortic trunk bifurcates, each moiety arching backward to the median axis of the body posterior to the heart,

whence it very soon unites with its fellow to form a single tube, the dorsal aorta. Anterior to the bifurcations of the truncus arteriosus three arterial arches have developed in turn, and posteriorly two, making in all the six primitive arterial arches. Briefly the normal changes that take place in these arches in mammals are:—

(*a*) The first and second arches disappear.

(*b*) The dorsal trunk between the third and fourth arches disappears.

(*c*) The third arch together with the anterior portion of the dorsal aorta thus cut off forms the internal carotid.

The ventral trunk anterior to the origin of the third arch forms the external carotid, and the intervening ventral portion between the third and fourth arches becomes the common carotid.

(*d*) The left moiety of the fourth arch together with the posterior portion of the left dorsal aorta becomes the permanent mammalian aortic arch.

(*e*) The fifth arch, which from the beginning is rudimentary, disappears.

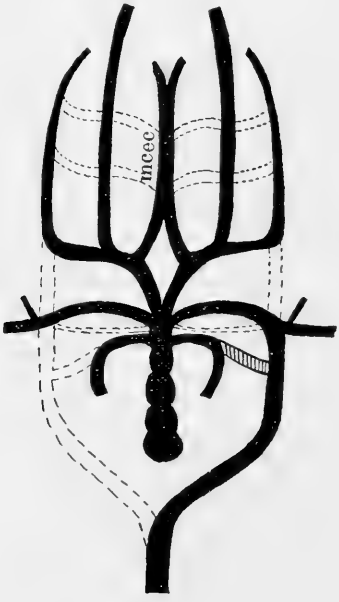
(*f*) A portion of the sixth arch becomes the pulmonary artery. On the right, the remainder of the arch disappears, but the corresponding portion on the left side remains in connection with the permanent aortic arch during fœtal life as the ductus Botalli.

(*g*) When the aortic bulb divides longitudinally, the sixth arch comes to communicate with the right ventricle, and the remaining vessels with the left ventricle.

In the diagram representing the condition in Teras XII at this early embryological period (text figure 2), it will be seen that the heart and arches six, five and four are normal, and that as the divergence anteriorly begins to be felt, the anterior arches show corresponding changes, and in proportion as the amount of duplication is slight, so also the modifications of the arterial arches are slight, the only difference from normal being an increase in the ventral trunk of the third arch, which anteriorly gives rise to the median compound external carotid.

In the double lamb (Teras XV) it is obvious that there has been from the beginning a greater degree of doubling of these elementary blood vessels. There is present the beginning of two hearts and two sets of arterial arches (Text figure 3). Already the aortic bulb has divided, and the semi-lunar valve has developed between the ventricle and the new bulbus arteriosus. Posterior to the bulbus the heart shows no duplicating tendencies. The communicating branch which passes from one aortic

trunk to the other is probably a portion of the fifth arch that has persisted, for its origin from component A is above the semi-lunar valve and its insertion into component B is below the normal aortic arch. It has no connection with the pulmonary system, and therefore cannot be a portion of the sixth arch. The dorsal origin of the right subclavian is an anomaly of common occurrence (Quain), but the present case differs from the usual condition under such circumstances in that the dorsal portion utilized in forming the subclavian also gives rise to the right

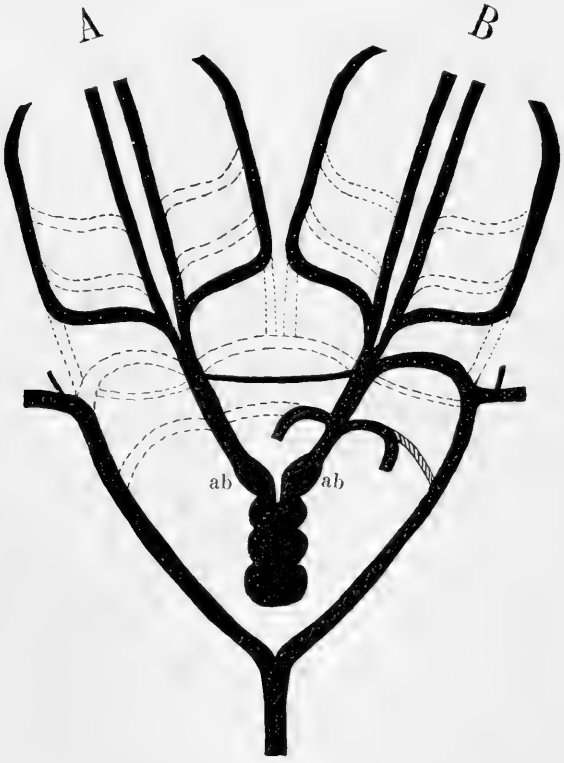


Text Fig. 2. Diagram showing the transformations in the primitive arterial arches in Teras XII.

vertebral, whereas usually, under a like condition, the anterior portion of the right fourth arch becomes the vertebral. The first, second and third arches are obviously normal, but in duplicate. Such an embryonal vascular condition, although suppositional, would fix the future development of the organism of which it is a part, and, it seems to me, would terminate in such an adult condition as exists permanently in Teras XV.

The next and final cosmobion in the series that I have to present will demonstrate the hypothesis that as the doubling extends farther and farther posteriorly, the heart becomes more and more involved. This

stage is represented by a two-headed turtle, Teras XX. Its gross anatomy has already been described and needs no repetition. The blood vessels in this organism were followed with some difficulty, owing to the smallness of the specimen and the fact that the blood vessels were not injected, and the animal had been preserved by being thrown alive into alcohol of



Text Fig. 3. Diagram showing the transformations in the primitive arterial arches in Teras XV.

unknown strength before it came into the hands of scientific persons. Although phylogenetically Teras XX is more primitive than the other specimens studied, its position in the cosmobiotic series is not altered, for cosmobia are not limited to any one genus and species, the qualities involved being applicable to all vertebrates.

The duplicating tendency has progressed so far in this specimen that not only the heads, but also the necks are entirely separate and distinct

as far posteriorly as the shoulder girdles, where, it will be remembered, the anlage of a median pair of fore-limbs and a median double shoulder girdle are present [Plate IV, Fig. 3, a and b].

If the cosmobiotic theory is tenable, the heart of Teras XX may be expected to show a greater degree of doubling than does the heart of the preceding Teras. An examination of Plate VII will support this hypothesis, for it is at once obvious that there are present two separate hearts, each supplying a complete normal set of arteries to each component and connected one with the other only by a very short communicating branch between the inner subclavians which pass to the anlage of the median pair of fore-limbs. For the sake of clearness the arteries have been separated somewhat more in the illustration than they are in the specimen, and the sinus venosi and branches of the dorsal aorta have been omitted.

A description of a normal chelonian heart will suffice for the hearts of Teras XX, and for the sake of easy comparison I repeat here very briefly the conditions found. The heart of a turtle has but three chambers, one ventricle and two auricles. The ventricle is not divided by a septum into two complete cavities as in the mammals studied, but only partially so, hence there is a vital difference in the character of the blood passing to and from the heart. But it is outside of the limits of the present investigation to go into details of reptilian versus mammalian circulation, since the difference would have no direct bearing upon the cosmobiotic series. Owing to the smallness of Teras XX, it would have been impossible to study the interior of the hearts without making serial sections, and that seemed hardly necessary, for all the other circulatory conditions being normal, it seems wholly probable that the interior of the hearts is also normal. The right auricle receives venous blood from the body, the left the oxygenated blood from the lungs through the pulmonary veins. The single ventricle lies posterior to the auricles and is partially divided into a right and left portion, the right one being known as the cavum pulmonale. The left portion is the larger of the two and is subdivided into a cavum arteriosum on the left, and a cavum venosum on the right.

The pulmonary artery of each component arises as in normal from the cavum pulmonale and almost at its beginning bifurcates into right and left branches, which supply the right and left lung respectively. The right branch passes dorsally to the other vessels arising from the right hand portion of the ventricle and courses parallel to the right aorta for some

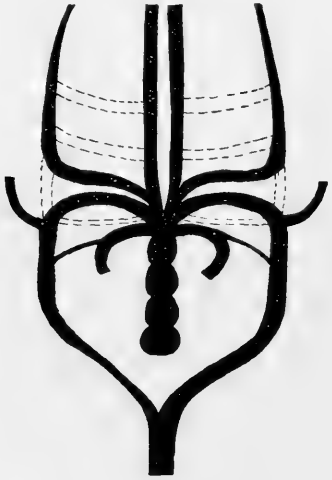
distance, it then crosses ventrally to the right aorta and enters the lung. The left pulmonary branch passes more directly to its lung, but courses parallel to the left aorta for a portion of the way. The artery arising apparently next to the pulmonary is the left aorta and the third vessel to take origin from the ventricle is the right aorta; each crosses the other close to the heart. Thus it is seen that in turtles (and all other reptiles) two aortic arches are present, in mammals only one.

The right aorta arches over the right pulmonary artery and bronchus, and receives a communicating branch from the left aorta about opposite the fourth dorsal vertebra. The left aorta passes round the left bronchus and pulmonary artery to a dorsal position and ends by dividing into three main trunks, a gastric artery, superior mesenteric, and a gastro-duodenal artery. A portion of the gastric artery continues as the communicating branch to the right aorta. In the plate these branches have been omitted in order to render the illustration more simple.

The right aorta is covered close to the heart by an innominate artery, which it gives off. The innominate divides almost immediately into the right and left subclavians, and the right and left common carotid arteries. The subclavians are at first ventral to the carotids, but soon diverge. Each gives off a minute thyroid, an ascending cervical, a vertebral, axillary and brachial arteries. The remainder of the subclavian continues posteriorly along the edge of the carapace in the hollow of the marginal plate as the internal mammary, and anastomoses with the epigastric. It was impossible to follow all of these subclavian branches in Teras XX, but otherwise Plate VII demonstrates a perfectly normal arterial distribution to each component, the only connection between the duplicated parts being through a short communicating branch between the inner subclavians (Plate VII, x).

If the vascular condition in the double lamb be recalled and a comparison be made between it and the two-headed turtle, it is at once obvious that in the latter the division of the component parts of the heart and anterior arteries has progressed farther. In the lamb only the bulbus arteriosus had divided, but in the turtle the division has extended through the common ventricle, auricle and sinus, thus dividing the heart into two identical halves, or in other words, forming two distinct hearts, each destined to give a normal arterial supply to an anterior moiety of the monster, and retaining only a slight communication with each other through a small branch from the inner subclavians.

Since Teras XX presents a normal, but double arterial supply, it is not difficult to represent diagrammatically the transformations of the primitive heart and arterial arches. Text figure 4, illustrating the normal changes in a chelonian, is inserted for ready comparison. It differs from the normal mammalian changes in two respects, first, both the right and left fourth arches persist, second, the ductus Botalli functions permanently throughout the life of a chelonian. A comparison of this diagram with text figure 5, which represents the underlying condition in Teras XX, will show at once that in the latter each moiety is identical



Text Fig. 4. Diagram showing the transformation in the primitive arterial arches in a normal reptile.

with that represented in the former, and that the communicating branch between them may suggest a slight increase in the fourth arch in the median region. Although in the diagram the hearts are rather widely separated, it should be mentioned that in the specimen they are quite close together, the sinus venosi being adjacent, and the heart of component B has a slightly more anterior position than that of its fellow; a line drawn across the ventral border of the auricles of the heart of A would be on a level with the most posterior portion of the ventricle of heart of B.

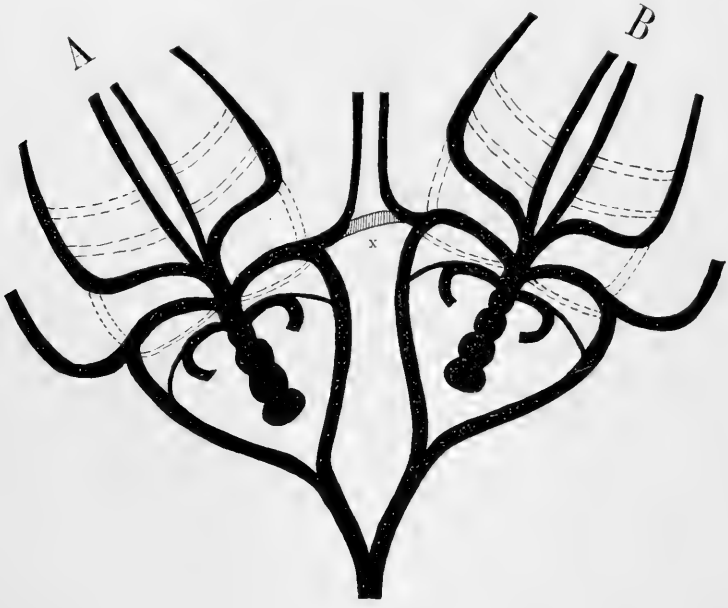
Summary.

Four cosmobia have been studied and general comparisons made. Of three of them the heart and anterior arteries have been made the subject of special investigation. The study has demonstrated:—

(1) That primarily each Teras has developed in an orderly, symmetrical manner in accordance with the laws of growth inherent within it.

(2) That as the structural parts of the components diverge, the arteries in the region involved reflect the deviation part for part, and the more posteriorly the divergence passes the more the heart becomes involved.

(3) That the divergence of all the parts involved is perfectly uniform and symmetrical.



Text Fig. 5. Diagram showing the transformations in the primitive arterial arches in Teras XX.

(4) That in each case it has been possible to refer the vascular arrangement back to an embryonic condition known in normal organisms by considering this latter condition as modified through various degrees of doubling. This has been done by reducing the teratological conditions to diagrams.

(5) That it should be emphasized that in explaining these cases they must be considered double to a definite extent from their beginning.

and that the embryonic arterial conditions in the Terata did not pass from single to double during individual development, but unfolded themselves from the first in accordance with the diagrams given to explain each case.

(6) That starting from such a condition, each case was modified by its physiological necessities.

(7) That it is possible, therefore, to conceive of these terata as representing progressive stages in a single series of "orderly living beings," which begins with organisms less than a single individual and approaches duplicate twins as the other limit, and includes between these limits normal beings and creatures of more than one but less than two complete individuals.

(8) That such a cosmobiotic series is not confined to any one genus or species, but is applicable to all vertebrates.

In conclusion, I take pleasure in expressing my thanks to Dr. H. H. Wilder, whose interest in the present research has been unceasing, and whose practical suggestions and many kindnesses have been invaluable.

Smith College, Northampton, Mass.,
May 20, 1908.

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(Asterisk indicates the literature not seen by the writer.)

EXPLANATION OF PLATES.

In all A the right component, B the left component.

In Plates V, VI, VII branches of the main arteries are indicated, but not named.

Plate I.

External appearance of Teras XII.

Fig. 1. Semi-profile from right side.

Fig. 2. Dorsal view.

Fig. 3. Ventral view.

a., Median eye; b., Everted brain tissue; c., Papilla-like protuberance from inner side of each mouth; d., Right external ear; e., Right (outer) eye of A; f., Median protuberance formed by the rami of the two inner mandibles; g., Left (outer) eye of B; h., Throat warts.

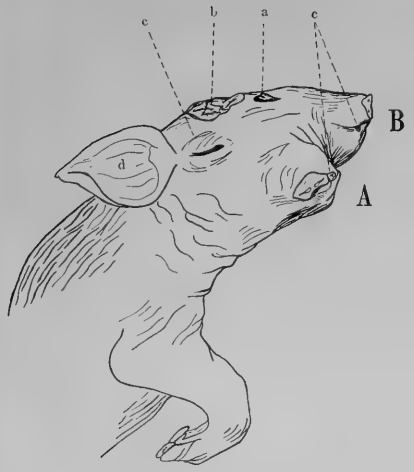

Fig. 1

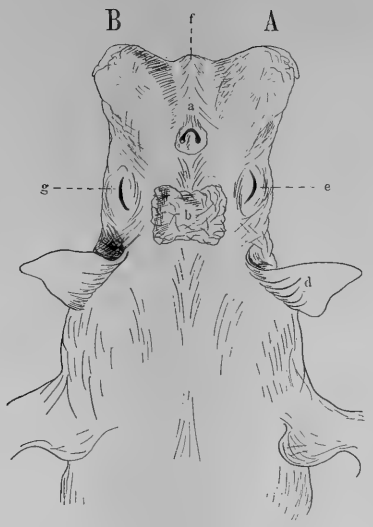

Fig. 2

Fig. 3

Plate II.

External appearance of Teras I.

Fig. 1. Three-quarter front view from the right.

Fig. 2. Ventral view.

a., Median eye; b., right (outer) eye of A; b′., Right (outer) ear of A; c., Left (outer) eye of B; c′., Left (outer) ear of B; d., Snout of A; e., Snout of B; f., Right fore limb; g., Left fore limb; h., Right hind limb; i., Left hind limb; t., Tail; u., umbilical cord.

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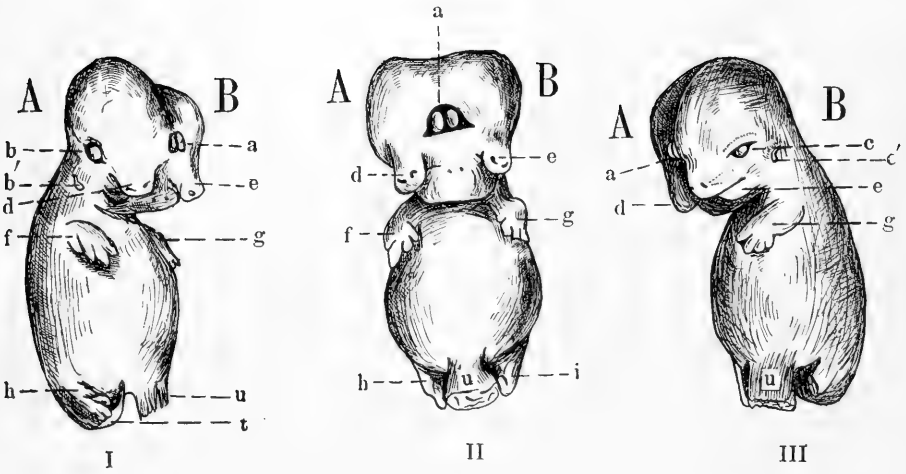

Plate III.

External appearance of Teras XV.

Roof of the cranium removed and the heads denuded. Body opened and spread out.

a., Left ear of component A; b., Right ear of component B; c., Right eye of B; d., Left eye of A; l., Larynx of A; l′., Larynx of B; t., Trachea common to both components.

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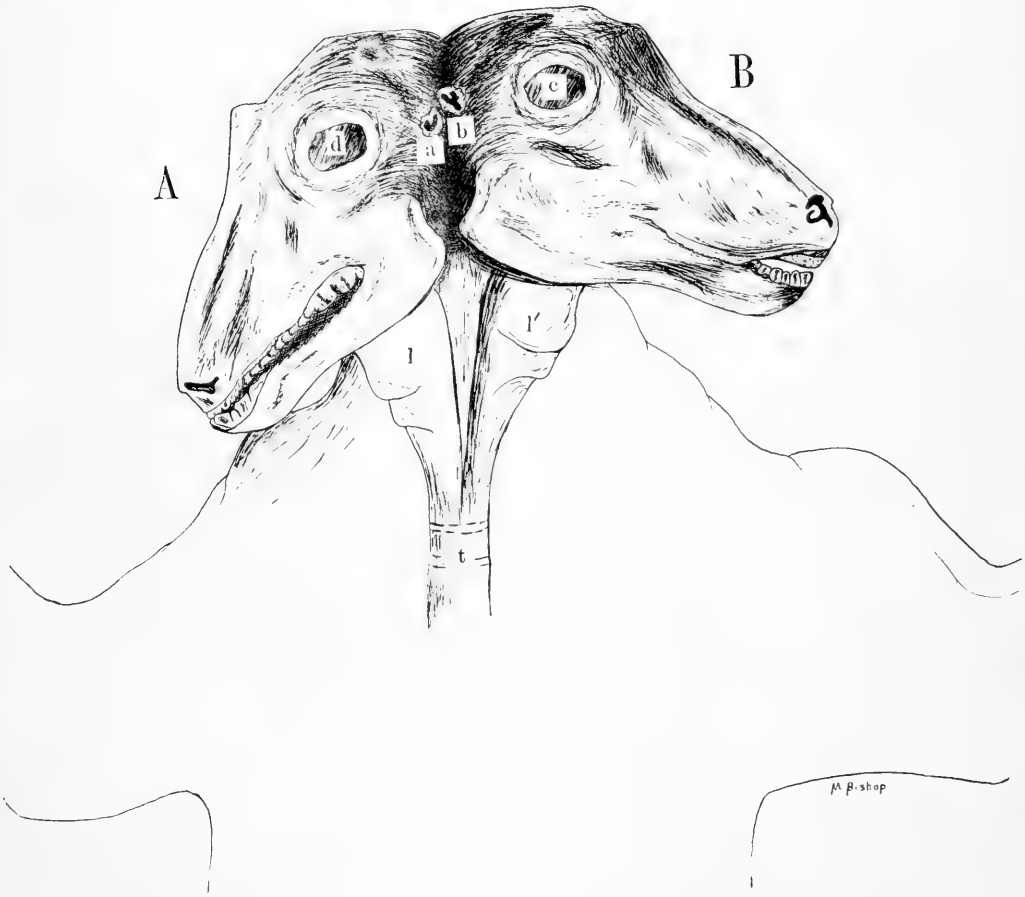

Plate IV.

External appearance of Teras XX.

Fig. 1. Dorsal view.

Fig. 2. Ventral view.

Fig. 3. Ventral view, plastron removed.

a., Anlage of median pair of fore limbs; b., Anlage of median double shoulder girdle; c., Right epicorocoid cartilage; c′., Left epicorocoid cartilage; u., Umbilicus; x, Region of doubling of the anterior plates of the carapace; y, Region of doubling of the anterior plates of the plastron.

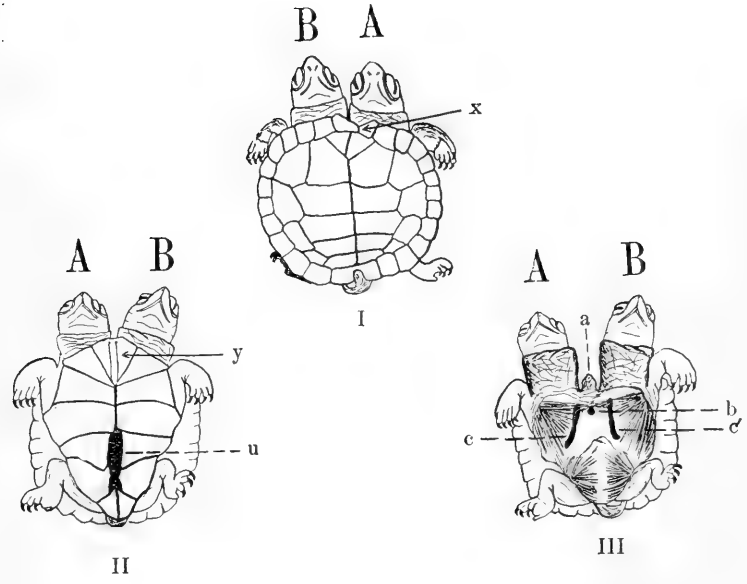
B A
x
I
A B
y
u
II
A B
a
b
c
d
III

PLATE V.

Diagram of the arteries in Teras XII.

a., Aorta; ant. a., Outer anterior auricular of A; ant. a′., Outer anterior auricular of B; da., Dorsal aorta; db., Ductus Botalli; f., Right facial of A; ff., Left facial of A; f′., Left facial of B., ff′., Right facial of B; i., Innominate; i. o. a., Infraorbital artery of A; i. o. a′., Infraorbital artery of B; i. o. for., Infraorbital foramina; i. t., Right and left inferior thyroids; l., lingual of A; l′., Placed between the right and left linguals of B; la., Left auricle; lcc., Left common carotid; l. ext. car., Left (outer) external carotid of B; lg. th., Right long thoracic; lg. th′., Left long thoracic; l. int. car., Left internal carotid; l. oc., Left occipital; l. s-cl., Left subclavian; l. st., Left superficial temporal of A; l. v., Left ventricle; m. c. ec., Median compound external carotid; m. c. i. mx., Median compound internal maxillary; o. i. mx., Outer internal maxillary of A; o. i. mx′., Outer internal maxillary of B; p., Pulmonary; p. a., Outer posterior auricular of A; p. a′., Outer posterior auricular of B; r. a., Right auricle; r. cc., Right common carotid; r. ext. car., Right (outer) external carotid of A; r. int. car., Right internal carotid; r. oc., Right occipital; r. s-cl., Right subclavian; r. st., Right superficial temporal of B; rv., Right ventricle; ss., Subsymphysial arteries; ss. for., Subsymphysial foramina; st., Outer superficial temporal of A; st′., Outer superficial temporal of B; sup. th., Right and left superior thyroids; ta., Right thyroid axis; ta′, Left thyroid axis; v., Right vertebral; v′., Left vertebral; x., Hypothetical connection between the outer external carotid of A and the median compound external carotid; x′., Hypothetical former condition of the left lingual artery of A; I., First rib; II., Second rib; III., Median eye; IV., Symphysis uniting the inner mandibles.

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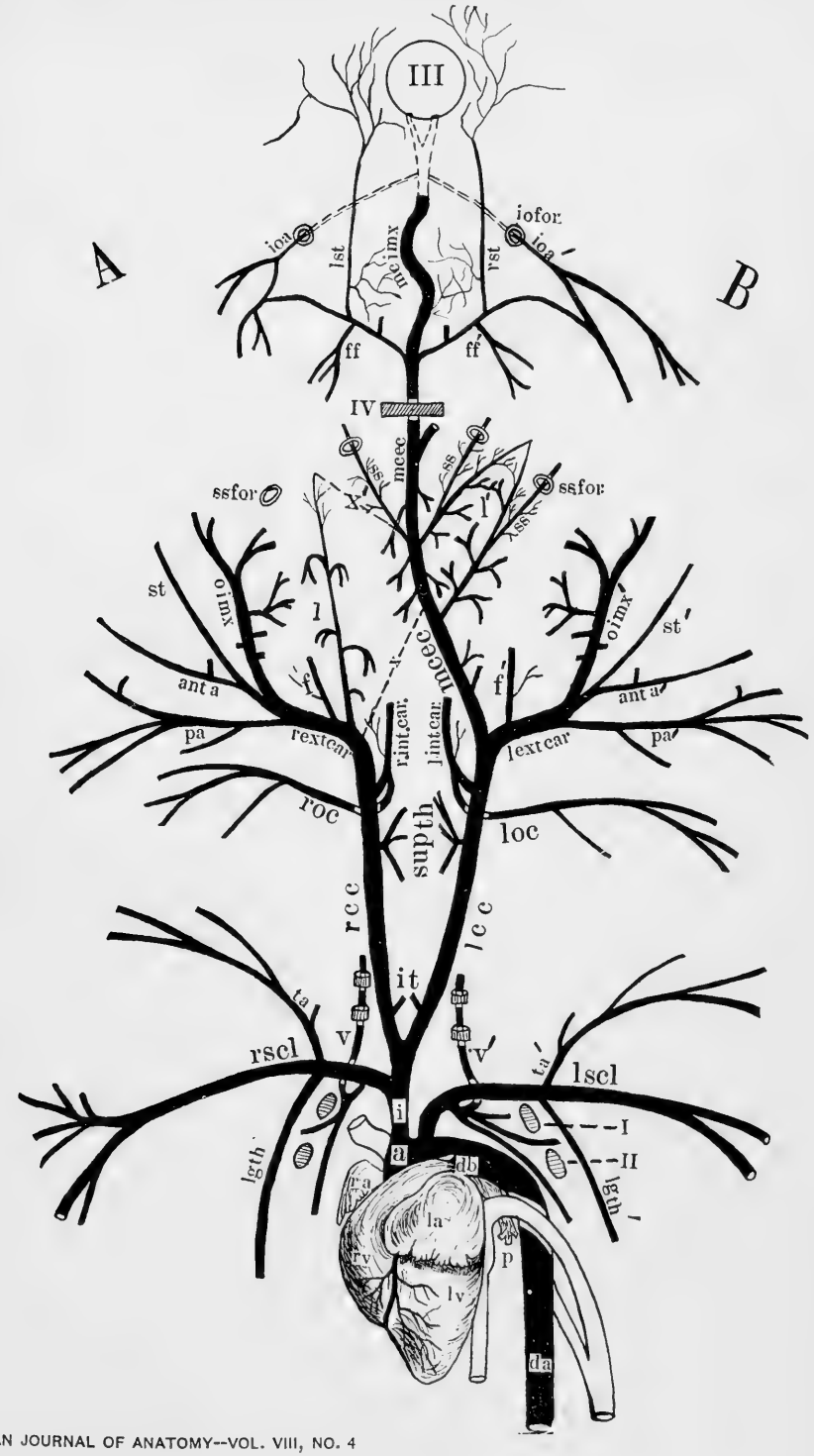

Plate VI.

Diagram of the arteries in Teras XV.

aa., Anterior aorta; at., Aortic trunk; ao. cef., Aorto-cephalic trunk to head A; cef., Cephalic artery to head B; db., Ductus Botalli; la., Left auricle; lv., Left ventricle; l. s-cl., Left subclavian; p., Pulmonary (left); p. a., Posterior aorta; r. a., Right auricle; r. v., Right ventricle; r. s-cl., Right subclavian; v., Right vertebral; v'., Left vertebral; I., First rib; II., Second rib; III., Diagram representing digastric muscle in heads A and B.

Arteries in component A:

f., Facial; it., Inferior thyroids; l. Lingual; lac., Right lacrymal; lac'. Left lachrymal; L. ant. a., Left anterior auricular; lcc., Left common carotid; l. ext. car., Left external carotid; l. int. mx., Left internal maxillary; l. oc., Left occipital; l. pa., Left posterior auricular; l. sup. tem., Left superficial temporal; l. tr. f., Left transverse facial; m. br., Muscular branch; o., Right orbital; o'. Left orbital; p. gl., Right pharnygeal; p. gl'., Left pharyngeal; r. ant. a., Right anterior auricular; rcc., Right common carotid; r. ext. car., Right external carotid; r. int. car., Right internal carotid; r. int. mx., Right internal maxillary; r. oc., Right occipital; r. pa., Right posterior auricular; r. sup tem., Right superficial temporal; sup. th., Right superior thyroid; sup. th'., Left superior thyroid; tr. f., Right transverse facial.

Arteries in component B:

f., Right facial; f'., Left facial; it., Inferior thyroids; l., Linguals; lac., Lacrymals; l. ant. a., Left anterior auricular; l. cc., left common carotid; l. ext. car., Left external carotid; l. int. car., Left internal carotid; l. int. mx., Left internal maxillary; l. oc., Left occipital; l. pa., Left posterior auricular; l. sup. tem., Left superficial temporal; l. tr. f., Left transverse facial; m. br., Muscular branch; o., right orbital; o'., Left orbital; pgl., Right pharyngeal; pgl'., Left pharyngeal; r. ant. a., Right anterior auricular; rcc., right common carotid; r. ext. car., Right external carotid; r. int. mx., Right internal maxillary; r. oc., Right occipital; r. pa., Right posterior auricular; r. sup. tem., Right superficial temporal; r. tr. f., Right transverse facial; sup. th., Right superior thyroid; sup. th'., Left superior thyroid.


A
B
III
III
lca
lcc
lca
lcc
it
it
lsel
lsel
lv
rv
ra
la
I
II
I
II

PLATE VII.

Diagram of the arteries in Teras XX.

a., Aortic arches; b., Right common carotids; b′., Left common carotids; d., Right subclavian to A; e., Left subclavian to B; f., Subclavian to left portion of anlage of median pair of fore limbs belonging to A; f′., Right subclavian to portion of anlage of median pair of fore limbs belonging to B; g., Anlage of median pair of fore limbs; h., Right ascending cervicals; h′., Left ascending cervicals; p., pulmonaries (right); p′., Pulmonaries (left); pa., Posterior aorta; x., Placed upon the connecting branch betweeen components A and B.

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