A STUDY OF ATROPHIC DEVELOPMENT

by

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The embryo which forms the subject of this investigation, and which is designated Embryo A hereafter, was obtained from a patient who aborted eight weeks after her last menstruation. The actual period of gestation, however, will be considered in the sequel.

The other embryo, marked B in the figures, which has been used to some extent for comparison, was found among blood clot and decidual shreds sent to me for examination by Dr. Chalmers, Dumfries; Dr. Chalmers' patient had been suffering for some months

from uterine haemorrhages occurring about every fortnight. The conditions, therefore, under which the ovum had begun to develop were pathological, and the suspicion attaches to this, as to nearly all specimens of early human embryos, that its unfavourable surroundings may have so acted on it as to cause it to develop abnormally. But, although the right side is badly damaged (Fig. 2), and the front slightly so, the left side is intact (Fig. 1), and its general aspect is such that one may fairly say there has been no marked deviation from the normal. This opinion, of course, rests only on the general similarity of its appearance to that of the embryos of other animals, and to the few specimens of early human embryos which have been described and been considered normal. I cannot refer to any figure of an exactly similar specimen: but were I able to do so, while this would strengthen the opinion given, it would leave it ultimately upon the same basis.

The points of special note in Embryo B are the great dorsal curvature; the absence of any appearance of the eyes externally, or of the nasal or auditory pits; the absence of the visceral clefts and arches; the looplike form of the heart and its forward prominence; and the still open condition of the medullary canal at its caudal end.

In strong contrast with the appearance of Embryo B is that of Embryo A. This contrast is specially shown in Figure 39 where the "shadows" of both, drawn with the camera lucida to the same magnification, are superposed. Embryo A is a mere nodule, which would readily have been passed over as a small lobule of fat had it occurred loose among other fragments of tissue with no clue to its origin. To the naked eye it shows only as a rounded body hanging from a thread, and having a small outgrowth at one end and a larger one at the other. With a knowledge of its origin in pregnancy one recognises these parts as the trunk, umbilical cord, tail and head of an embryo. Examined in profile with a pocket lens, the most striking feature in the general form is the rectilinear character of the outline, (Fig. 5). The ventral boundary of the trunk is almost parallel with the dorsal line, while the tail is at right angles to the spinal axis, and the long axis of the head makes with the same line an angle very little greater than a right angle. Viewed from the front the body is pear-shaped, the greatest transverse diameter being at the junction of the middle and lower thirds (Fig. 6).

The head is subcylindrical in shape with a very slight protuberance of the surface anteriorly. It is joined to the trunk by a neck which from before backwards is quite two-thirds the length of the head in the same direction; so that there is thus only a comparatively shallow cleft between the fore part of the head and the upper front of the trunk. On the left side of the neck but not on the right, there is a quadrilateral depression with a shallow groove in its middle running backwards and upwards. The groove is probably the beginning of one of the visceral clefts, but there is no communication through it with the interior; and the posterior boundary of the quadrilateral space is seen in the sections to be a slight ridge running downwards from the site of the auditory vesicle, being perhaps a rudiment of the visceral arches.

At the front upper angle of the trunk there is a distinct rounded protuberance, and the middle region of the front and sides is marked off from the rest of the body by a surrounding groove, the whole of this area being divided into two by an anterior mesial sulcus. The rounded protuberance was thought to be due to the bulging forward of the heart, and the middle area was taken to be the abdominal region as distinguished from the thoracic region above and the pelvic region below. But, as the sections show, the heart has not been formed at all: and nothing can be detected within the body corresponding to the other surface markings. Nevertheless, I still think that these features have reference to the heart and the great divisions of the trunk. The contours of the body are not wholly subject in development to the internal conformation; for there is less interdependence of parts in an organism during development than there is after development is completed. Most organs are composite in origin, more than one factor contributing to their formation, and the failure to act of one among the factors does not necessarily involve the failure of the others. An involution of the epiblast, for instance, and the formation of the lens from it, is necessary to the production of the complete organ of vision: but the involution of the epiblast may not take place, and the lens be absent, while the organ is otherwise perfect. There may even occur so futile a thing as the existence of a set of ocular muscles where there is not even a rudiment of a globe on which they could act. I have recorded an instance of this phenomenon in connection with a case of diprosopus diophthalmus in a calf (Veterinarian August. 1900)

It is quite possible then that the somatopleure may proceed to develop regularly, even to the formation of the surface markings, in spite of the failure of the usually concurrent processes. Indeed the present specimen proves that at least the general form of the body may be fairly maintained in the presence of greatly defective and abnormal development of the internal organs.

The umbilical cord or abdominal stalk is very thin and situated very low down. The caudal extremity ends in a short distinct tail. There is no trace without or within of the protovertebrae or of the limbs, and no external indication of any of the sense organs. The body walls are completely closed.

INTERNAL STRUCTURE - METHOD OF EXAMINATION. The embryo having been stained with borax-carmine and imbedded in paraffin was cut into 156 sections. As the specimen measured to begin with 2.6 millimetres in its greatest length, each section was therefore 1/60th of a millimetre in thickness. The outlines of all the sections were then drawn with the camera lucida to a magnification of 60 diameters, and having been cut out in cardboard 1 millimetre in thickness and the pieces put together, it was found that the model thus constructed agreed very faithfully with the original (Fig. 8). The plane of section was ascertained to be at right angles to the frontal plane of the body, and having only a very slight obliquity with reference to the sagittal plane. It was seen from the model also that there had been some shrinkage in the upper part of the trunk, and a considerable falling in of the middle region. Accordingly these points were taken into account in the interpretation of the sections. The reconstruction, however, added nothing further to the knowledge already obtained of the external form. Very few of the sections were damaged in the cutting.

The treatment of Embryo B was not so successful. The utmost care had been used in the manipulation, the microtome and all the re-agents having been tested with chick embryos immediately beforehand. The sections were well cut, but they failed to adhere to the slide, and when the paraffin was dissolved most of them broke up into a powdery debris. It may be that decomposition had made considerable progress before the specimen came into my hands, two days having elapsed without anything having been done towards its preservation. Embryo B is therefore not available for a comparison of its internal structure with that of Embryo A.

In the description that follows, the same terms of position are used as are employed in the descriptive anatomy of the adult body.

THE CENTRAL NERVOUS SYSTEM. This can be traced through the body to the caudal extremity, but is not carried forward into the short free portion of the tail. In general it keeps fairly in the middle line, but where the single left Wolffian body is developed it is thrown to the right, and where the umbilical cord arises, somewhat to the right of the mesial plane, the medullary canal is diverted to the left. The characteristic spindle-celled epithelium is for the most part very poorly developed, but, such as it is, it can be seen on the dorsal aspect of the canal in all the sections. Anteriorly, however, it frequently passes into the primitive round-celled tissue of which the mesoblast is composed, and generally the lumen of the tube is partly or wholly filled by these round cells, even where the circumference is fully formed by the typical cells. The medullary substance lies close to the surface in all places, there being usually only a thin layer of mesoblast, sometimes nothing at all between it and the epiblast.

Taking the presence of the spindle-shaped cells as the only available guide, the form of the nervous system of this embryo is described as follows. Beginning at the tail in a blunt extremity the tube is irregularly oval in section with the long diameter running antero-posteriorly. As it passes upwards it becomes nearly cylindrical, swells slightly and is broken into by the round cells in front. Contracting again, its least diameter is found at section 70, nearly the middle point of the long axis of the body. From there upwards it enlarges and becomes again oval in section, the long diameter of the oval now lying transversely. In the cervical region the front wall disappears and the section takes the shape of a horseshoe. This shape is maintained well into the head, the while the sides are pinched in, so that a prominent fold or ridge is formed posteriorly, with a smaller ridge on each side, all of them running longitudinally. At the same time the points of the horseshoe grow forward till they touch the lower borders of the otic vesicles on the inner sides of these and then pass in a horizontal direction to join the lower (actually the posterior) wall of the first primary cerebral vesicle. This portion of the encephalon, clearly distinguished by the optic vesicles springing from it, is flattened from side to side. Taking the origin of the optic diverticula as its anterior limit, it expands in front of this into the prosencephalon, circular in section and without any trace of division (Figs. 9,10,11,15,21.).

Above and behind the thalamencephalon the pineal diverticulum is prominent. Behind this again there is one continuous cavity not divisible except by the presence of the longitudinal ridges above mentioned, below and posteriorly, and their absence from the remaining portion. These ridges, I take it, roof over the third primary cerebral vesicle and the rest of the cavity is the middle vesicle.

The thalamencephalon and prosencephalon are fully formed, but there is no distinct floor to the second and third primary vesicles, their roofs passing at the sides into a mass of round-celled tissue which grows up from the neck into the centre of the head, and which is covered by the vesicles as by a hood. Except in the prosencephalon the cavity of the cerebral vesicles has not the tubular or globular form that is proper to it, but is encroached upon by the undifferentiated tissue to such an extent as to be almost obliterated. The same kind of tissue intrudes into the prosencephalon and optic vesicles.

THE OPTIC VESICLES are pear-shaped outgrowths of the thalamencephalon, directed upwards in relation to the long axis of the whole body, but backwards relatively to the cerebro-spinal axis. Their stalks are still hollow and only slightly constricted from above downwards. The vesicles are lined thickly with spindle cells and they show no cupping. A thin layer of mesoblast intervenes between them and the epiblast, but there is no thickening of the latter towards the formation of a lens (Fig. 12.).

THE OTIC VESICLES are ovoid in form and situated between the epithelium of the encephalon and the epiblast, all traces of their origin as involutions of the latter having disappeared. They are lined by a single layer of cubical epithelium and their cavities are filled with round cells (Fig. 13.).

A SINGLE NASAL PIT can be seen on the right side running inwards and backwards from the surface towards the end of the prosencephalon (Fig. 21.)

THE CRANIAL FLEXURE is much exaggerated so that the whole encephalon forms a semicircle and the lamina terminalis looks directly downwards. In consequence of the excessive curvature the auditory lie somewhat higher than the optic vesicles, parts of both pairs being seen in the same section (Fig. 20).

THE CHORDA DORSALIS. In only two or three of the sections in the region of the neck can there be recognised a group of cells which from their position and darker staining must be considered to represent the chorda dorsalis. In all other parts the region immediately anterior to the medullary canal is occupied by the mass of undifferentiated spherical cells.

THE CERVICAL REGION AND UPPER PART OF THE TRUNK.

Figs. 22 & 23. All the interior in these portions of the embryo is occupied by round-celled tissue with irregular spaces between the clumps of cells. In the upper part of the trunk the tissue is more condensed than it is higher up, due probably to the greater shrinking here as indicated by the reconstruction. Here also between the central mass and the lateral body walls there is on each side a free space that gradually widens out into the cavity of the gut below. At the same place the body wall anteriorly is thickened in the situation corresponding to the bulging seen externally, and between this and the cells which are in continuity with the notochordal region there is a layer of protoplasmic substance devoid of nuclei, its condition, I consider, being due to degeneration. So wanting in definite shape is the central mass of cells that it is impossible to reconstruct it in any way that will make it even remotely resemble the heart in any stage of development. Not only is the heart entirely absent, but there is not the least appearance of a bloodvessel throughout the whole body. I regard this spongy tissue as an extension downwards of that part of the undivided mesoblast which normally lies immediately below the cerebral vesicles.

SPLANCHNOPLEURE AND SOMATOPLEURE. The real cleavage of the mesoblast does not begin until the ig. 25 93rd section is reached, about the middle of the trunk, and is carried as far downwards as the termination of the gut, just above the origin of the umbilical cord. It does not, however, extend completely round the anterior wall. From the point where the cleavage begins the histological character of the mesoblast changes. The protoplasm around the nuclei is increased in amount and is drawn out into processes.

THE GUT is in the form of an irregular cone with its base uppermost. It is enormously distended and gives to the front of the body its globular appearance. The hypoblast is distinguishable, but it is broken through by an intrusion of round cells from the notochordal region, that largely occupy the upper part of the cavity. A thin sheet of splanchnic mesoblast, the mesentery, runs for a short distance between the dorsal wall of the body cavity and the gut. The body cavity is thus divided into two in its upper part, but in its lower part it is single and throughout its lining of mesoblastic epithelium is differentiated. (Figs. 11. 17. 24, 25)

THE WOLFFIAN BODY. Projecting into the left half of the body cavity a column of cells is seen which in its position represents the Wolffian body of that side, but there is no corresponding body on the other side. Running through a few sections of this column there is found a small tubular cavity, but it is not formed by specialised cells and has merely the appearance of an intercellular space (Fig. 16.

A complete scheme of the anatomy is exhibited in Fig. 11.

THE EXTRA-EMBRYONIC STRUCTURES. In the drawing (Fig. 35.) is shown the ovum as it appeared when found imbedded in blood clot, some of the clot having been removed in order to display it. The chorion has been opened, and there is seen within it another body nearly filling its cavity. This proved to be the large saccular allantois, which abruptly contracts at the end uppermost in the drawing into the thin umbilical cord. The cord is in continuity with one side of the allantois only, for the rest of the circumference of the sac in this neighbourhood presents a considerable breach of continuity. The gap, however, is possibly a rupture from the compression which the ovum must have undergone during the uterine contractions. From the chorion the allantois is easily separable in all places except at the distal end. Here microscopic examination of sections discovers no organic connection between the two, and no extension into the chorionic villi. (Fig. 32) The allantoic cavity runs through the cord to near the body of the embryo, but the proximal end of the cord itself is solid (Figs. 33. 34). There are no signs of blood-vessels anywhere on the organ.

Branched villi were found sparingly distributed on each of several pieces of the chorion submitted to the microscope, but no special investigation was made to determine whether they were more numerous at one place than another and no difference in this respect presented itself so far as the examination went.

THE YOLK SAC lay between the allantois and the chorion. It was flattened out as one finds it in abortions of two or three months, and measured 3.5 millimetres by 2 millimetres. Its stalk, bound to the allantois by the reflected amnion, could not be traced into the umbilical cord, but from its origin to the abdominal wall it must have extended nearly a centimetre. Examined from the surface with a low power objective the yolk sac was seen to consist of a fibrillar stroma containing fine granules and granular corpuscles of various sizes, the average being about .01 millimetres in diameter (Fig. 36.). The lobulated appearance seen in Fig. 37. is due to a channelling of the substance and the crowding of the corpuscles at the sides of the channels.

THE AMNION extended over the allantois for about a third of its surface and was then reflected to the chorion (Fig. 38).

The disposition of these several structures is displayed in Fig. 38. approximately in their relative dimensions.

THE AGE OF THE EMBRYOS. Compare Embryo B with one figured by His in his monograph Anatomie Menschlicher Embryonen (Atlas, Taf. IX, Fig. 1) and catalogued by him as LXVIII (Lg.) (Text, Heft II, s. 7 and Anhang s. 88): and with another in the same work designated LXVII (Lr.) (Atlas, Taf. IX, Fig. 13. Text, Heft II, s. 90) The author's drawings of both are copied in Figs. 40 & 41.

It will be seen that Embryo B departs from the form of LXVIII (Lg.) and approaches to that of LXVII (Lr.) in the greater curvature of the back, the larger size of the head and the closure of the auditory pit. It approaches to LXVII (Lr.) and departs from LXVIII (Lg.) in the greater prominence of the heart, and the less distinct visceral clefts. In the degree of closure of the abdominal wall it is probably intermediate between the two. In regard to size, while LXVIII (Lg.) was 2.15 millimetres in length, and LXVII (Lr.) was 4.2, Embryo B measured 2.8 millimetres. On the whole Embryo B appears to come nearer in age to LXVIII (Lg.) than to LXVII (Lr.).

The facts in regard to LXVIII (Lg.) fixed its age very satisfactorily at twelve days; but the estimate of the age of LXVII (Lr.) is founded on less trustworthy data, and it can be given only approximately as three weeks. If Embryo B is considered as one of fourteen to sixteen days' development, this will make its age equal to the interval between the last two haemorrhages, which is said to have been "about a fortnight." It is to be noted, however, that while in B the substitution of a ventral for the dorsal flexure indicates a greater advance in development, the still open condition of the medullary canal points to an earlier condition than that of LXVII (Lr.), but doubtless the times of completion of different stages of development are liable to some variation.

Compare now Embryo A with Embryo B. Size as an indication of age is more to be depended upon in the early embryo than in the foetus of the later months of pregnancy. If it were an absolutely reliable criterion the smaller Embryo A would be younger than the larger Embryo B; and some of the developmental marks in A would be quite consistent with this view, such as the nearly straight dorsal contour, the faint and indefinite indication of the visceral clefts, and the very rudimentary condition of the internal structures. On the other hand, the complete closure of the anterior wall, the cutting off of the yolk sac, and the great development of the amnion and allantois are altogether opposed to it. The latter group of facts is, I believe, a truer index to the age than is the former group, and points to an advancement beyond the stage of even the three weeks embryo LXVII (Lr.).

By way of extrinsic evidence as to the duration of the development in Embryo A there are the following facts. The menstrual period which was due in July 1900 did not occur. The woman, however, did not attribute its suppression to pregnancy. She had gone to the coast, and shortly after her arrival there her eldest boy was removed to hospital suffering from scarlet fever. Under similar conditions of mental and bodily stress there had been on a former occasion suppression without pregnancy. When therefore a flow of blood set in at the time when the August period was expected, the woman regarded it as perfectly natural. Indeed it appears to have been a quite regular menstruation until, after it had lasted about a week, there was a sudden greatly increased flow caused by the patient straining in turning a bed. It was only then that she suspected pregnancy and an impending miscarriage, and on the following day I removed the ovum through the dilated os.

From the termination of the June menses till the expulsion of the ovum there is an interval of nine weeks. From just before the suppressed period in July till the same date the interval is six weeks. If the suppression in July was not due to pregnancy the next occasion on which fertilisation was most likely to occur was just before the August menstruation. Assuming that fertilisation did occur at this time and that development went on during the flow of the week preceding the onset of sharp haemorrhage, which is quite possible, the life of the embryo would thus have lasted eight or ten days. So short an interval could hardly be sufficient for the formation of the less advanced features of the embryo, and is quite inadequate to the production of the more advanced characters. If the days before the August menstruation must be rejected as the time of fertilisation - and I think they must be - there are then two probable periods to be considered during which development may have gone on, one of nine weeks and one of six weeks, following the prevailing opinion that rupture of the Graafian follicle takes place immediately before or during the menstrual flow, and that fertilisation is effected very shortly thereafter in the Fallopian tube.

It is customary to calculate the onset of parturition at forty weeks from the last natural menstruation. In the great majority of cases this calculation is borne out by the event, but in a considerable number of instances it is found to be three weeks too short. The discrepancy, however, is removed if in the cases where the apparent delay occurs the forty weeks' reckoning is made from the first suppressed menses, and not from the last obvious illness, and in that way the general constancy of the period of gestation is maintained. On these considerations it appears that fertilisation in this case is most likely to have happened at the time of the last occurring menstruation, but also very likely to have been effected just before the one that was missed. As my contention is that the life of Embryo A was considerably longer than one would infer from its size and degree of development, it will be sufficient if I show as well as may be that it continued from the suppressed period of July 18th till the expulsion of the ovum on the 31st of August following.

First of all, it is necessary to exclude the chance of the embryo having been retained in the uterus for a length of time after its death.

I have examined the product of abortion in very many cases - to be numbered by dozens, I should think, and except in these two instances I have never found a very young embryo. Where the decidual sac has been ruptured the embryo may, of course, have escaped: yet even when the sac is unruptured one generally finds only a little clear fluid within it. Considering that a foetus of the later months of pregnancy retained in utero for a fortnight after its death is so macerated that the brain is liquefied, the skull collapsed, the body softened and the epidermis peeled off in large patches - considering this, one would expect that the more delicate embryo of the early weeks would very speedily dissolve. A few days would probably be sufficient for its dissolution to be effected.

This opinion no doubt is at variance with that of His, who says:- "Sehr bemerkenswerth erscheint es mir, dass ich niemals leeren Fruchten begegnet bin," and further on, "So lange das Chorion bez. dessen Elementartheile lebend sind, scheint es den Inhalt vor Faulniss und selbst vor Macerations-zerfall zu bewahren." (Anatomie Menschlicher Embryonen, Heft II, page 20.) If the experience of His were general, early embryos would be more plentiful than they are, and why the chorion should protect the dead embryo from maceration and be no protection to the dead foetus is not at all evident.

Embryo A was in an excellent state of preservation even to the epiblast, though this would be most exposed to maceration. (See the photomicrographs, especially Figs. 12, 14 & 17.) These facts, it seems to me, are sufficient warrant for the inference that it was alive till very nearly the time of its expulsion, most likely till the onset of the sharp haemorrhage at the time when the woman strained herself. This fixes the termination of embryonic life at the 31st August, and the question is narrowed to this, when did it begin?

The closing of the body walls and the constriction of the originally wide connection between the embryo and the vitelline sac so proceeds that early in the second month the process is complete and the true umbilical cord is formed. Fig. 43 copied from His (Text Heft II pg. 48) shows an embryo at this stage. The specimen from which the figure was drawn measured 11.5 millimetres in length, and according to the author's scale of length to age, it was between 4½ and 5 weeks development. It is also stated in connection with this embryo (pg. 96) that the umbilical vesicle was connected to the body by a stalk 8½ millimetres in length, a point in which the specimen resembles Embryo A.

If the extrusion of the yolk sac to this extent and the closure of the body walls requires an interval of five weeks, and was not effected prematurely in Embryo A, but occurred at the regular time, then A was not less than five weeks of age; and as the missed period in July was in every way the most probable time of fertilisation, it is fair to conclude that individual life began at that date, and so had lasted for six weeks.

THE NATURE OF THE MALDEVELOPMENT. To apply the term arrested development to the condition of Embryo A is not satisfactory either as a theory of causation, or as a determination of its place in teratological classification. As a theory of causation, while it ascribes the condition to a stoppage in development, it takes no account of the occasion of the stoppage itself. That there had been a retardation of development in parts and an inequality over all must be admitted; but that development had definitely ceased in any part at a particular stage may well be doubted.

As the denomination of a class of malformations the term arrested development is, or ought to be, restricted to the members of a group that have a common and well defined mode of origin. Though greatly differing according to the part affected and the amount of deformity, all the cases that properly belong to this group agree in this that in a single organ, or in a limited region, development has stopped prematurely, while the rest of the organism has gone on to the attainment of the mature conformation. A dwarfed limb is not an arrest of development, if it is possessed of all its members, although it has failed to keep pace in growth with the rest of the body to which it belongs. In cases of arrested development properly so called, we find one region in an embryonic state out of which it should have passed; and, allowing for the modification produced in it by the continued growth and development of the adjacent organs and tissues we can recognise the exact stage in development at which the arrest has occurred. The localisation of the deformity to a single organ or limited region is an essential feature of the process. It is conceivable doubtless, that development may cease throughout, and the organism continue to live, and even to grow, for a time thereafter; but practically speaking, since development may be said to be the one function of the early embryo, total cessation of it is equivalent to death. At all events such complete cessation, with no other manifestation of defect, could never be demonstrated.

Now in Embryo A it cannot be said that maldevelopment is confined to one organ or system of organs or to one morphological region. It cannot be said, for instance, that the central nervous system is in a definite and regular stage of its evolution, while the alimentary canal is in another more advanced or more backward definite and regular stage. A general arrest, or perhaps more correctly, a general retardation of development there has been, but this is not a complete expression of all the phenomena in the case. There is besides entire absence of parts, the vascular system and one Wolffian body for example; there is vitiation in the conformation of those that are present; and, most of all, the amount of growth or increase of mass is incommensurate with the age of the embryo as indicated by the closure of the body walls.

The absence of the heart suggests the question, whether we have to do with a case of acardiacus, although absence of that organ is not the true diagnostic sign of this variety of malformation. The vascular and other anomalies in acardiacus are secondary to the reversal of the circulation owing to the anastomosis of the allantoic vessels of the embryo with those of a more vigorous twin. (Ahlfeld: Missbildungen des Menschen, pg. 36.) In the present case there was no possibility of the presence of a twin having been overlooked: and besides there was no evidence of any circulation whatever having been carried on through the umbilical cord.

CAUSATION. It is obvious that no hostile agent having merely a local action can be taken into account as a possible cause of the condition to be accounted for. The cause must have been such a one as would affect the embryo as a whole.

A fruitful source of malformations is the adhesion of the amnion to the developing embryo, or the presence in the amniotic fluid of a glutinous substance taking the form of membranelike shreds and bands that attach themselves to various places. In Fig. 42 there is a photograph of a drawing made by me some years ago from a specimen in the Maternity Hospital collection, which shows some of the effects of these adhesions. Besides causing the typical intra-uterine amputation, the amniotic bands have brought about coalescence between adjacent parts. The right foot has only four toes, but the second one, between which and the first the band is adherent, is as broad as two and probably contains the elements of two. Such interference with the outward form must be accompanied by corresponding changes in the internal anatomy; and, as happens in malformations generally, the internal disturbance is apt to be more extensive than the external appearance would lead one to expect. Early amniotic adhesions then to the body of a very young embryo might produce a very profound effect on its whole internal economy. It could hardly do so, however, without disturbing the outward symmetry; and in Embryo A the external aspect is almost perfectly symmetrical.

A too closely fitting amnion is stated to be sometimes a cause of defective development; but whether such a pathological condition ever really exists is very problematical. If it did at one time exist in this case, it had passed away, for when the ovum was opened it was found that the amniotic sac was much larger than was commensurate with the size of the embryo.

That pathological conditions of the uterus are among the most frequent causes of abortion goes almost without saying, and it is very probable that they have an influence on the development of the embryo, but it is not possible to assign particular manifestations of maldevelopment to their action. Among uterine disorders one would expect that endometritis, which is an accompaniment of most diseased states of the organ, would be the most important factor in the etiology of malformations so far as they may be ascribed to the uterus. I am not unfamiliar with the effects of endometritis on the fruit of conception, and if I may trust my own observation these are limited to engorgement of and haemorrhage into the decidua, and the destruction of the ovum in this way. They are of comparatively late occurrence in fact, and until the allantoic circulation is established, the healthy or unhealthy state of the endometrium can have little influence on the development of the embryo. Be that as it may, however, this patient has had no symptoms of any uterine ailment during the eight or nine years of my professional acquaintance with her.

The cause of the maldevelopment in Embryo A. it seems to me, is not to be looked for among external agencies but in the ovum itself, either as a vice of its original constitution or as an interference with its early nutrition. That this ovum entered upon life with vitality below the normal is made highly probable by the history of child-bearing in the woman.

In 1894 the first child was born. He is still alive, but has always been delicate. The second child, a female, was born prematurely in 1895, and lived for only 32 hours. The birth of the third occurred at full term in 1896. This boy died at the beginning of the present year from uraemia coming on without warning three months after recovery from scarlet fever, and proving fatal in 24 hours. The fourth pregnancy, in 1898, ended in the birth of a macerated foetus of the ninth month.

The fifth, in 1899, went to the full time, and a live male child was born, who, however, succumbed to an attack of broncho-pneumonia after only a day's illness, when three or four months old. In 1900 occurred the miscarriage by which Embryo A was obtained; and a week ago, 15th May 1901, I again delivered her of a macerated foetus in the sixth month of pregnancy.

Except the one mentioned there were no miscarriages, yet the history is very suggestive of a syphilitic taint. Neither husband nor wife, however, nor any of the children have shown the least sign of that disease.

The husband is a strong robust man, and his mother who is still alive has also been healthy during the ten years that she has been known to me. Of his father, or whether he had any brothers or sisters I can say nothing, as having learned that he was illegitimate but not a son of the man whom his mother had married late in life, I refrained from enquiring further into his family history.

The family history of the wife is very instructive as tending to show a constitutional weakness on her side. A sister, Mrs. McC., also a patient of mine, has been married for a shorter time than Mrs. L. Her first child born in the same week as Mrs. L.'s first stillborn one, was stillborn and macerated. Her second child, born in August 1900, died a few days ago from bronchitis and convulsions. Her husband is a healthy man except for occasional attacks of renal colic. Another sister is married and has had one child, but I have no other information regarding her. A fourth sister is imbecile and ill grown. One brother, known to me, is not a strong man in appearance, but I am not aware of his having had any illness during the last half dozen years. The remaining one of this generation of the family lives away from home and is described as a ne'er-do-well. The parents of all these, both still living, have been much addicted to alcohol, and especially so in their early married life. The mother also is of unstable mind and a sister of hers is said to be weak-minded, while her brother is the well known idiot of an Ayrshire village.

With these facts before one, it is a reasonable conclusion that in Mrs. L. the ovarian ovum is ill endowed with vitality, and not only has it a bad start in life, but it is also handicapped by circumstances unfavourable to its proper nutrition after fertilisation. During the woman's second pregnancy a slight oedema of the face called for an examination of the urine, and it was discovered to contain albumen. This albuminuria has continued ever since both during pregnancy and in the intervals between her pregnancies, as proved by very frequent examinations. Never has there been found with the microscope any evidence of destructive disease of the renal tubules in the shape of casts or desquamated epithelium, and there has not been any apparent effect on her general health. The albumen varies in amount, but never, or only for very short intervals, quite disappears; and no treatment has been of any avail to check it.

I am not disposed to over-estimate the importance of albumen in the urine of pregnant women. In an experience of nearly a thousand cases of midwifery, I have had only one of puerperal eclampsia, yet I find albumen in a very large number. I cannot give accurate figures, but 30%, I think, is not putting it too high. On that account I seldom anticipate the occurrence of convulsions in labour; but always when the albuminuria is pronounced I expect the death or enfeeblement of the child, and this expectation is rarely falsified in the event. To quote an illustrative case which happened to be under observation during the progress of this work. A patient, a primipara, developed marked oedema a month before her expected confinement. The whole of the subcutaneous tissue was affected, the face swollen out of recognition, and the urine on boiling became almost solid. There was no improvement with treatment, yet the labour passed without incident, the oedema disappeared a few days after, and there was no albumen six weeks later. The child was very small and feeble, but has survived.

I attribute therefore great importance to the fact of albuminuria in the etiology of the case under investigation. I regard the condition indeed as chiefly one of malnutrition, and the defect in growth as more pronounced than the defect in development. It is true that a vascular connection with the uterus had not been established, but the mass of the embryo and its adnexa was very much greater than could have been contained in the original ovarian ovum. The material for the building up of this mass must have come from the maternal blood, and would be obtained as individual cells in the body obtain their pabulum, by osmosis. But the maternal blood was in an abnormal state as evidenced by the albumen in the urine, its presence there pointing at least to the diminution by so much of the nutritive value of the blood. I interpret the transition of the spindle cells of the nervous centres into round cells as an evidence of defective nutrition. Cell multiplication had been going on, but the young cells did not rise to the specialised form proper to their situation, but remained in the more primitive state.

The conclusions that I have come to then in regard to the causation of the maldevelopment in

Embryo A may be summed up in the following propositions.

The ovum was originally of vicious constitution and deficient in vitality, and

It suffered from malnutrition owing to the abnormal state of the maternal blood.

That this embryo should have been more affected than others from the same source may have been due to an exaggeration in the unfavourable circumstances in consequence of the mental and bodily strain to which the woman was subjected at the time of this pregnancy.

In applying the term atrophy to this example of maldevelopment I follow the etymology of the word and the example of His. "Unter dem Nammen atrophischer Formen habe ich einige Bildungen zusammengestellt, die bei allen sonstigen verschiedenheiten doch darin mit einander ubereinstimmen, dass zwar der Embryo seiner allgemeinen Gestalt nach deutlich angelegt, aber abnorm verbildet und jedenfalls weit unter der dem Choriondurchmesser entsprechenden Gesammtgrösse ist." (Anatomie

Menschlicher Embryonen Heft II, s. 99) Atrophy in the sense of defective nutrition is not the same as the atrophy of the pathologists, which is a retrogressive change resulting in the destruction of the proper tissue of an organ.

Plate I.

Fig. 1. Embryo B.
Left Side.

Fig. 2. Embryo B.
Right Side.

Fig. 3. Embryo B.
Profile.

Fig. 4. Embryo B
Front aspect.

Plate II.

Fig. 5. Embryo A.
Profile.

Fig. 6. Embryo A.
Front Aspect.

Fig. 7. Embryo A.

Fig. 8. Embryo A: Reconstruction.

Plate III

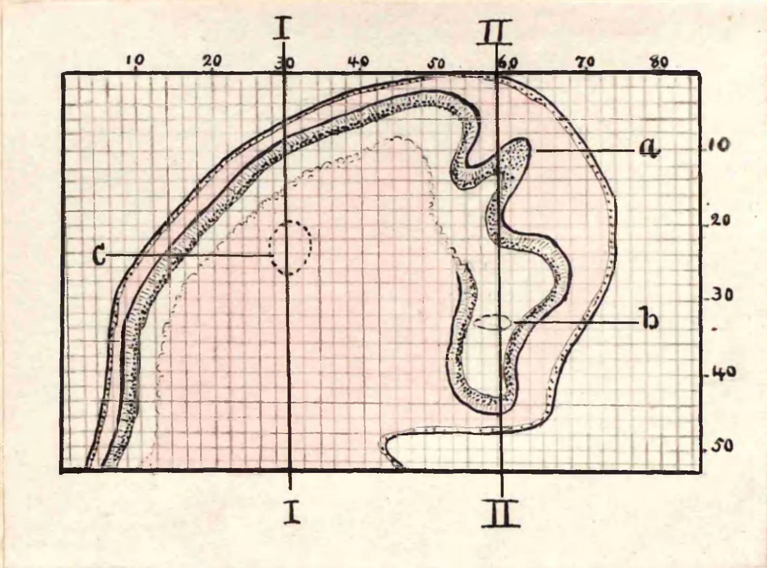


Fig. 9. Longitudinal Section of the Head.

a. Pineal Diverticulum. b. Opening into Opt. Vesicle
c. Site of Otic Vesicle.
I – I Plane of Section of A. Fig. 10.
II – II " " " " B " "

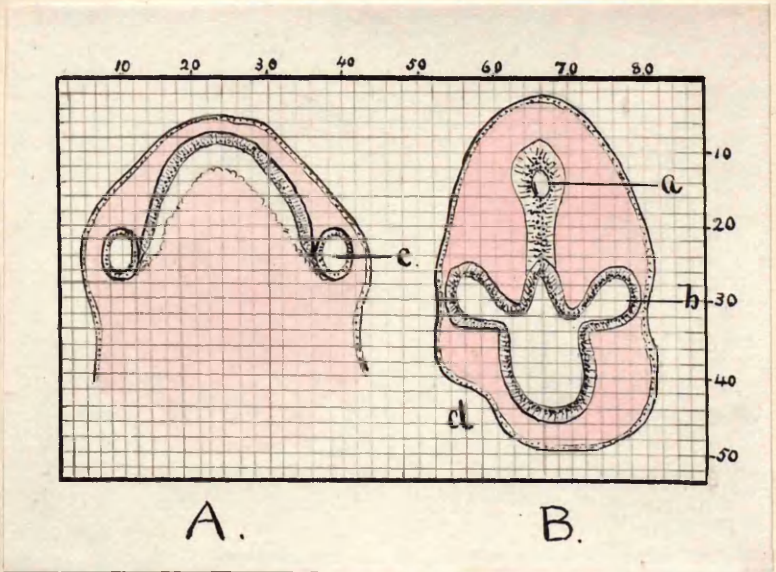


Fig. 10. Frontal Sections of the Head.

For positions see Fig. 9.

a. Pineal Diverticulum. b. Optic Vesicle
c. Otic Vesicle. d. Olfactory Pit.

Plate IV.

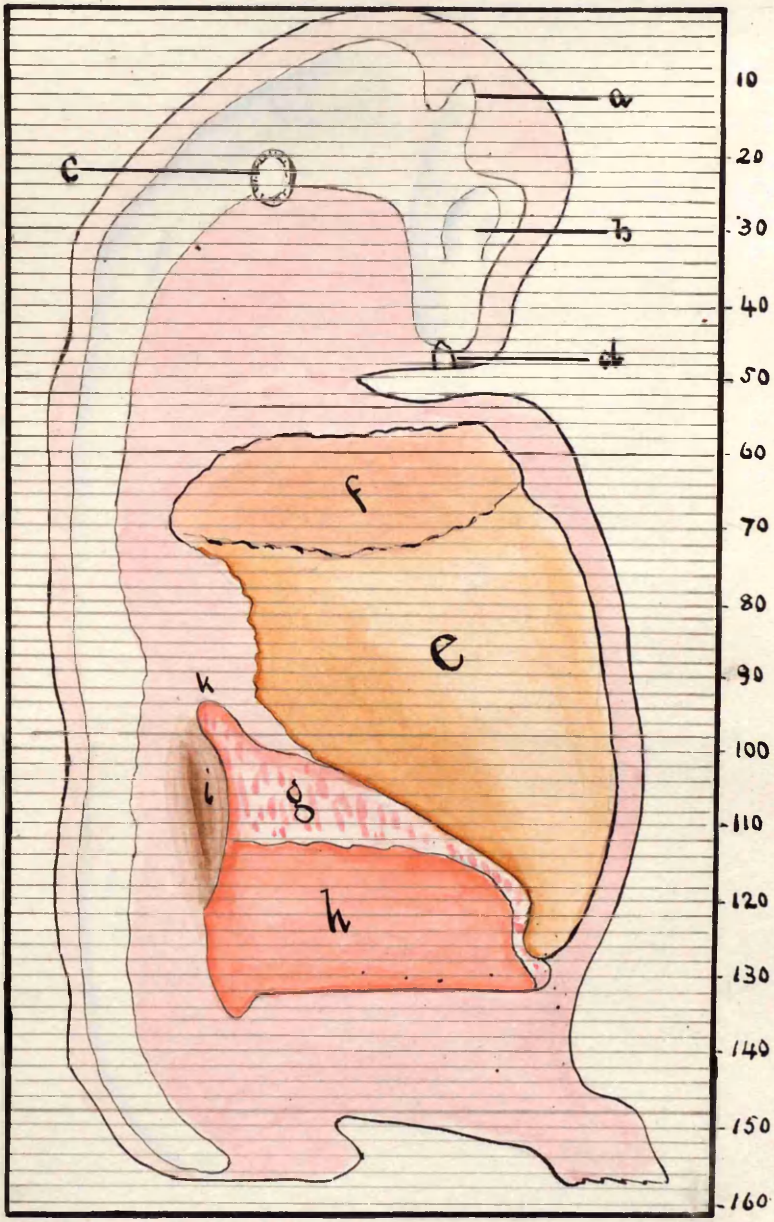


Fig. 11. Scheme of the Internal Anatomy.

The distance between the parallels represents thickness of 2 sections.
a. Pineal Diverticulum. b. Optic Vesicle. c. Otic Vesicle. d. Nasal Pit. e Gut.
f. Extension of Mesoblast into Gut. g. Mesentery. h. Lower undivided
part of Body Cavity. i. Wolffian Body (here represented on right side)
K. Beginning Cleavage of the Mesoblast.

Plate V.

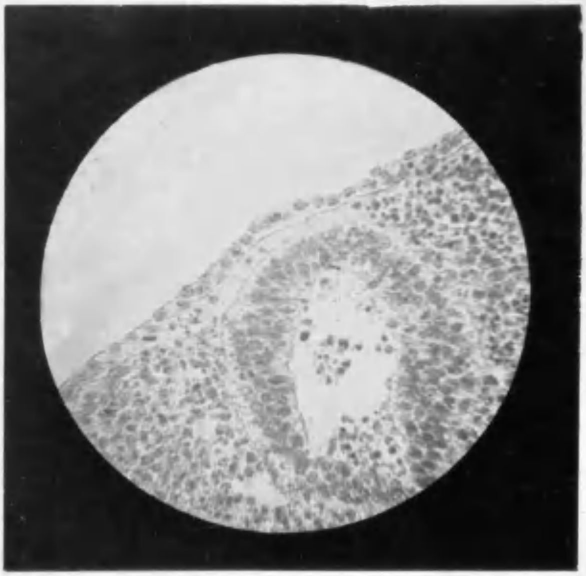


Fig. 12. The Optic Vesicle.
Shows unthickened Epiblast.

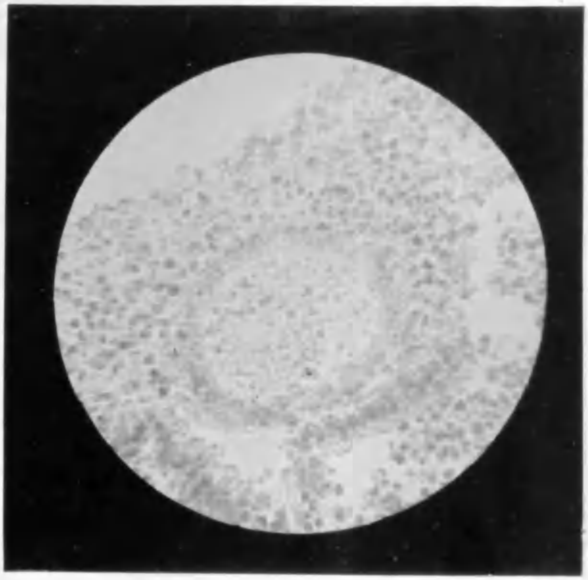


Fig. 13. The Otic Vesicle
shows round cells in interior.

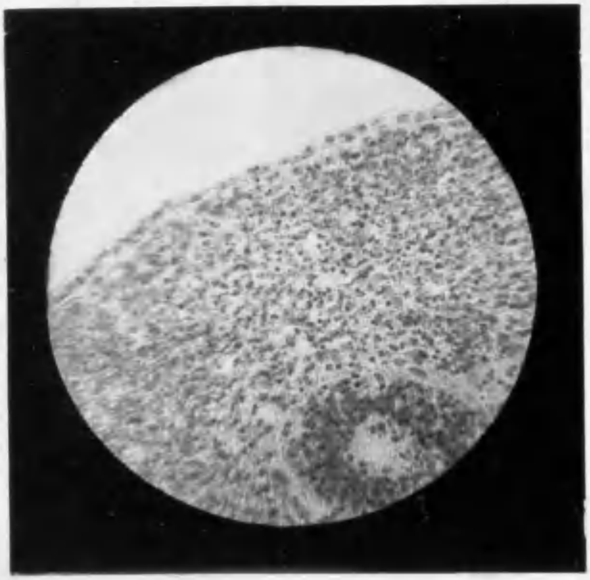


Fig. 14. Epiblast, Mesoblast and Cerebral Vesicle.

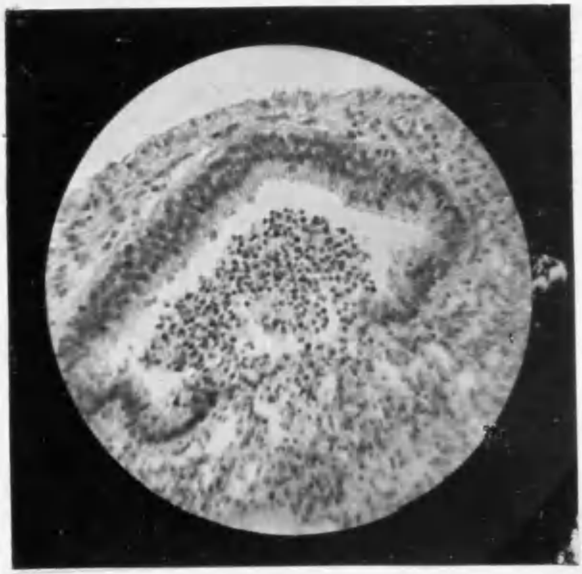


Fig. 15. Medullary Canal.
Shows transition of spindle cells into round cells.

Plate VI.

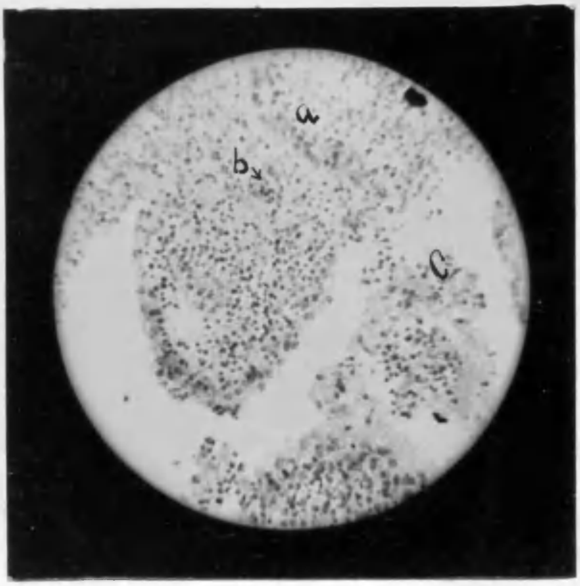


Fig. 16. The Wolffian Body.

a. Neural Canal. b Chorda Dorsalis.

c. Mesoblast of the Mesentery.

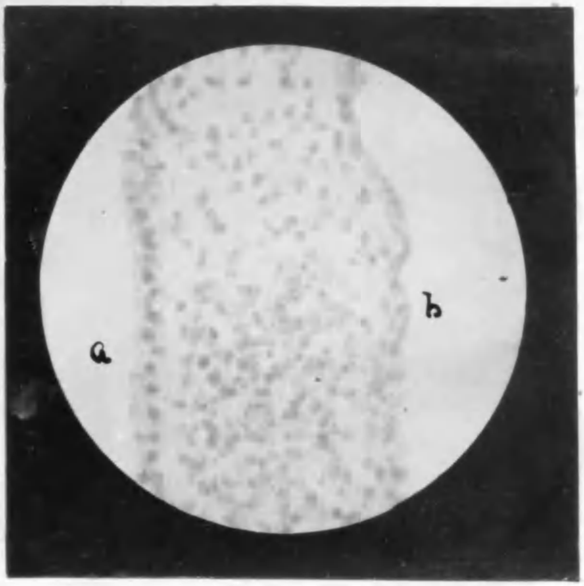


Fig 17. The Somatopleure

a. Epiblast.

b. Epithelioid Layer. (Peritoneum.)

Fig. 18. Section 15.

a. Solid part of Pineal Body. b Middle Cereb. vesicle. c. Central core of round-celled tissue.

Fig. 19. Section 19.

a. Hollow part of the Pineal Body.

Fig. 20. Section 28.

a. Optic Vesicle.

b. Otic Vesicle.

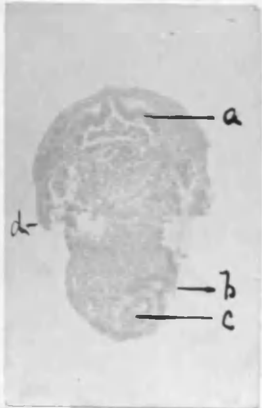


Fig. 21. Section 47.

a. Roof of 3rd Cerebral Ves.?

b. Olfactory Pit.

c. Prosencephalon.

d. Visceral Arch?

Note. Owing to the transparency of the sections good photographs could not be got with the low power.

Plate VII.

Fig. 22. Section 53

Fig. 23. Section 61.

Fig. 24. Section 80.

Fig. 25 Section 94
a. Somatopleure
b. Splanchnopleure
c. Body Cavity.
d. Gut.

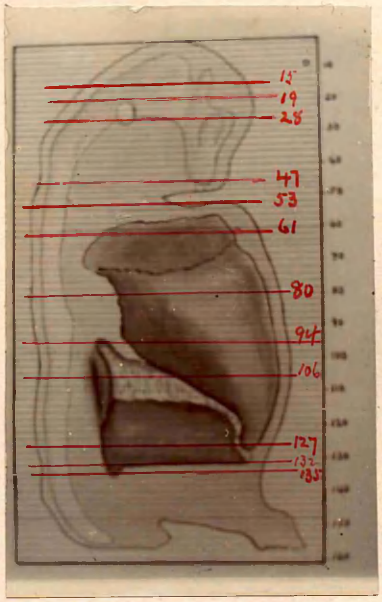


Fig. 26. Position of Sections

Fig. 27. Section 106
a. Wolffian Body
b. Mesentery
c. Gut

Fig. 28. Section 127.
a. Body Cavity
b. Gut.

Fig. 29. Section 132.
a. Body Cavity

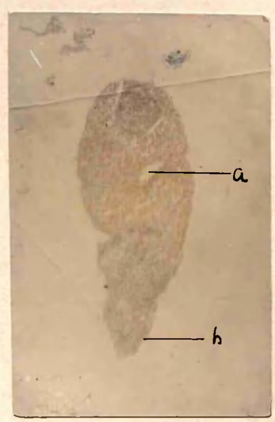


Fig. 30 Section 135
a. Body Cavity
b. Umbilical Cord.

Plate VIII

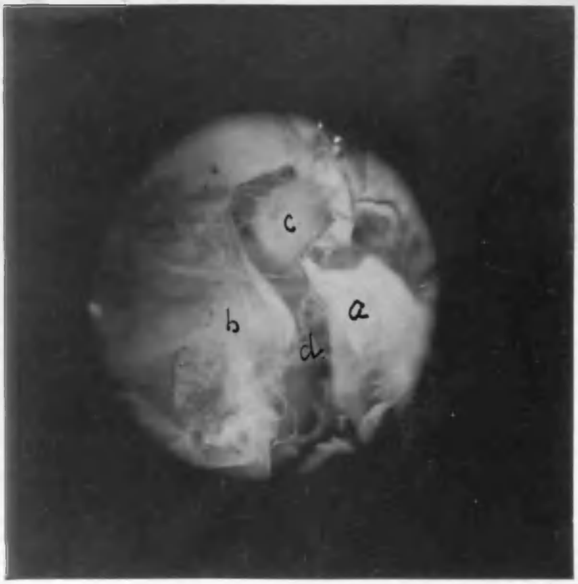


Fig. 31. Chorion, Allantois & Amnion.
a. Chorion reflected; b. Allantois: c, Embryo.
d. Amnion passing from Allantois to Chorion.

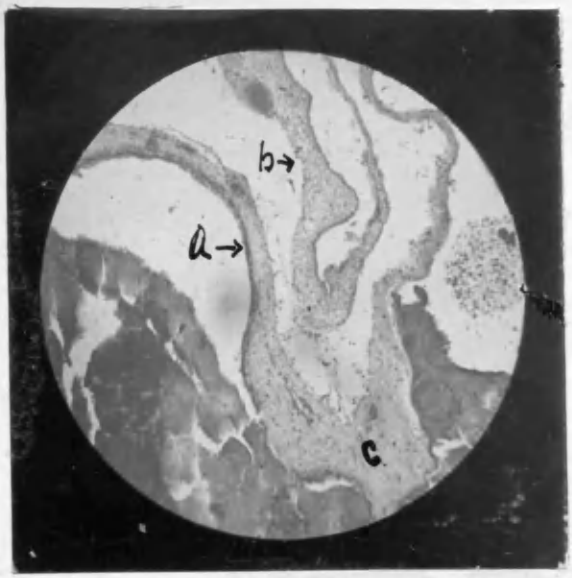


Fig. 32. Shows relation of Allantois to Chorion.
a. Chorion: b. Allantois: c. Chorionic Villus.

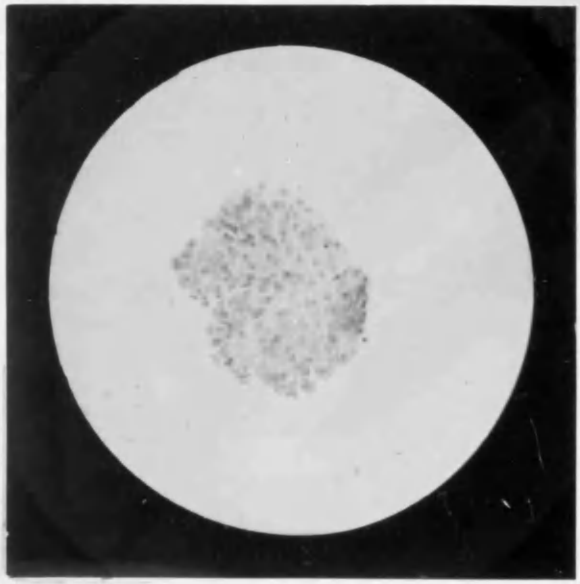


Fig. 33. Umbilical Cord, close to the Embryo.

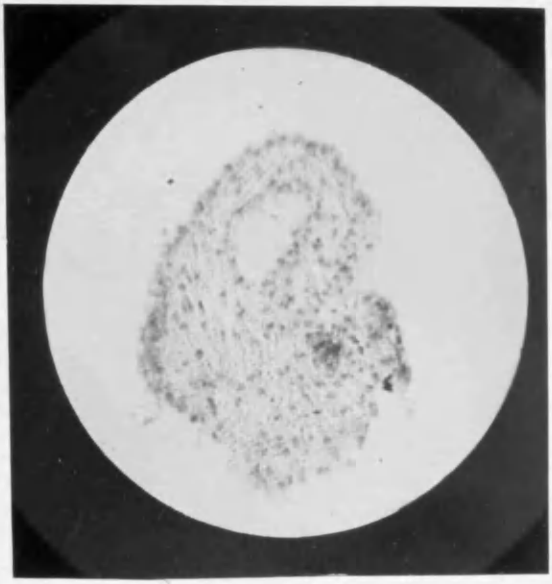


Fig. 34. Umbilical Cord more distant from the Embryo than Fig. 33. Shows the hollow stalk of the Allantois.

Plate IX.

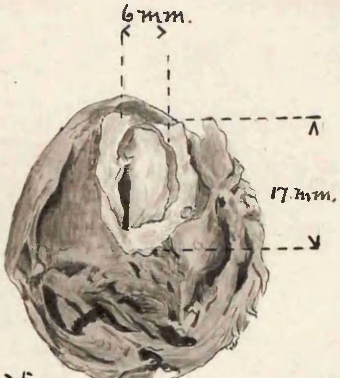


Fig. 35.
Ovum imbedded in Clot.
natural Size.

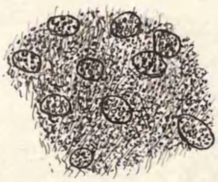
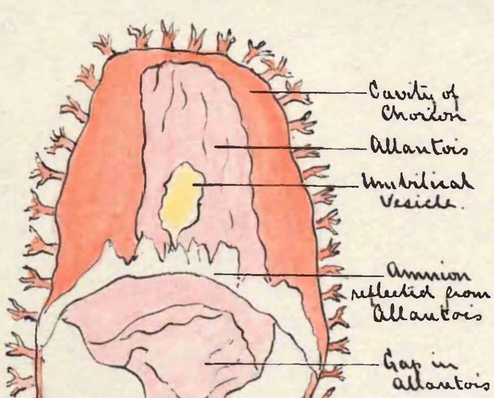


Fig. 36.
Surface view of Umbil. Vesicle
(magnified.)

Fig. 37. Umbilical Vesicle of Embryo A.
(by 25 diameters)



To show (approximately) the relative size of Embryo A and its membranes.
Enlarged about 4 diameters.

Fig 38.

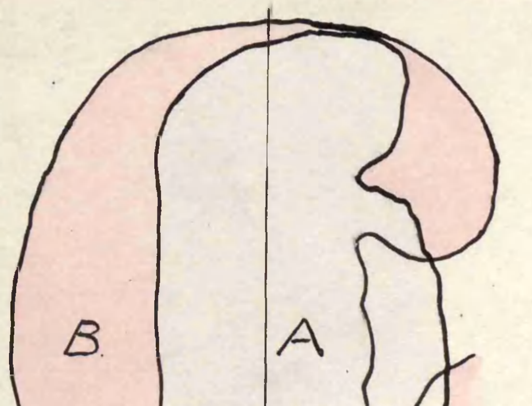


Fig. 39.

Embryos A and B superposed.

Plate X

Fig. 40. Embryo of about 12 days (His)
LXVIII. (Lg)

Fig. 41. Embryo of about 3 weeks (His).
LXVII (Lr.)

Fig. 42. Shows the effects of Amniotic Adhesions. (drawn from a specimen).

Fig. 43. Human Embryo at time when Body Walls are first completely closed. (His)