THE DEVELOPMENT OF THE ANTERIOR ABDOMINAL WALL, WITH REMARKS ON THE AETIOLOGY OF ASSOCIATED ABNORMALITIES.

BY

GEORGE M. WYBURN, M.B., CH.B.

PRESENTED AS A THESIS FOR THE DEGREE OF DOCTOR OF SCIENCE.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

THE DEVELOPMENT OF THE INFRA-UMBILICAL PORTION OF THE ABDOMINAL WALL, WITH REMARKS ON THE AETIOLOGY OF ECTOPIA VESICAE

BY

GEORGE M. WYBURN, M.B., CH.B., F.R.F.P.S.G.

REPRINTED FROM THE JOURNAL OF ANATOMY
VOL. LXXI, PART II, JANUARY 1937

CAMBRIDGE
AT THE UNIVERSITY PRESS

PRINTED IN GREAT BRITAIN

[Reprinted from the JOURNAL OF ANATOMY
Vol. LXXI, Part II, January 1937]
 PRINTED IN GREAT BRITAIN

THE DEVELOPMENT OF THE INFRA-UMBILICAL PORTION OF THE ABDOMINAL WALL, WITH REMARKS ON THE AETIOLOGY OF ECTOPIA VESICAE

By GEORGE M. WYBURN, M.B., Ch.B., F.R.F.P.S.G.
Senior Demonstrator of Anatomy in the University of Glasgow

CONTENTS

INTRODUCTION

The umbilical region of the human embryo has at all times attracted much interest as a prolific source of congenital defects and abnormalities, in spite of which, perhaps because of which, there still exists some gaps in our knowledge regarding the method of closure and completion of the belly wall.

An examination of the sections of a human embryo of 4·5 mm. in length (McIntyre II), with a favourable history, and showing the yolk sac with connecting duct, seemed to offer a fruitful field for study. The impossibility of limiting observation to the umbilicus alone was soon apparent, and it became obvious that satisfactory results could only be procured by a more comprehensive survey embracing the whole question of the development of the anterior abdominal wall.

The initial absence of a ventral wall to the embryo is found in all vertebrates with the exception of some of the Amphibia.

In the frog with its small, yolked, holoblastic egg gastrulation is complete—the blastopore forms at the equator with dorsal, lateral and ventral lips and wholly encloses the yolk cells of the vegetative pole. The yolk is thus taken into the body of the embryo and lies in the floor of the gut.

In the Elasmobranchs the large amount of yolk impedes cell division so that segmentation is meroblastic. The resulting blastoderm corresponds to the cells of the animal pole of the frog's egg. The embryo arises from the posteromedian portion of the blastoderm, so that only the dorsal lip of the blastopore is intra-embryonic, while the lateral and ventral lips, formed of the extra-embryonic

blastoderm, grow and enclose the yolk, the resultant sac being outside the body of the embryo to which it is connected by a stalk. Thus at an early stage the embryo is devoid of a ventral wall. The midgut, for a varying period, communicates with the yolk sac by the yolk stalk; this connexion is later obliterated.

In the Gymnophiona the anterior edge and the major portion of the lateral edges of the blastoderm take no part in the formation of the blastopore, and there is not only an absence of ventral wall, but the yolk remains uncovered.

The embryonic shield of the Amniota, according to Jenkinson, is the equivalent of the blastoderm of Gymnophiona. Blastopore formation affects only the shield, there being no true ventral lip. The edge of the extra-embryonic blastoderm grows steadily round the yolk entirely independent of blastopore formation, and finally encloses it at the vegetative pole. The yolk sac is extra-embryonic.

In the chick the enveloping blastoderm is continuous with the false amnion or chorion and is gradually separated from the yolk sac by the encroachment of the extra-embryonic coelom between somatopleure and splanchnopleure.

In placental mammals the egg has undergone loss of yolk and cleavage is accordingly holoblastic. The blastocyst with its surrounding trophoblast and enclosed embryonic material is possibly a modification to meet nutritional and protective requirements. The trophoblast, which from an early stage surrounds the yolk sac, is analogous with, if not the homologue of, the false amnion of the chick. This (the false amnion) is comparable to the extra-embryonic blastoderm of the Anamnia which encircles the yolk. The modified form of blastopore formation affects only the embryonic shield. The embryo is therefore without a ventral wall and the yolk sac is extra-embryonic. The completion and closure of the anterior abdominal wall occurs at a late stage of development in placental mammals.

It is the opinion of Keith that the trophoblast in the human blastocyst can be regarded as the precociously developed belly wall of the embryo. In view of the comparative lack of knowledge of the earliest stages in the formation of the human blastocyst, which acquires in a relatively short time its own salient characteristics, and taking into account the fundamental differences in the early ontogeny of the placental mammals which represent not a simple or common evolutionary plan but rather a great diversity of methods of attaining similar physiological requirements, it seems a hazardous experiment to affix a phylogenetic label to any portion of the human blastocyst.

In the heavily yolked eggs the inert yolk substance is responsible for the partial cleavage and limitation of gastrulation to the more active animal pole. The placental mammals show the early differentiation of the tissues concerned with protection and nourishment, and gastrulation is again much modified.

The absence of a true ventral wall in the early stages and the extra-embryonic position of the yolk sac may perhaps be regarded as a modification incurred by nutritional necessity, which modification could be explained as a

concomitant of incomplete and suppressed gastrulation following on the more prolonged embryological phase with its demand for "yolk" or "membranes".

The anterior abdominal wall in its development falls naturally into three parts—supra-umbilical, umbilical and infra-umbilical. The present portion of the work deals with the infra-umbilical abdominal wall.

THE INFRA-UMBILICAL ABDOMINAL WALL

This part of the ventral wall cannot be said to exist until the appearance of the genital tubercle with the subsequent development of an interval between the tubercle and lower attachment of the body stalk. In the series examined the interval first becomes apparent in an embryo of 12·5 mm. which shows a well-marked genital tubercle with a narrow dense band of mesoderm between it and the attachment of the stalk. Keibel & Mall give the first appearance of the tubercle as occurring in an embryo of 13 mm. This mesoderm, caudally merging into the genital tubercle and superiorly continuous with the tissue of the stalk, would therefore seem to be the basis of the future infra-umbilical portion of the belly wall.

An endeavour to trace the origin of this mesodermal mass through a series of younger embryos in the Glasgow Collection has involved a consideration of the primitive streak, of the cloacal membrane, of the mesoderm in general, and has led to a study of existing descriptions of early embryos in connexion with the individual points within this question.

EMBRYO McINTYRE I

The first of the series examined was embryo McIntyre I. Observations on this embryo were published by Bryce (1924), but in his paper particular interest was centred on the more cranial sections of the embryonic shield. The embryo is of the presomite class, having a pronounced ventral curve at the hinder end, a primitive streak measuring 0·33 mm., the major portion of which occupies the ventral aspect of the caudal flexure, and a total length of 1·4 mm., including the primitive streak.

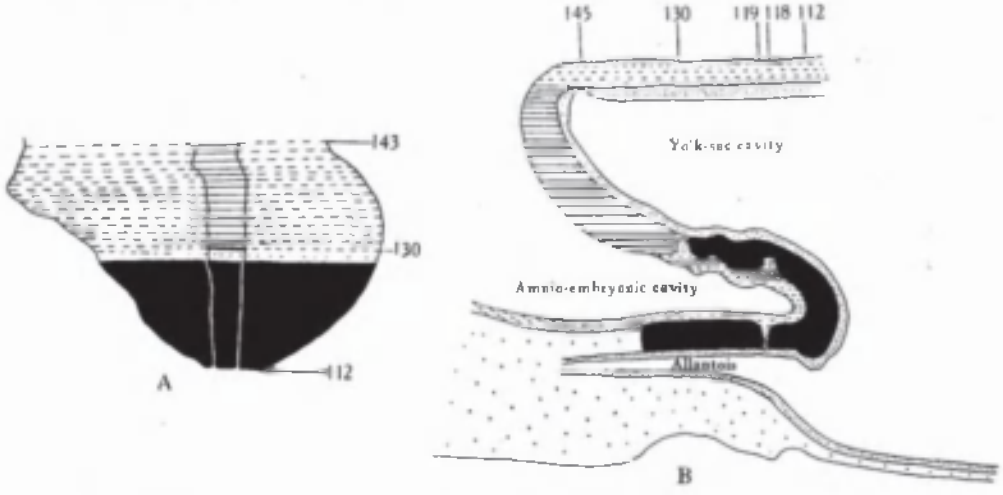
Bryce is of the opinion that the McIntyre embryo is younger than embryo Gle (Graf v. Spee) and embryo Vull (Eternod), to which it bears a close resemblance and is probably a stage succeeding that of Ingalls in which, however, the disc has the dimensions of $2 \times 0{\cdot}75$ mm.

A graphic reconstruction was made of the caudal half of the embryo from sections 109–150 (Text-fig. 1A, B), the exact position of the sections being indicated on the drawing of the wax models (Pl. I, fig. 1).

Section 146 (Pl I, fig. 3) is placed at the flexure and shows the opening of the archenteric canal. Sections 150–147 are through the region of the caudal bend, consequently there is some difficulty in interpreting the nature of the tissues and it is impossible to discriminate between ectoderm and mesoderm, but from the position it is probable that the section is cut through Hensen's knot,

Cranial to 146 the sections show the primitive groove and primitive streak on the ventral aspect, i.e. on the caudal portion of the shield which has been bent round ventrally to become continuous with the body stalk.

From sections 145 to 142 (Pl. I, fig. 4) the primitive streak appears as a fusion between the ectoderm and mesoderm. The endoderm dorsally is in contiguity with the mesoderm, but there is no distinct fusion of the layers. In the sections cranial to 142 the primitive streak on the ventral aspect has the appearance of mesoderm budding off from the ectoderm, more especially from the walls of the primitive groove. The endoderm forms a distinct layer connected to the mesoderm by a few cellular strands. This appearance persists in the next twelve sections, the only change being a gradual deepening of the yolk-sac pocket with consequent approximation of endoderm and ectoderm, and decrease of intervening mesoderm.



Text-fig. 1. Embryo McIntyre I. × 100. The numbers refer to the sections. A. Reconstruction of the surface of the caudal portion of the embryonic shield, i.e. the portion bent ventrally to form the tail fold. In the midline is the primitive groove. Area in which mesoderm crosses the midline is shown in black. B. Reconstruction of a median sagittal section (see Pl. I, fig. 1). Description in text. Ectoderm—interrupted horizontal lines; endoderm—fine stippling; dense mesoderm—black; primitive streak—horizontal lines.

Section 130 (Pl. II, fig. 5). The primitive groove is still present. The ectoderm forms a thickened cord of cells with the endoderm lying immediately above. There is no intervening mesoderm, but mesoderm is seen extending laterally on each side, separated by an interval from the ectoderm and endoderm. The appearance is that of a cloacal membrane, and extends only over one section.

Sections 129–127 (Pl. II, fig. 6) again show mesoderm between the ectoderm and the endoderm with a gradual flattening out of the primitive groove. The amount of mesoderm between the two layers gradually increases. There is

no sign of budding off of the mesoderm from the ectoderm, and while the three layers are in contiguity at the midline this may be in some measure artificial, as both ectoderm and endoderm can be traced as distinct layers while the mesoderm stretches across from side to side between them.

Section 126. There is no primitive groove. The ectoderm seems to be thickened in the midline, forming a plate of cells which at first glance would appear to extend up to and establish contact with the endoderm. On further examination with an apochromatic 4 mm. lens this resemblance to a cloacal plate is found to be due to shrinkage of the mesoderm on each side leaving an apparent space between the "plate" and the mesoderm. Similar spaces can be seen in the mesoderm more laterally as a result of formalin fixation. The ectoderm and endoderm can again be traced as distinct layers across the middle line.

Section 125 (Pl. II, fig. 7). Is similar to 126, but the resemblance to a cloacal plate is even more striking.

Sections 124–120 (Pl. II, fig. 8). Mesoderm is again visible separating the ectoderm and endoderm.

Section 119 (Pl. III, fig. 9). The amniotic space between the disc and body stalk is diamond-shaped in the section. From the lower apex a distinct cord composed of a double row of cells can be made out extending down to and establishing contact with the endoderm of the allantois which at this level is oval in section and extending up the cord.

Section 118 (Pl. III, fig. 10). The amniotic space is still diamond-shaped. The cord of cells noted in the previous section is not now evident, the amnion and allantois being separated by definite mesoderm. From the upper angle of the space a short process extends up to but does not reach the endoderm of the yolk-sac diverticulum, a single row of mesodermal cells intervening.

Sections 117–109 (Pl. III, fig. 11). The amniotic space gradually diminishes and disappears, the mesoderm of the disc fusing with that of the body stalk, the resultant mass being placed between the endoderm of the yolk sac dorsally and that of allantois ventrally.

Bryce (1924) in the description of the embryo states that the primitive streak extends up to section 117, from which point it is replaced by the cloacal plate connecting the yolk-sac diverticulum with the ectoderm and found up to the commencement of the allantoic duct proper. As before mentioned, in the original description, interest was focused almost entirely on the cranial sections and not on the region now examined.

No evidence of a cloacal plate is to be found in section 117, or those cranial to that; in fact in those sections where the amniotic space is gradually closing in, the ectoderm can be distinguished only with difficulty and ultimately disappears entirely.

Definite contact between ectoderm and endoderm is established at two points, viz. sections 130 and 119. The possibility of a cloacal plate in sections 125 and 126 has been rejected because of the alternative explanation of an artefact during fixation. In this embryo there are therefore two points at which

an undoubted cloacal membrane can be said to exist. Between these two points mesoderm is continuous on the one hand with that of the primitive streak and on the other with the mesodermal basis of the body stalk.

Regarding these findings there are two questions which occur—(A) the source of the mesoderm of the body stalk; (B) an explanation of the division of the cloacal membrane.

SOURCE OF MESODERM OF THE BODY STALK

It is firstly necessary that there should be a clear conception of the structure of the primitive streak.

Bryce (1924) states that all three layers are fused over the length of the streak, but while the mesoderm can be observed budding off from the ectoderm, the basal part of which is indistinguishable from that layer, the endoderm, except in the most caudal section where it is not present, preserves its identity and can be traced as a distinct layer across the middle line. There is certainly no interval between the mesoderm and endoderm, but in none of the sections of the primitive streak did there appear to be any actual budding off of mesoderm from endoderm.

Hill & Florian (1931), describing the primitive streak of the "Dobbin" embryo (0·98 mm.), state that the endoderm is clearly visible on the ventral aspect of the streak. Ingalls (1918) in his embryo of 2 mm. describes a considerable interval between the endoderm and the primitive streak, while Heuser (1930), in one of 1·6 mm., shows the streak as a fusion of ectoderm and mesoderm, the endoderm lying quite free. Debeyre (1912), on the other hand, states of the region of the primitive streak: "Tout le long de la ligne primitive ou à son niveau on remarkera l'union intime qui existe entre les feuillets." Florian (1934), from reconstructions of embryos WO, Op. and Fetzer, is of the opinion that in the primitive streak primordium there is a fusion of endoderm and mesoderm in the midline and that this persists for some time, while Rossenbeck (1923), writing on the embryo Peh-Hochstetter, considers the primitive streak as a fusion of ectoderm and mesoderm, the endoderm being separated by an interval from the actual primitive streak.

This disparity in the description of the character of the streak is probably due to variations in its form according to the degree of development, not necessarily corresponding to the size of the embryonic shield; but most observers seem agreed that while there is a fusion of all three layers in the region of Henson's knot, the actual streak itself is represented by a fusion of ectoderm and mesoderm. Grosser (1927) expresses the opinion that the primitive groove is due to a sinking of the ectoderm on account of the heavy emigration of mesodermal cells.

The blastocyst of man and higher mammals is characterized by the precocious development of mesoderm, which being in the later stages an angio-

blastic tissue arises in accordance with the mode of nutrition of the embryo (Bryce).

Of three of the earliest ova showing the embryonic rudiment, in that of Peters (1899) the amniotic and yolk-sac vesicles are separated by mesoderm except in the middle line at the cranial end; in T.B. I (1908) there is a considerable interval between the two vesicles which are situated in a cavity already filled with mesenchyme—the unusual distance between the amniotic cavity and the yolk sac may be to some degree artificial; Streeter (1927) in a description of section 4 of the Miller ovum—the sixth section through the rudiment—states that the amniotic and yolk-sac cavities are in a common compartment surrounded by mesenchyme, the ectoderm of the amnion being in contact with the endoderm of the yolk sac with but a narrow intervening cleft. There is, however, some doubt as to what constitutes the yolk sac in the Miller ovum.

Fetzer (1910), describing an embryo of 0·23 mm. in length, states that there is no primitive groove, medullary fold, or neurenteric canal. Nevertheless the yolk-sac endoderm and ectoderm of the shield are separated by a layer of mesenchymal cells passing towards the cranial end and fusing in the midline with the ectoderm. According to Rossenbeck this is undoubtedly the primitive streak.

Graf von Spee, discussing Peter's ovum, is of the opinion that the anterior and posterior poles of the amniotic and yolk-sac vesicles grow into the solid mesenchyme separating them from the chorion which mesenchyme, acting as a wedge, ultimately completely separates the ectoderm and endoderm except for an area in the midline at the caudal end—the cloacal membrane.

It is now well known that the primary mesenchyme in the human ovum and that of the higher primates makes its appearance long before there is any indication of a primitive streak, thereby differing fundamentally from that in the lower mammals.

Streeter (1927) is of the opinion that this mesenchyme arises either from the inner cell mass during the formation of the segmentation cavity or alternately is split off from the trophoblast. The close relation of the mesenchyme to the trophoblast inclines him to the latter explanation.

Bryce (1924) accepts the former hypothesis and regards the differentiation of the primitive mesenchyme as simultaneous with that of ectoderm and endoderm from the formative cell mass.

Strahl & Beneke (1910) express the opinion that the primary mesoderm is split off at the morula stage, the ectoderm and endoderm remaining widely connected in the early stages. Later this connexion is restricted to the primitive streak region.

Hubrecht (1909) finds that in *Tarsius* the mesoderm of the connecting stalk is derived from a proliferation of the ectoderm at the posterior margin of the shield which Bryce (Quain) suggests is a precocious development of the primitive streak formed later as an extension of this area.

In a history of the primates Hill (1932) shows four stages in the genesis of the body stalk:

(1) Lemur, e.g. *Loris*, where the mesoderm arises relatively late (blastocyst 8 mm.) and both extra- and intra-embryonic mesoderm are derived from a primitive streak. The mesenchyme of the allantoic outgrowth which is the homologue of the connecting stalk is formed from the primitive streak, arising from its hind end and extending round the cloacal membrane.

(2) In *Tarsius* the connecting stalk mesenchyme is in the first instance a proliferation of the posterior margin of the shield ectoderm, later being reinforced by a backward extension from the primitive streak.

(3) In "*Hapale*" embryo there is an area of proliferating mesenchyme at the caudal margin of the shield which Hill suggests corresponds to the precociously developed hinder end of the primitive streak in *Tarsius* and which in his opinion forms the whole of the primary mesoderm, including that of the stalk. The extra-embryonic mesenchyme is differentiated some considerable time before the appearance of the primitive streak.

(4) The fourth stage is the human embryo.

Florian (1930) has demonstrated the existence of a proliferating area in the posteromedial margin of the shield ectoderm in the embryo Fetzer and believes this to be the source of the stalk mesenchyme and the major portion of the rest of the primary mesenchyme in the human. In a recent publication (1933) he avers to have satisfied himself as to the existence of such a region in the embryos Peters, Werner, and von Mollendorff's Wo and Op. This accords with the views of Rossenbeck that in the human the primitive streak forms relatively little of the mesoderm.

It is to be noted that in the embryos of *Loris*, *Tarsius* and Selenka's Kleim S., the ectoderm and endoderm of the rudiment are in contact in the early stages; the duration of contact diminishes as the scale is ascended.

In answer to question A (p. 206) it can therefore be stated that in the human the mesenchyme of the stalk is in all probability derived from a proliferation of the caudal margin of the shield ectoderm, and one can postulate a stage, perhaps transient, when the ectoderm and endoderm are connected in the midline over a considerable extent of the embryonic shield. As seen in the sections of McIntyre I and also demonstrated by Florian (1934) in embryo Beneke (size 0·75 mm.) and by Hill and Florian (1931) in the Dobbin embryo (0·98 mm.), the mesoderm of the primitive streak is continuous round the cloacal membrane with that of the stalk.

As there is no histological difference between the primary as compared with the secondary mesoderm it is impossible from a study of the sections to say where the one ends and the other begins, but it is reasonable to assume that the mass of mesoderm beyond the cloacal membrane and on the caudal aspect of the stalk is compounded of primary and secondary mesoderm.

DIVISION OF THE CLOACAL MEMBRANE

Until the recent work of Florian, scant attention was given by embryologists to the caudal region of the human embryo. Any semblance of union between the ectoderm and endoderm in the expected region by direct apposition or indefinite cords of cells was designated "cloacal membrane". The approximation of endoderm and ectoderm with no intervening mesoderm in section 130 of McIntyre I gives the appearance of an undoubted cloacal membrane. Similarly the connecting cord of cells from the amniotic ectoderm to the endoderm of the allantois is clearly demonstrable in section 119. On the other hand, a cursory examination of sections 125 and 126 might lead to their interpretation as cloacal plates, whereas a more careful study shows the impossibility of excluding mesoderm intervention.

Section 118 with the cord of cells from the amnion extending almost to the endoderm suggests that at this point former fusion between the two layers is being broken down by a pressing in of mesoderm from each side.

Most observers are agreed as to the difficulty in defining the limits of the cloacal membrane. Hill & Florian (1931), describing the Dobbin embryo, comment on this, more especially the differentiation between the membrane and the primitive streak. Of this region Debeyre (1912) says: "A son extrémité postérieure comme dans l'embryon de Keibel-Frassi (1907) se trouve l'ébauche d'une membrane cloacale très probablement au moins (bien que nous ne puissons le vérifier directement sur les coupes)." Much of this difficulty, however, arose from the failure to recognize the incompleteness of fusion in many parts of the "membrane".

Sternberg (1927), in an embryo of 4 somites, described a fusion of ectoderm and hindgut endoderm, and also separate connexions between amniotic ectoderm and the endoderm of the allantois. Since then similar conditions have been noted in other specimens—Florian (1930) in embryo Bi II (also of 4 somites); Hill and Florian (1931) in the Dobbin embryo; and West (1930), describing an embryo of 8 somites, states that the cloacal membrane is very indefinite, actual contact being established in only two sections.

In the Ingalls (1918) embryo there exists what the author designates as an amnio-allantoic duct characterized by a pocketing of the amniotic cavity towards the allantois with contiguity of ectoderm and endoderm. Rossenbeck (1928), after noting the cloacal membrane as a cord of cells from the ectoderm to the endoderm in the Peh-Hochstetter embryo, in a subsequent paragraph describes an apposition of the dorsal wall of the allantoic passage with the floor of the amniotic cavity.

From a study of McIntyre I, along with the facts available from recent work on this subject, more especially the researches of Florian, I am of the opinion that the primordium of the cloacal membrane is in the early stages relatively extensive, the caudal fusion of endoderm and ectoderm being between the amnion and the future allantois, at this stage not yet separated off from the

Table I. *Table showing extent of cloacal membrane relative to the size of the embryo*

Embryo	Length of embryonic disc Presomite	Cloacal membrane
W.O. (V. Mollendorff, 1925)	0·25 mm.	What von Mollendorff describes as the cloacal membrane is, according to Florian, the primitive streak, and von Mollendorff's allantois is the cloacal membrane of Florian
"Fetzer" (*Fetzer & Florian, 1930*)	0·26 mm.	The cloacal membrane is separated by an interval from the primitive streak
T. F. (Florian (1928))	0·4 mm.	The cloacal membrane is a cord of cells which extends on to and connects the allantoic endoderm with the amniotic ectoderm
Bi I	?	Primitive streak reaches the cloacal membrane
Bi 24	0·625 mm.	Length 0·06 mm.
"Hugo" Stieve (1926)	0·635 mm.	Length 0·035 mm.
"Beneke" (Strahl & Beneke, 1910)	0·75 mm.	Cloacal membrane separated by an interval from the primitive streak
W.A. 17 (Grosser, 1930–1)	0·85 mm.	Length 0·13 mm. and extends on to the allantois
"Dobbin" (Hill & Florian, 1931)	0·98 mm.	Length 0·08 mm.
Peh-Hochstetter Rossenbeck (1923)	1·4 mm.	Cloacal membrane extends well on to allantois
Heuser (1930)	1·6 mm.	Cloacal membrane extends well on to allantois
Ingalls (1918)	2·0 mm.	Length 0·12 mm., and there is an additional connexion between the allantoic endoderm and amniotic ectoderm
	Somites	
F. von Orts Llorca (1934)	2	Cloacal membrane in two parts—one of which is allantoic
H 3 (Wilson)	2–3	Cloacal membrane at the commencement of allantois
Bi II	4	Cloacal membrane broken up—one portion involving allantois
Sternberg (1927)	4	Cloacal membrane is in four portions
Pfannenstiel-Kromer	5–6	Very short cloacal membrane extending some distance into the allantois
Dandy (1910)	7	Not mentioned
Payne (1925)	7	Not mentioned
West (1930)	8	Length 0·09 mm.
Eternod (1899)	8	Length 0·05 mm.
Corner (1929)	10	Cloacal membrane terminates before reaching the allantois
Embryo Bl. XI	10	Cloacal membrane terminates before reaching the allantois
Pfannenstiel III	13–14	Has trebled its length compared to Pfannenstiel-Kromer
Heuser (1930)	14	Length 0·18 mm.
Atwell (1930)	17	Length 0·18 mm. Extends to the allantois
Davis (1924)	20	Length 0·16 mm.

yolk sac. At a subsequent period the allantoic portion of the connexion is broken down by an extension of the mesoderm in towards the middle line, the chordal[1] part remaining as the site of the permanent cloacal membrane. This undergoes extension later along with the growth of the cloaca and embryo as a whole.

Table I is a series of embryos arranged according to size, with, as far as can be obtained, the available data regarding the cloacal membrane.

In the earliest specimens before the appearance of the allantois the fusion of ectoderm and endoderm occurs at the caudal end of the disc cranial to the attachment of the body stalk. In later embryos of the presomite class, in every case the membrane includes the allantois, and this condition remains up to the stage of about 4 somites. At this time the connexion with the amnion is being interrupted by mesoderm, and in the immediately older embryos of about 5–8 somites the cloacal membrane will be relatively much reduced. This is exemplified in the Pfannenstiel-Krömer embryo of 5–6 somites, and may account for its apparent absence in that of Dandy (1910)—7 somites—and Payne (1925)—7 somites. After the 10-somite stage the cloacal membrane seems to undergo proportionate development, although according to Heuser there are variations in its extent which have no relation to the size of the embryo.

The inferences deduced from the table, owing to the small series and lack of mathematical measurements, can only of course be accepted in a broad sense, but are of interest as coinciding with the suggestions made from observations on embryo McIntyre I. It should be noted that in the Dobbin embryo Hill and Florian observed the presence of granules in the cells of the cloacal membrane which in the opinion of Florian are to be regarded as indicative of degeneration of the cells. These granules occurred in the areas of incomplete fusion. F. von Orts Llorca (1934) has demonstrated a very similar condition to that in in McIntyre I in an embryo of 2 somites where he shows the cloacal membrane in two parts, (1) at the junction of allantois and yolk sac, (2) between the amnion and allantois. Regarding the membrane he states: "Da in dieser Gegend zahlreiche absterbende Zellen vorhanden sind, scheint es, dass die Kloakenmembran in frühen Entwicklungsstadien eine grössere Ausdehnung besitzt und dass sie zunächst bis auf das Allantoisdivertikel übergreift, während später der der Allantois entsprechende Teil der Kloakenmembran verschwindet und das Mesoderm zwischen das Amnion- und das Allantoisepithel vordringt."

The terminal point of the primitive streak is still a matter of controversy. In embryo McIntyre I, as already noted, sections 142–131 show the mesoderm distinctly budding off from the ectoderm of the primitive groove, whereas in the sections after the first part of the cloacal membrane, i.e. in 129–119, while the mesoderm and ectoderm are in continuity there is no actual formation of

[1] In this paper the portion of the cloacal membrane nearest the body stalk will be designated the "allantoic end", and the portion most distant from the body stalk the "chordal end".

mesoderm. One would therefore infer that the primitive streak terminates at the cloacal membrane.

Keibel and Elze express the opinion that the cloacal membrane should be regarded as a modified part of the primitive streak which reaches up to the body stalk. Their views are based on the presence of thickening of the ectoderm which stretches down almost to the allantois. This I would regard as a partially obliterated cloacal membrane and not primitive streak. Grosser (1927) implies that the streak becomes divided, a part growing into the tail bud, and the remainder being represented by the cloacal membrane. He also states that the primitive streak does not appear until the disc is 0·5 mm. long. The cloacal membrane has been shown to exist when the anlage of the primitive streak is represented only by a nodal fusion of all three layers (Florian, 1934). In the same monograph Florian has also demonstrated in E. Beneke and Fetzer an interval between what he regards as the cloacal membrane and the primitive streak in which all three layers are distinct and separate. In the later stages the primitive streak grows down to the cloacal membrane.

The name primitive streak was first given to the appearance observed in the chick embryo, the "streak" being essentially caused by the formation of mesoderm from the ectoderm at that particular region. As there is no mesoderm in the formation of the cloacal membrane it can be assumed that the actual streak as observed in the chick does not include the membrane. Keibel argues that the membrane is a secondary formation, the approximation of the ventral rim of the cloaca and ectoderm pressing the mesoderm from the midline. Recent work has negatived this as the union of ectoderm and endoderm at the caudal end of the shield occurs as early as, if not before, the primordium of the primitive streak.

Grosser (1927) inclines to the view that the ectoderm and endoderm of the embryonic disc are everywhere separated by an interrupted layer of primitive mesoderm, but quotes von Mollendorff's assertion of a ribbon-like connexion between the layers in the midline caudally which Rossenbeck regards as a connexion from the morula stage.

Strahl & Beneke (1910) express the opinion that the ectoderm and endoderm remain widely connected in the early stages, this connexion being later restricted to the primitive streak region.

Opinion seems unanimous that some degree of contact is maintained in the midline, and it is not unreasonable to conclude that in man as in lower mammals there is continuity along the length of the disc, separation being effected as suggested.

The hypothesis advanced here is as follows. Despite the precocious development of the primary mesenchyme in the human, it seems reasonable from phylogeny to postulate a stage when the ectoderm and endoderm are in contact in the midline. The appearance of the primordium of the primitive streak representing the fused lips of the blastopore acclaims the formation of secondary mesoderm separating the ectoderm and endoderm in this region.

The invagination of the dorsal lip with the pushing forward of the head process intervenes between the two layers of the disc cranially. Anterior to the head process the layers remain in contact—the site of the buccopharyngeal membrane.

Caudal to the fused lips of the blastopore and reaching to the attachment of the stalk remains a relatively extensive area of contact, the anlage of the cloacal membrane. The yolk-sac endoderm of the caudal portion of the membrane is predestined to become the epithelium of the allantoic diverticulum, and, as suggested above, the ectoderm and endoderm are here later separated by incursions of mesoderm. The cloacal membrane would thus be the homologue of the ventral lip of the blastopore and adjacent area.

From the cranial end of the primitive streak wings of mesoderm extend forwards on each side of the head process fusing anteriorly in the region of the mesodermal field of the protocardial area. Similarly from the caudal end of the streak as seen in McIntyre I, mesodermal processes extend round the cloacal membrane fusing with the stalk tissue in the region of the posterior mesodermal field. There would therefore be a close analogy in the development of the poles of the disc, the more rapid progress of the caudal end in the human obscuring many of the features.

The above assumption is compatible with the facts as observed at a later stage of development.

The bearing of these findings and conclusions on the problem of ectopia vesicae will be discussed later.

DESCRIPTION OF EMBRYOS FROM 2·4 TO 40 MM.

2·4-*mm. embryo*

The next of the Glasgow series to be examined is an embryo of 2·4 mm. in length. This was obtained as a result of abortion, and although seeming for the most part morphologically normal the tissues show some pathological change and the region of the tail fold is abnormal. This and the plane in which the sections were cut forbid any definite statement regarding the position and size of the cloacal membrane.

A photograph of a wax plate model of the embryo is given in Pl. III, fig. 12, and it is evident that there is some degree of torsion on a longitudinal axis, the attachment of the stalk and yolk sac being twisted to the right, while the caudal extremity turns to the left.

Section 84 (Pl. I, fig. 2) shows a mesodermal mass on the caudal aspect of the stalk attachment, and the graphic reconstruction of a coronal and sagittal plane give some idea of the extent of this tissue (Text-fig. 2A, B).

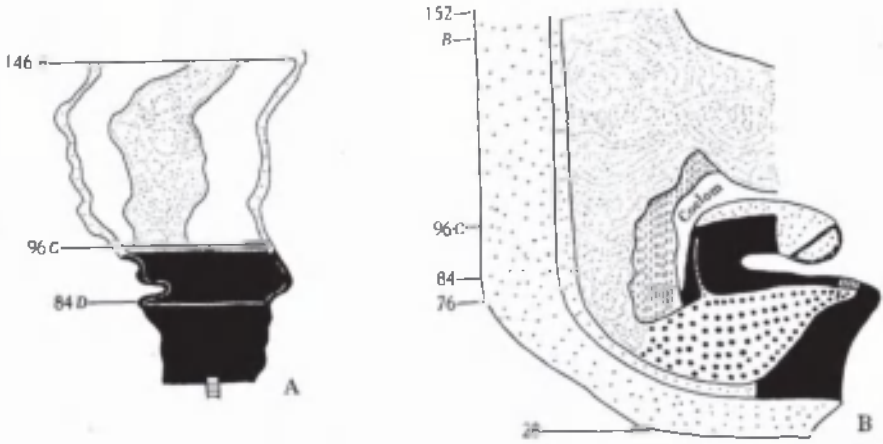
It envelops the embryonal end of the stalk, extending for a short distance only into the stalk substance and becoming continuous below with the mesoderm forming the ventral wall of the caudal end. As has been stated, the mesodermal mass is composed of primitive and secondary mesoderm (the secondary

mesoderm extending in wing-like processes round the cloacal membrane), the two fusing and forming the tissue seen in the figure, and illustrated in the reconstruction.

It is to be noted that at this stage there is no anterior abdominal wall, the entire ventral aspect below the septum transversum being occupied by the wide communication with the yolk sac and the attachment of the stalk. The allantoic end of the cloacal membrane is some distance from the stalk attachment.

4·5-mm. embryo (***McIntyre II***)

This embryo was obtained following a hysterectomy and sterilization in a case of mitral stenosis and incompetence with a history of cardiac trouble during previous pregnancies. When brought into the Department the vesicle



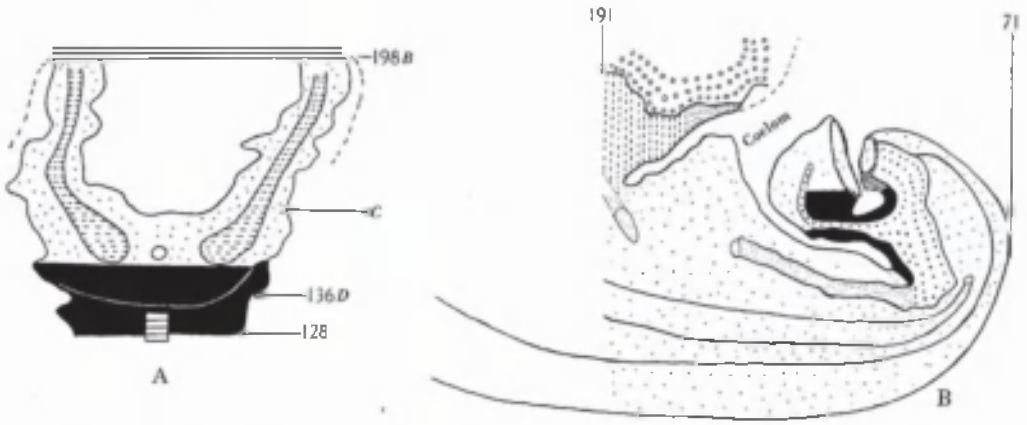
Text-fig. 2. Embryo 2·4 mm. ×50. Numbers refer to the sections. A. Reconstruction of the ventral surface from the septum transversum to the cloacal membrane. B. Reconstruction of a median sagittal section (see Pl. III, fig. 12). Description in text. Gut and yolk sac—fine stippling; cloaca and allantois—large dots; cloacal membrane—straight lines; dense mesoderm—black; splanchnopleure—interrupted lines. Between *B* and *C* the ventral wall is occupied by the mouth of the yolk sac. *D.* = the level of the caudal attachment of the body stalk.

was perfectly clear and transparent with no magma present. On opening the vesicle the umbilical arteries could be seen actually pulsating. There is therefore every probability of a normal structure, and considerable weight may be attached to the findings in this case.

Pl. VI, fig. 21, is a photograph of a wax-plate reconstruction from which it is observed that the ventral wall is still occupied by the communication with the yolk sac considerably narrowed from that in the 2·4 mm. Below this is the stalk attachment.

The embryo was cut transversely in a cranio-caudal direction, and Text-fig. 3A shows a graphic reconstruction of the ventral surface from the septum

transversum to the region of the cloacal membrane. The caudal end is represented straightened out and the approximate position of the cloacal membrane indicated. Text-fig. 3B is a graphic reconstruction in a plane indicated in Pl. VI, fig. 21. The cloacal membrane extends over twenty sections, each of 10 μ, and has therefore a total length of 0·2 mm. Owing to the direction of the sections and the folding of the caudal end, the distance of the membrane from the stalk attachment cannot be accurately measured, but it is apparent from a study of the reconstruction that the allantoic end of the cloacal membrane is some distance below the lower attachment of the stalk.



Text-fig. 3. Embryo 4·5 mm. (McIntyre II). ×50. The numbers refer to the sections. A. Reconstruction of the ventral surface from septum transversum to cloacal membrane. The tail is represented straightened out. B. Reconstruction of median sagittal section (see Pl. VI, fig. 21). The yolk sac is not shown. Description in text. Gut—fine stippling; cloaca and allantois—large dots; dense mesoderm—black; cloacal membrane—horizontal lines; allantoic vessels—interrupted horizontal lines; septum transversum—interrupted vertical lines; liver—small circles. The interval between *B* and *C* is the communication between extra- and intra-embryonic coelom. *D* = the level of the caudal attachment of the body stalk.

Section 136 (Pl. IV, fig. 13) shows the lower attachment of the stalk and the hindgut with its dorsal mesentery. There is no indication of the cloacal membrane, indeed the cloaca itself only comes into view in the more caudal sections.

Pl. IV, fig. 14, is a photograph of section 131 and is the allantoic end of the cloacal membrane. It can be seen that the section is at the head of the tail fold and some distance from the stalk attachment.

Section 138 (Pl. IV, fig. 15) is at the caudal limit of the attachment of the stalk. There is a strong mesodermal condensation at the embryonal end of the stalk. Section 144 (Pl. IV, fig. 16) is the site of the cranial attachment, and the loose texture of the tissue is apparent in comparison with that in section 138.

This mesodermal condensation at the lower aspect of the stalk, as can be seen from the reconstructions, is continuous with and prolonged into the tissue of the ventral wall below the stalk attachment, extending down to the cloacal

membrane. It has increased relatively from the corresponding mass in the 2·4-mm. embryo and represents the primordium of the genital tubercle and ventral parts of the infra-umbilical abdominal wall.

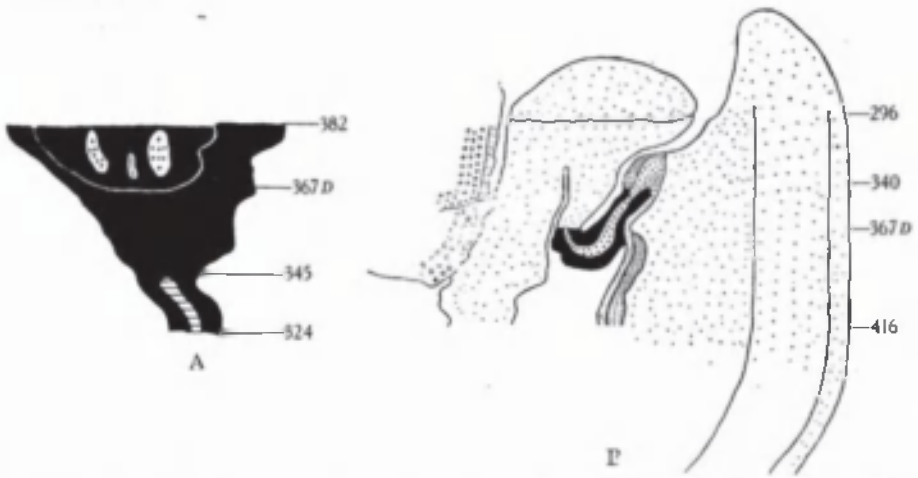
Keibel & Mall give a reconstruction of the embryo Pfannensteil-Kromer of 1·38 mm., showing a cloacal membrane of 0·02 mm. length extending up to the attachment of the stalk, and also a reconstruction of Pfannenstiel III of 2·6 mm.—with a cloacal membrane 0·13 mm. long extending up to and a short distance along the body stalk. Most authors seem to be in agreement with this, including Bryce (Quain's *Anatomy*, vol. i), Keith and Frazer.

In the embryo just examined there is quite a definite interval between the cloacal membrane and the stalk. In one of his later publications a similar mesodermal separation was shown by Keibel in embryo "EB", and has been demonstrated by Sternberg (1926) in embryo B of 18 somites and embryo F of 4 mm.

The question will be later discussed in relation to the problem of extroversion of the bladder.

7-mm. embryo

This specimen was obtained following curettage and cut transversely at 10 μ in a cranio-caudal direction. Pl. V, fig. 17, is a drawing of a wax model reconstruction.



Text-fig. 4. Embryo 7 mm. Numbers refer to the sections. A. Reconstruction of the caudal portion of the ventral surface. × *circa* 50. The tail is straightened out. B. Reconstruction of a median sagittal section. × 25. See Pl. V, fig. 17. Gut—fine stippling; cloaca and allantois—large dots; dense mesoderm—black; cloacal membrane—horizontal lines; mesentery—interrupted horizontal lines; septum transversum—interrupted vertical lines; liver—small circles; heart and allantoic vessels—crosses. *D* = the level of the caudal attachment of body stalk.

The cloacal membrane stretches over sixteen sections, giving a total length of 0·16 mm. Section 329 illustrates the chordal end of the membrane, and section 345 the allantoic end (Pl. V, figs. 18–20), and it is to be noted that in

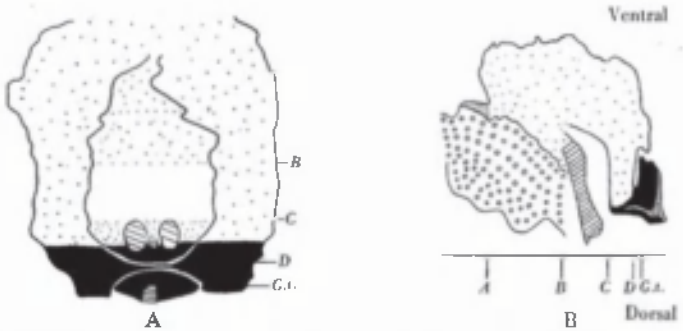
this specimen there is no membrane as represented by the coaptation of two layers of cells, but rather as a cord or plate of cells several rows thick, the major portion of the plate seeming to be derived from the endoderm. Section 867 is through the caudal attachment of the stalk; the allantoic end of the cloacal membrane is therefore 0·24 mm. from the stalk.

Section 873 (Pl. V, fig. 19) affords comparison between the caudal and cranial regions of the body stalk, the former exhibiting a fairly dense mesenchyme around and on the superficial aspect of the vessels, while the latter shows the typical loose texture of stalk tissue.

As can be observed in the graphic reconstruction of a medial sagittal section (Text-fig. 4A, B), the mesodermal condensation in the stalk is continuous with and merges into the dense tissue intervening between the ventral part of the cloaca and the surface. It extends on either side of the cloacal membrane as part of the mesodermal bed of the cloaca.

12·5-*mm. embryo*

This embryo was obtained during operation for a ruptured ectopic pregnancy, the history of acute haemorrhage suggesting the recent death of the foetus.



Text-fig. 5. Embryo 12·5 mm. Description in text. A. Reconstruction of ventral surface from septum transversum to cloacal membrane. × *circa* 12. B. Reconstruction of median sagittal section of same. × 10. Dense mesoderm—black; ventral cloaca and allantois—large dots; cloacal membrane—horizontal lines; blood vessels—oblique lines; liver—circles. *A* = section 675 at the level of the cranial attachment of body stalk; *B* = section 775; *C* = section 825; interval between *B* and *C* is the extension of the coelom into the stalk and occupied by midgut loop; *D* = section 875 at the level of caudal attachment of the stalk; *G.t.* = section 888 at the level of the genital tubercle.

It is the first of the series in which the genital tubercle appears, and the small area between the tubercle and the stalk may be said to be the commencement of a true infra-umbilical portion of the abdominal wall.

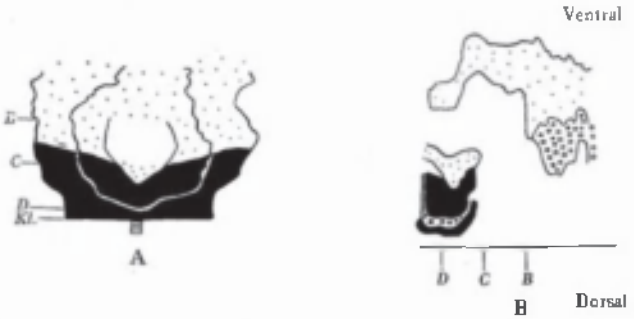
Section 864 (Pl. VI, fig. 28) shows the mesodermal condensation in the lower portion of the stalk and caudal to the vessels. It is becoming more marked and extends laterally to meet the paraxial downgrowth into the abdominal wall.

The relations can be followed from the reconstructions of the ventral wall (Text-fig. 5A) and a median sagittal section (Text-fig. 5B). The condensation can be traced caudally as it passes round the cloacal membrane to fuse with the general mesoderm on each side of the cloaca. It forms the basis of the genital tubercle which carries the membrane on its lower surface. The "infra-umbilical" area extends over eight sections measuring therefore about 0·08 mm.

13-mm. embryo

Obtained following abortion, this embryo, despite its greater size, is probably an earlier stage than the preceding. There is no genital tubercle and the tissues of the specimen show pathological changes.

The mesodermal condensation in the caudal portion of the stalk is, however, evident, and reference to the graphic reconstruction (Text-figs. 6A, B) shows again the continuation of this tissue down to and round the cloacal membrane. The allantoic end of the membrane itself is separated by a short interval from the stalk attachment.



Text-fig. 6. Embryo 13 mm. × *circa* 12. A. Reconstruction of lower ventral surface. B. Reconstruction of median sagittal section of ventral wall. Cloacal membrane—horizontal lines; dense mesoderm—black; ventral cloaca and allantois—large dots; liver—circles; *B* = section 910; *C* = section 954; interval between *B* and *C* is the extension of the coelom into the stalk and occupied by the midgut loop. *D* = section 1002 at the level of caudal attachment of the body stalk. *Kl.* = cloacal membrane.

14-mm. embryo

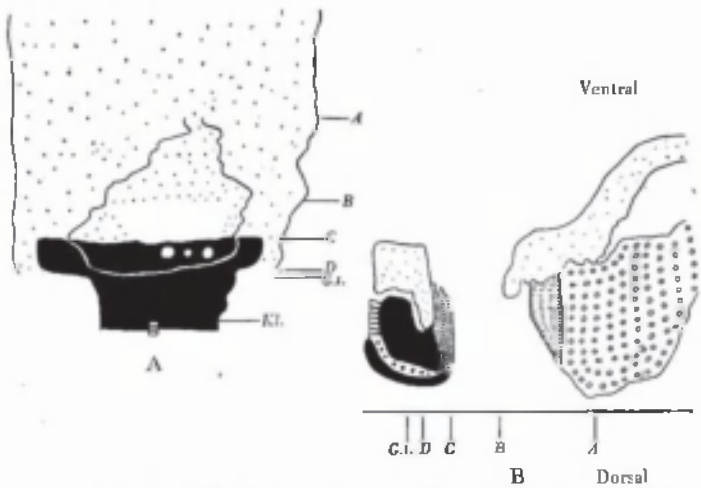
Obtained at operation and fixed while still transparent. Before fixation this embryo measured 15·5 mm. The sections were cut transversely.

The sections cranial to the stalk and intestinal loop show the ventral downgrowths from the paraxial mesoderm. These downgrowths exhibit some tendency to divide into strata foreshadowing the muscular layers of the anterior abdominal wall (Pl. VII, fig. 24). Ventrally the wall is completed by mucoid tissue.

Caudally the downgrowths from the paraxial mesoderm become less marked until they ultimately disappear entirely, but ventrally the mucoid tissue merges into a mesodermal condensation which in the lower sections is

well marked, and at the level of the caudal attachment of the stalk appears as a thick band of tissue on the superficial aspect of the allantoic vessels (Pl. VII, fig. 25). More caudally the band is continuous with the genital tubercle. The extent and relations of the mesodermal mass are shown in the graphic reconstructions (Text-figs. 7A, B).

The sections show clearly that the mesodermal condensation of the ventral portion of the infra-umbilical abdominal wall is not derived from the paraxial downgrowths, but has a separate origin. This part of the abdominal wall, as represented by the interval between the attachment of the stalk and the genital tubercle, has increased in length as compared with the 12·5-mm. embryo.



Text-fig. 7. Embryo 14 mm. × 10. A. Reconstruction of the ventral surface caudal to the septum transversum. B. Reconstruction of a median sagittal section of ventral wall. Dense mesoderm—black; cloaca and allantois—large dots; cloacal membrane—horizontal lines; liver—circles; blood vessels—interrupted horizontal lines. *A* = section 872 at the level of cranial attachment of the stalk. *B* = section 972; *C* = section 1044; interval between *B* and *C* is the extension of the coelom occupied by the midgut loop. *D* = section 1052 at the level of caudal attachment of stalk; *G.t.* = section 1060 at the level of genital tubercle. *Kl.* = cloacal membrane.

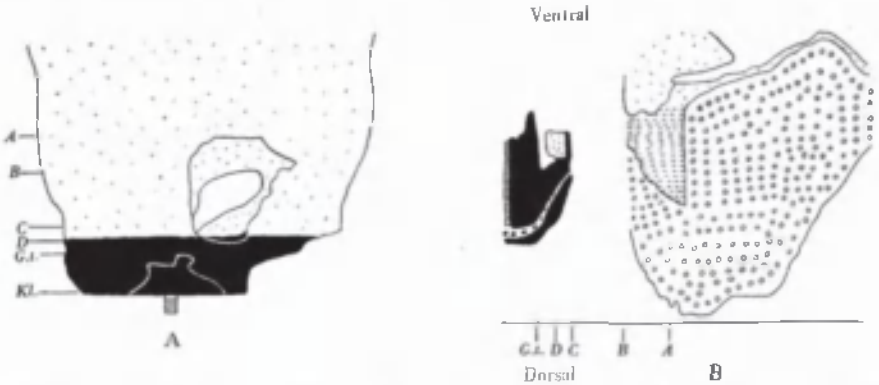
16·1-*mm. embryo*

Obtained following abortion.

The sections show the downgrowths from the paraxial mesoderm dividing into three strata.

These persist into the lower portion of the abdominal wall. In the upper sections (Pl. VII, fig. 26) the downgrowths reach about half-way round, but below the stalk they become continuous with the mesodermal thickening which commences on the caudal aspect of the stalk, and inferiorly forms the genital tubercle (Pl. VII, fig. 27). As can be seen from the graphs (Text-fig. 8A, B) this mesoderm forms the increasing infra-umbilical abdominal wall, the

genital tubercle, and the tissue between the cloaca and the ventral surface. The cloacal membrane, represented by a deep cleft, is on the caudal aspect of the genital tubercle.

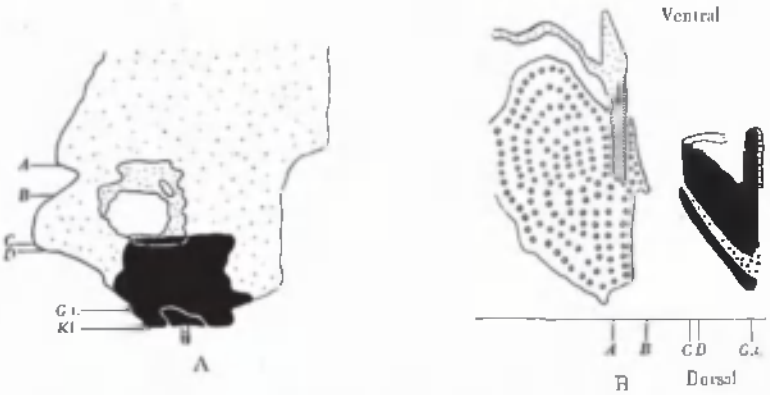


Text-fig. 8. Embryo 16·1 mm. × *circa* 12. A. Reconstruction of the ventral surface below the septum transversum. B. Reconstruction of a median sagittal section of ventral wall. Dense mesoderm—black; cloacal membrane—horizontal lines; ventral cloaca and allantois—large dots; liver—circles; blood vessel—interrupted horizontal lines. *A* = section 1148 at the level of the cranial attachment of the body stalk. *B* = section 1200. *C* = section 1256. *B–C* = extension of the coelom occupied by the midgut loop. *D* = section 1272 at the level of the caudal attachment of the stalk. *G.t.* = section 1282 at the level of the genital tubercle. *Kl.* = cloacal membrane.

23-mm. embryo

No history.

The downgrowths from the dorsal mesoderm are clearly divisible into three strata uniting in front. Above the body stalk the ventral junction is some



Text-fig. 9. Embryo 23 mm. × *circa* 12. A. Reconstruction of the ventral surface below the septum transversum. B. Reconstruction of a median sagittal section of ventral wall. Dense mesoderm—black; cloacal membrane—horizontal lines; ventral cloaca and allantois—black dots; liver—circles; blood vessels—interrupted horizontal lines. *A* = section 825 at the level of the cranial attachment of body stalk. *B* = section 857; *C* = section 913. Between *B* and *C* is the extension of the coelom occupied by the midgut loop. *D* = section 921 at the level of the caudal attachment of the stalk. *G.t.* = section 977 at the level of the genital tubercle. *Kl.* = cloacal membrane.

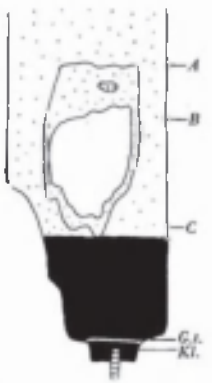
distance from the midline where the body wall is composed of tissue of loose texture (Pl. VIII, fig. 28). At the level of the body stalk the thickening forming the rectus muscle is visible; the splitting to form its sheath can be discerned. Below the body stalk the rectus sheath runs into a mesodermal mass forming the midventral wall (Pl. VIII, fig. 29). The infra-umbilical abdominal wall has increased considerably from that of the 16·1 embryo.

The mesodermal mass forms not only the ventral portion of the abdominal wall but the entire thickness of tissue superficial to the allantois and bladder (Text-fig. 9 A, B).

30-mm. embryo

Obtained following abortion; sections cut longitudinally.

The graph (Text-fig. 10) shows the extent of the mesoderm and Pl. VI, fig. 22, is a section almost through the midsagittal plane, demonstrating the continuity of the stalk mesoderm with that forming the lower abdominal wall and genital tubercle.



Text-fig. 10. Embryo 30 mm. × *circa* 12. Reconstruction of the ventral surface below the septum transversum. Dense mesoderm—black; cloacal membrane—horizontal lines; blood vessel—interrupted horizontal lines. *A* = cranial attachment of body stalk; between *B* and *C* is the extension of the coelom occupied by the midgut loop; *D* = the caudal attachment of the stalk; *G.t.* = genital tubercle. *Kl.* = cloacal membrane.

40-mm. embryo

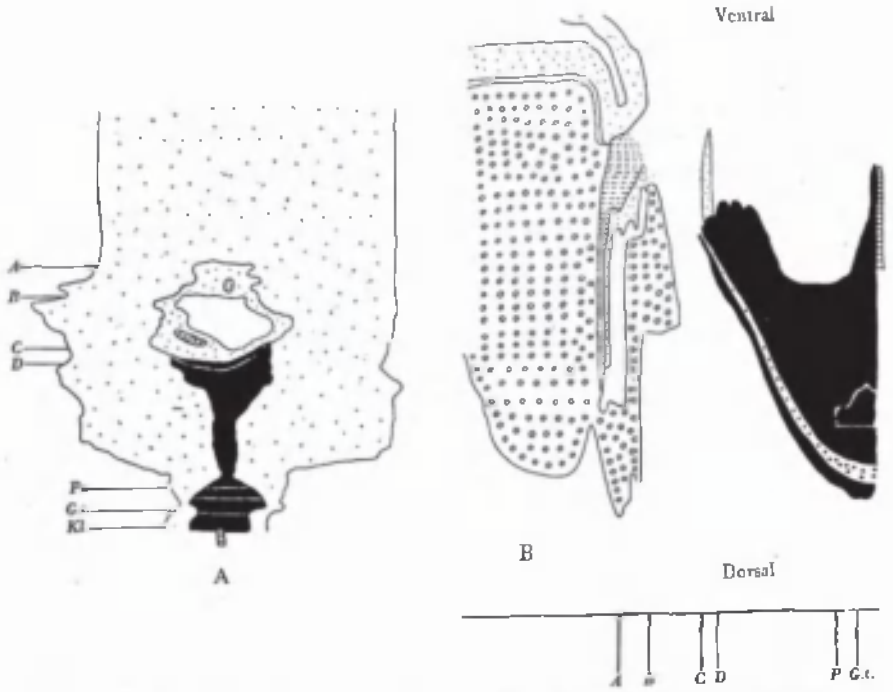
No history.

The ventral wall again shows the three muscular sheets terminating in the rectus in front.

The increasing thickness of the abdominal wall, well marked in this embryo, appears to be due to the somatopleure mesoderm rather than the paraxial myogenic downgrowths. The umbilical cord appears to be sunk in a depression in the anterior abdominal wall (Pl. VIII, fig. 30), which may be caused by a failure of the thickening to reach the midventral line owing to fixation at the umbilicus. The interval between the recti decreases in the more caudal sections.

The mesodermal mass in the midventral portion of the infra-umbilical wall, now of considerable length, is reinforced by extensions from the rectus sheath. It is also increased in thickness, stretching from the surface to the bladder and allantois internally.

In this embryo the condensations forming the pubic portions of the pelvis are present (Pl. VIII, fig. 31), and it is apparent that these arise from the central mesodermal mass (see graphs—Text-figs. 11A, B). Caudally the mesoderm forms the genital tubercle.



Text-fig. 11. Embryo 40 mm. × *circa* 12. A. Reconstruction of the ventral surface below the septum transversum. B. Reconstruction of a median sagittal section of ventral wall. Dense mesoderm—black; cloacal membrane—horizontal lines; ventral cloaca and allantois—black dots; liver—circles; blood vessels—interrupted horizontal lines. *A* = section 1152 at the level of the cranial attachment of body stalk; *B* = section 1184; *C* = section 1236; between *B* and *C* is extension of coelom; *D* = section 1252 at the level of the caudal attachment of stalk; *G.t.* = section 1408 at the level of the genital tubercle; *Kl.* = cloacal membrane; *P* = section 1384 at the level of the pubic condensations.

DISCUSSION

In the earliest embryo studied (the McIntyre I of 1·4 mm.) there is present a band of mesodermal tissue passing from the caudal aspect of the stalk round the cloacal membrane to the region of the termination of the primitive streak.

From the graphic reconstructions of the various stages up to that of 40 mm. the growth and development of this band of tissue can be traced; it is apparent

that from it are formed the structures in the midventral line of the infra-umbilical part of the body wall including the abdominal wall itself, the genital tubercle, cloacal fold, symphysis pubis, and the muscular coat of the bladder.

At the body stalk this mesoderm envelops the caudal aspect extending only a short distance along the stalk and surrounding not only the proximal portion of the allantois and allantoic vessels but furnishing a distinct band of tissue on the deep surface of the body wall caudal to the umbilicus in which are placed these structures; it becomes continuous with the mesoderm round the cloaca.

The more dense character of the tissue on this portion of the stalk as compared with the looser texture and mucoid appearance of the remainder is particularly well marked up to the 23-mm. stage. In the 30 and 40 mm., while still apparent, it does not so sharply contrast with the surrounding tissue in the stalk or upper half of the abdominal wall, as though its strength were becoming exhausted by a "paying-out" to its derivatives.

The question of the origin of the umbilical part of the mesoderm has already been discussed and the conclusion formed that it arises from the primitive mesoderm representing the site of the posterior mesodermal field of the embryonic shield. Extending as wing-like processes round the cloacal membrane it becomes continuous with the secondary mesoderm from the end of the primitive streak.

The observations leading to the assumption that the primitive streak terminates at or even before the commencement of the cloacal membrane are recorded earlier, and the reasons given for discarding the suggestion of Keibel and others that the cloacal membrane itself is a modification of the primitive streak which may extend as far as or even on to the body stalk.

The first indication of the existence of a body wall below the attachment of the stalk is in the 12·5-mm. embryo, where the interval between the genital tubercle and the stalk is occupied by the mesodermal mass under discussion. This also shows lateral extensions passing some distance round the body wall and on each side of the genital tubercle forming the cloacal folds.

The relative decrease in the breadth of attachment of the body stalk, with the consequent ventral encroachment of the paraxial downgrowths into the somatopleure in the older embryos, minimizes the actual area of abdominal wall formed by this mesoderm, but it can be observed in its position in the midventral line up to the 40-mm. stage and is probably ultimately represented in the adult body wall by the symphysis pubis, lower part of the rectus sheath and infra-umbilical portion of the linea alba.

The extension of the 'coelom' into the pelvis follows a 'taking in' of the stalk into the body of the embryo with a prolongation of the 'umbilical coelom' (i.e. that part of the body cavity passing into the stalk) between the hind-gut and the ventral wall containing the allantois and the vessels. This can be seen in the reconstruction of the 4·5- and 7-mm. embryos. The mesoderm of the caudal end, in which is embedded the cloaca, remains unsplit, and thus that

portion which passes from the hind end of the primitive streak to become continuous with the downgrowth from the stalk is equivalent to somatopleure and splanchnopleure, forming not only part of the parietes, but the fibrous and muscular coats of the bladder. The condensations forming the pubes seen in the 30- and 40-mm. embryos are obviously arising in the midline from the mesoderm in this region.

ECTOPIA VESICAE AND EPISPADIAS

Any investigation of the embryology of this region inevitably involves the problem of ectopia vesicae and epispadias and the plethora of suggestion—much of it empirical, most of it unsatisfactory—which has been offered to account for this congenital defect.

On the question of the aetiology of extroversion of the bladder and epispadias most surgical text-books are content with the statement that the deformity can be ascribed to arrested development of the lower abdominal parietes. Others elaborate ingenious mechanical theories to account for the condition, for example, "pressure of the umbilical cord which passes between the lower limbs of the foetus to a dorsally placed placenta" (*Surgery of Childhood*, J. Fraser); or again, "Epispadias is really a hypospadias in which torsion of the penis has occurred at an early stage of foetal life so that the under surface becomes the upper" (*System of Surgery*, Choyce, vol. II, 1932).

For some time the views of Keibel were very generally accepted. According to this author the cloacal membrane should be regarded as a modified part of the primitive streak and ectopia vesicae as a persistent portion of the blastopore.

Keibel and Elze believe "that the primitive streak extends along the body stalk, as in some sections the ectoderm covering the body stalk shows a local thickening which is nearly in contact with the allantoic duct". The description is more akin to that of the cloacal membrane becoming obliterated by the incursion of mesoderm than to that of a primitive streak.

Keith agrees with Berry Hart that the primitive streak forms the post-umbilical wall and suggests that extroversion of the bladder is an unclosed condition of the streak. Should this be so, is there any reason why the non-closure of the blastopore should be confined to the allantoic portion of the ventral wall of the cloaca? Would it not be reasonable to assume that amongst the many recorded cases of this condition a few would show more extensive or additional defects involving perhaps the anal region or some degree of spina bifida which, according to Grosser (1927), is a non-fusion of the lips of the primitive groove? Or, again, one would expect to find the condition in lower mammals where the primitive streak forms not only the secondary but the primary mesoderm.

Cogent reasons have earlier been advanced for the rejection of the averment that the primitive streak extends on to the body stalk. There is neither

histological nor ontogenetical evidence to support the suggestion that the cloacal membrane is a modified primitive streak. The facts I have recorded as observed in McIntyre I, viz., that the primitive streak terminates at or even some distance before the commencement of the cloacal membrane, is in agreement with most of the recent work already referred to.

Keibel (1896) later retracts from his original position, and, having observed some diminution in the absolute length of the cloacal membrane in embryos of about 6 mm., is of the opinion that ectopia vesicae may result from a failure of shortening of the membrane at this stage and accordingly is of a later developmental period than was presumed in his previous observations.

Enderlen (1908) states that if such assumptions were correct, then the cloacal membrane must extend up to the body stalk, and in his opinion this is actually so up to the 9-mm. stage; the earlier the error occurs the more complete the defect, ranging from complete extroversion to hypospadias.

In the embryos 4·5 and 7 mm. of this series the cloacal membrane did not reach the body stalk, and similar observations on even earlier stages have been recorded.

Felix (1911) found that the cloacal membrane reaches the body stalk up to 18 somites.

From the study of this region in a series of embryos ranging from 1·4 to 40 mm. the following facts have been observed and are recounted graphically in the drawings.

Firstly, in the presomite-stage the cloacal membrane involves not only the cloaca, but exists as an area of contact between the amniotic ectoderm and allantoic endoderm. This is seen in section 119 of the McIntyre embryo and has been recorded by a number of observers including Florian (1930) in embryo Bi II and Sternberg (1927) in an embryo of 4 somites. The cloacal membrane is therefore at this stage relatively extensive reaching on to and along the proximal end of the connecting stalk. In the McIntyre embryo the "allantoic cloacal membrane" extends only over one section, and in the intervening area between that and the hindgut cloacal membrane, the ectoderm and endoderm are separated by mesoderm. In the Sternberg embryo there are three separate portions of the allantoic cloacal membrane, and two in the Bi II of Florian. In the next embryo studied of 2·4 mm. the cloacal membrane is limited to the cloaca proper, with a mesodermal interval between its allantoic extremity and the stalk.

It is therefore reasonable to assume that the interrupted contact of allantoic endoderm and ectoderm is evidence of the disappearance of the allantoic cloacal membrane, and not the commencement or extension of the existing cloacal membrane, and that, primarily, the "membrane" was an area of contact of ectoderm and endoderm extending from the hindgut cranially,[1] and caudally terminating some distance along the stalk.

[1] The terms "cranially" and "caudally" are here descriptive of the relations existing before the appearance of the tail fold.

The McIntyre I thus represents a stage showing the process of obliteration of the "allantoic cloacal membrane". Florian (1930) observed signs of degeneration in this part of the membrane.

Examination of the sections of this embryo leads to the conclusion that the separation of the ectoderm and endoderm in this region is effected by the mesoderm growing in towards and ultimately fusing in the midline. This mesoderm seems to be derived from the wing-like processes arising from the hind end of the primitive streak extending round on either side of the chordal portion of the cloacal membrane, and encroaching on the midline towards the allantoic end. One would therefore anticipate that at a later stage there would be evidence of a decrease in size and extent of the membrane, and a study of Table I discloses such a condition occurring in embryos of about 6–8 somites. It is of interest that the actual obliteration is in progress during what is probably the period of maximum activity of the primitive streak and when one would predict an optimum mesodermal energy.

In the 2·4 mm. and more definitely in the 4·5 mm. the cloacal membrane is placed some distance behind the caudal attachment of the stalk and is limited to the ventral aspect of the cloaca.

The processes of mesoderm encircling the membrane and fusing with the mesenchyme of the stalk form the band of denser tissue whose development has been followed up to the 40-mm. embryo. The extent covered by structures arising from this mesodermal tissue is indicated in the reconstructions by the areas shown in black from which it becomes evident that failure of this tissue to develop would result in the persistence of the original extensive cloacal membrane which would form the infra-umbilical portion of the ventral abdominal wall, the absence of the genital tubercle with defective formation of the external genitals, and deficiency of the symphysis pubis. With the breaking down and absorption of the cloacal membrane which normally occurs about the second month, the condition of ectopia vesicae would then be established. Minor mesodermal failure would be responsible for the lesser defect of epispadias.

The mesodermal septum dividing the cloaca into ventral and dorsal parts reaches the surface separating the anal from the urogenital orifice so that the extroversion is limited to the ventral cloaca, and the anal region develops normally.

As the mesodermal band has been shown to consist of primary and secondary mesoderm, the fault might be apportioned to the one or the other, or again could be accounted for by an undue adherence of amniotic ectoderm and allantoic endoderm, what Rossenbeck (1923) would term an "incomplete loosening" of the germinal layers preventing the mesodermal inroads.

Bearing in mind the role of the primitive streak and that it is less productive in the human than in any other form, one inclines to the view that the aetiological factor is deficiency and non-development of the mesodermal processes which normally arise from the hind end of the primitive streak, extend

on either side of the cloacal membrane, press in towards the midline, obliterate its allantoic extension, and, continuing on to the stalk, merge into the primary mesoderm.

Sternberg (1926), in a study of the cloacal membrane of young embryos, concludes that the period of shortening of the membrane coincides with the appearance of the first somites, and that therefore extroversion must occur before the degeneration of the allantoic cloacal membrane. He states of the condition: "Die teratogenetische terminationperiode der Bauchblasenspalte und der mit ihr verwandten missbildungen ist demnach wesentlich früher, als man bisher angenommen hatte und zwar etwa in jenes stadium zu verlegen im welchem sich die ersten Ursegmente ausbilden."

Extroversion of the bladder is a condition peculiar to the human species (Kermauner, 1909). This is probably due to the precocious development of the allantois, e.g. the Peh-Hochstetter embryo (Rossenbeck, 1923), in accordance with the mode of nutrition in the human, coupled with the diminished activity of the primitive streak. In *Tarsius* (Hubrecht, 1909) the primitive streak thickening appears as a forward extension of the proliferating caudal margin of the embryonic shield from which is formed the mesoderm of the connecting stalk, whereas in the human the origin of the primitive streak is much more cranial.

The "allantoic cloacal membrane" appears to be a human characteristic (Sternberg) and is possibly permitted by the more cranial origin of the streak with the consequent lessened mesodermal production at this point. Again, the extension of the cloacal membrane may be a secondary development due to the activity of the ectodermal cells of the amnion described by Florian (1930) which, encroaching on and destroying the mesoderm of the connecting stalk, thereby permits of the extension of the amniotic space at the expense of the stalk tissue.

The cloacal membrane appears at a relatively early stage in the human embryo (Fetzer-Florian embryo, 1930), and perhaps is not so much a development as an actual persistence of contact between the ectoderm and endoderm.

One concludes that ectopia vesicae is to be regarded as yet another of the long list of congenital defects to be laid to the account of the mesoderm and in some way occasioned by the declining activity of the primitive streak.

The determination of the causal factor effecting the mesodermal deficiency is a problem the answer to which may be found in the complicated mechanism of "organizers", the initiation of "Field Gradients" with their subtle interaction and susceptibility to adverse environmental conditions.

SUMMARY

1. A study has been made of a series of embryos ranging from 1·4 to 40 mm. in length, with graphic reconstructions, tracing the development of the infra-umbilical abdominal wall.

2. The infra-umbilical portion of the anterior abdominal wall, the genital tubercle, symphysis pubis, and muscular coat of the bladder, are formed from a well-defined band of mesoderm.

3. This band of mesoderm has a twofold origin: (*a*) from the caudal margin of the embryonic shield—primary mesenchyme; (*b*) processes of secondary mesoderm passing round the cloacal membrane from the hind end of the primitive streak.

4. In the embryo McIntyre I the cloacal membrane is in two parts, one of which implicates the allantoic diverticulum.

5. At an early stage the cloacal membrane is a relatively large area of contact of ectoderm and endoderm extending some distance along the allantoic diverticulum.

6. The allantoic cloacal membrane is later obliterated by the mesoderm pressing in towards the midventral line between the ectoderm and endoderm.

7. Extroversion of the bladder is due to mesodermal deficiency, particularly of the processes of secondary mesoderm arising from the hind end of the primitive streak, following on which there is persistence of the primary extensive cloacal membrane, impaired development of the muscular coat of the bladder, of the symphysis pubis, and of the formation of external genitals and infra-umbilical portion of anterior abdominal wall.

8. Epispadias is a similar mesodermal error in a minor form.

My thanks are due to my Chief, Prof. Blair, for his helpful criticism and valuable suggestion, and to Dr Norman H. W. Maclaren for his very generous assistance and advice.

The drawings of the wax plate reconstructions were made by Mr Alexander Rettie of this Department.

REFERENCES

Atwell, W. J. (1930). "A human embryo with seventeen pairs of somites." *Carneg. Instn Publ.* No. 407; *Contr. Embryol.* No. 118.

Bryce, T. H. (1908). *Quain's Anatomy*, 11th ed., vol. I. London.

—— (1924). "Observations on the early development of the human embryo." *Trans. roy. Soc. Edinb.*, vol. LIII, pt. iii, No. 26.

Bryce, T. H. & Teacher, J. H. (1908). *Contributions to the Study of the Early Development and Imbedding of the Human Ovum.* Glasgow: Maclehose.

Choyce. (1932). *System of Surgery*, vol. II.

Corner, G. W. (1929). "A well-preserved human embryo of ten somites." *Carneg. Instn Publ.* No. 394; *Contr. Embryol.* No. 112.

Dandy, W. E. (1910). "A human embryo with seven pairs of somites." *Amer. J. Anat.* vol. X.

Davis, C. L. (1924). "Description of a human embryo having twenty paired somites." *Carneg. Instn Publ.* No. 332; *Contr. Embryol.* No. 72.

Debeyre, A. (1912). "Description d'un Embryon humain de Onm. 9." *J. Anat.*, Paris, t. XLVIII.

Enderlen, E. (1908). "Über Blasenektopie." *Samml. klin. Vortr.* Nr. 472/73.

Éternod, A. C. F. (1869). "Il y a un Canal notochordal dans l'Embryon humain." *Anat. Anz.* Bd. XVI.

FELIX, W. (1911). "Die Entwicklung der Harn- und Geschlechtsorgane." In Keibel-Mall, *Handbuch der Entwicklungsgeschichte des Menschen.*

FETZER, M. (1910). "Über ein durch Operation gewonnenes menschliches Ei." *Anat. Anz.* Bd. XXXVII.

FETZER, M. & FLORIAN, J. (1930). "Der Embryo 'Fetzer' mit beginnender Axialmesodermbildung und bereits angelegter Kloakenmembran." *Z. mikr.-anat. Forsch.* Bd. XXI.

FLORIAN, J. (1928). "Ein junges menschliches Ei *in situ* (Embryo T.F. mit Primitivstreifen, ohne Kopffortsatz)." *Z. mikr.-anat. Forsch.* Bd. XIII.

—— (1930). "The formation of the connecting stalk and the extension of the amniotic cavity towards the tissue of the connecting stalk in young human embryos." *J. Anat.*, Lond., vol. LXIV, pt. iv.

—— (1933). "The early development of man, with special reference to the development of the mesoderm and cloacal membrane." *J. Anat.*, Lond., vol. LXVII.

—— (1934). "Ein Schema der Entwicklung der Axialgebilde des menschlichen Embryos bis in das Stadium von 10 Urwirbelpaaren." *Biol. gen.* Bd. x, Lief. 2.

FRAZER, J. (1926). *The Surgery of Childhood.* London: Arnold and Co.

FRASSI, L. (1907). "Über ein junges menschliches Ei *in situ*." *Arch. mikr. anat.* Bd. LXX.

FRAZER, E. (1931). *Manual of Embryology.* London: Baillière, Tindall and Cox.

GROSSER, O. (1927). *Frühentwicklung, Eihautbildung und Placentation.* Munich.

—— (1931). "Primitivstreifen und Kopffortsatz beim Menschen." *Anat. Anz.* Bd. LXXI.

HEUSER, C. H. (1930). "A presomite human embryo with definite chorda canal." *Carneg. Instn Publ.* No. 433; *Contr. Embryol.* No. 138.

—— (1930). "A human embryo with fourteen pairs of somites." *Carneg. Instn Publ.* No. 441; *Contr. Embryol.* No. 131.

HILL, J. P. (1932). "A developmental history of the primates." *Philos. Trans.* B, vol. CCXXI.

HILL, J. P. & FLORIAN, J. (1931). "A young human embryo (Embryo Dobbin) with head process and prochordal plate." *Philos. Trans.* B, vol. CCXIX.

HUBRECHT, A. A. W. (1909). "Early ontogenetic phenomena in mammals." *Quart. J. micr. Sci.* vol. LIII, N.S.

INGALLS, N. W. (1918). "A human embryo before the appearance of the myotomes." *Carneg. Instn Publ.* No. 227; *Contr. Embryol.* No. 23.

JENKINSON, J. W. (1913). *Vertebrate Embryology.* Oxford.

KEIBEL, F. (1896). "Zur Entwicklungsgeschichte des menschlichen Urogenitalapparats." *Arch. Anat. Physiol.*, Anat. Abt.

KEIBEL, F. & MALL, F. (1912). *Manual of Human Embryology.*

KEITH, A. (1921). *Manual of Embryology and Morphology,* 4th ed.

KERMAUNER, F. (1909). "Die Misabildungen des Rumpfes." In Schwalbe, *Die Morphologie der Missbildungen des Menschen und der Tiere.*

LLORCA, F. VON ORTS (1934). "Beschreibung eines menschlichen Embryo mit 4 Urwirbelpaaren." *Z. ges. Anat.* I. *Z. Anat. EntwGesch.* Bd. CIII, Heft 6.

MOLLENDORFF, VON (1925). "Das menschliche Ei. Wo(lfring) Implantation. Verschluss der Implantationsoffnung und Keimesentwicklung beim Menschen vor Bildung des Primitivstreifens." *Z. ges. Anat.* I. *Z. Anat. EntwGesch.* Bd. 76.

PAYNE, F. (1925). "General description of a seven-somite human embryo." *Carneg. Instn Publ.* No. 361; *Contr. Embryol.* No. 81.

PETERS, H. (1899). *Über die Einbettung des menschlichen Eies.* Leipzig u. Wien: Franz Deutike.

ROSSENBECK, H. (1923). "Ein junges menschliches Ei, Ovum Humanum Peh-Hochstetter." *Z. ges. Anat.* I. *Z. Anat. EntwGesch.* Bd. LXVIII.

STIEVE, H. (1926). "Ein 13½-Tage altes, in der Gebärmutter erhaltenes und durch Eingriff gewonnenes menschliches Ei." *Z. mikr.-anat. Forsch.* Bd. VII.

STERNBERG, H. (1926). "Zur formalen Genese der Bauchblasenspalte." *Virchows Arch.* Bd. CCLXIII.

—— (1927). "Beschreibung eines menschlichen Embryos mit vier Ursegmentpaaren." *Z. ges. Anat.* I. *Z. Anat. EntwGesch.* Bd. LXXXII.

Strahl, R. & Beneke, R. (1910). *Ein junges menschliches Embryo.* Wiesbaden.
Streeter, G. L. (1927). "The Miller ovum." *Carneg. Instn Publ.* No. 363; *Contr. Embryol.* No. 92.
Veit, O. & Esch, P. (1922). "Untersuchung eines *in situ* fixierten operativ gewonnenen menschlichen Eies der 4. Woche." *Z. ges. Anat.* I. *Z. Anat. EntwGesch.* Bd. LXIII.
Wilson, J. T. (1914). "Observations upon young human embryos." *J. Anat.*, Lond., vol. XLVIII.
West, C. M. (1930). "Description of an embryo of eight somites." *Carneg. Instn Publ.* No. 407; *Contr. Embryol.* No. 119.

EXPLANATION OF PLATES I–VIII

Plate I

Fig. 1. Photograph of a drawing of a wax plate reconstruction of embryo McIntyre I. × *circa* 40. The arrows indicate the plane of the graphic reconstruction (Text-fig. 1 B). The numbers refer to the sections limiting the area reconstructed in the graph.
Fig. 2. Section 84 of 2·4-mm. embryo. Photomicrograph × *circa* 80. *M.* = mesodermal condensation at the caudal attachment of the stalk.
Fig. 3. Section 146 of embryo McIntyre I. Photomicrograph × *circa* 140. Description in text. *Y.* = cavity of the yolk sac.
Fig. 4. Section 143 of embryo McIntyre I. Photomicrograph × *circa* 140. Description in text. *Y.* = cavity of the yolk sac.

Plate II

Sections of embryo McIntyre I. Photomicrographs × *circa* 140. Description in text.
Fig. 5. Section 130. *Y.* = cavity of yolk sac. *a.e.c.* = amnio-embryonic cavity.
Fig. 6. Section 129. *Y.* = cavity of yolk sac. *a.e.c.* = amnio-embryonic cavity.
Fig. 7. Section 125. *Y.* = cavity of yolk sac. *a.e.c.* = amnio-embryonic cavity.
Fig. 8. Section 122. A process of ectoderm can be seen extending up to yolk sac endoderm but separated from it by a small interval in which are mesodermal cells. *Y.* = cavity of the yolk sac. *a.e.c.* = amnio-embryonic cavity. *A.* = allantoic diverticulum.

Plate III

Figs. 9–11 are sections of embryo McIntyre I. Photomicrographs × *circa* 140. Description in text.
Fig. 9. Section 119. *Y.* = cavity of yolk sac. *a.e.c.* = amnio-embryonic cavity. *A.* = allantoic diverticulum.
Fig. 10. Section 118. *Y.* = cavity of yolk sac. *a.e.c.* = amnio-embryonic cavity. *A.* = allantoic diverticulum.
Fig. 11. Section 112. *Y.* = cavity of yolk sac.
Fig. 12. Photograph of a drawing of a wax plate reconstruction of embryo 2·4 mm. in length. × *circa* 40. The arrows indicate the plane of the graphic reconstruction (Text-fig. 2 B). The numbers refer to the sections limiting the area reconstructed in the graph.

Plate IV

Sections of embryo 4·5 mm. (McIntyre II). Photomicrographs × *circa* 110. Description in text.
Fig. 13. Section 136. *M.* = mesodermal condensation.
Fig. 14. Section 131. *Kl.* = cloacal membrane.
Fig. 15. Section 138. *M.* = mesodermal condensation.
Fig. 16. Section 144.

Plate V

Fig. 17. Photograph of a drawing of a wax plate reconstruction of a 7-mm. embryo. × *circa* 12. The arrows indicate the plane of the graphic reconstruction (Text-fig. 4 B). The numbers refer to the sections limiting the area reconstructed in the graph.
Figs. 18–20 are sections of embryo 7 mm. in length. Photomicrographs × *circa* 120. Description of sections in text.
Fig. 18. Section 329. *Kl.* = cloacal membrane.
Fig. 19. Section 373. *M.* = mesodermal condensation.
Fig. 20. Section 345. *Kl.* = cloacal membrane.

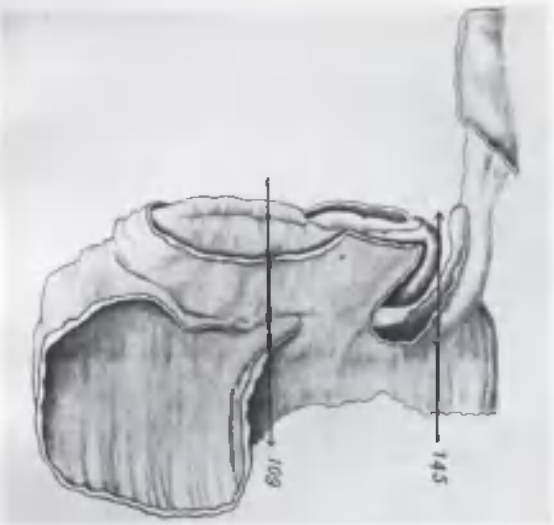


Fig. 1.

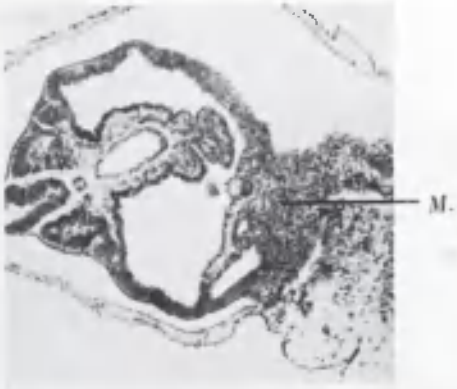


Fig. 2.

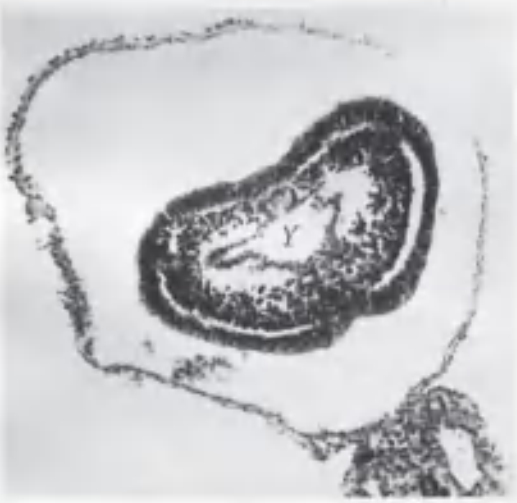


Fig. 3.

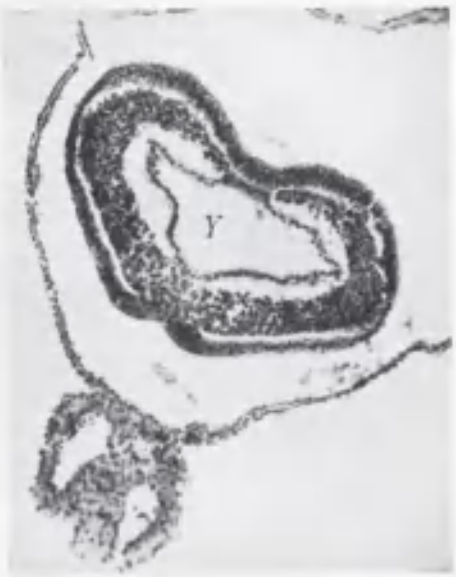


Fig. 4.

Fig. 5.

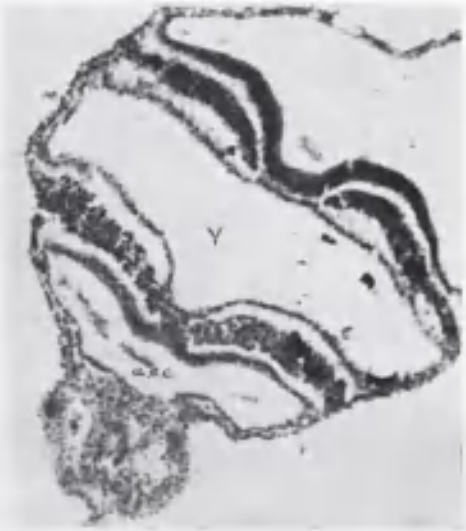


Fig. 6.

Fig. 7.

Fig. 8.

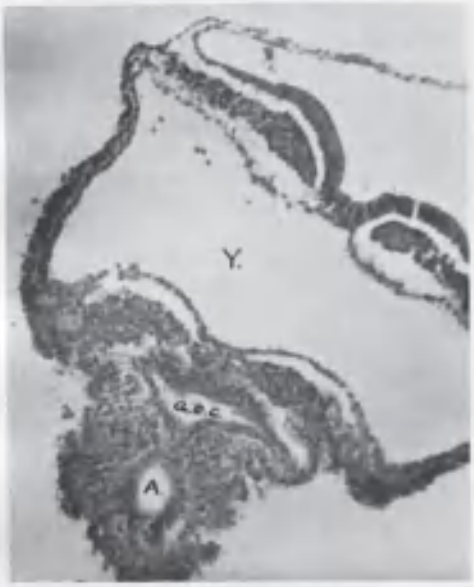


Fig. 9.

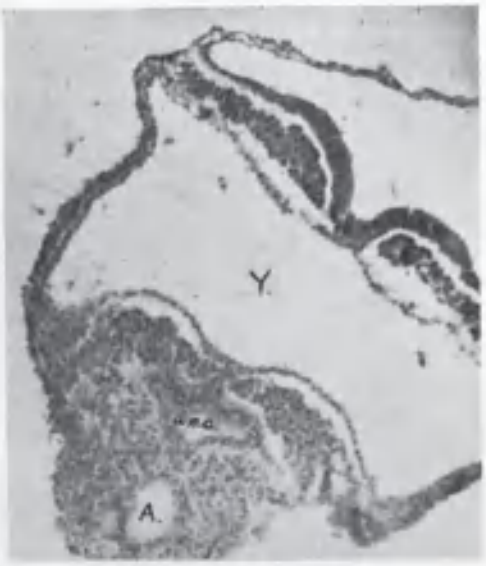


Fig. 10.

Fig. 11.

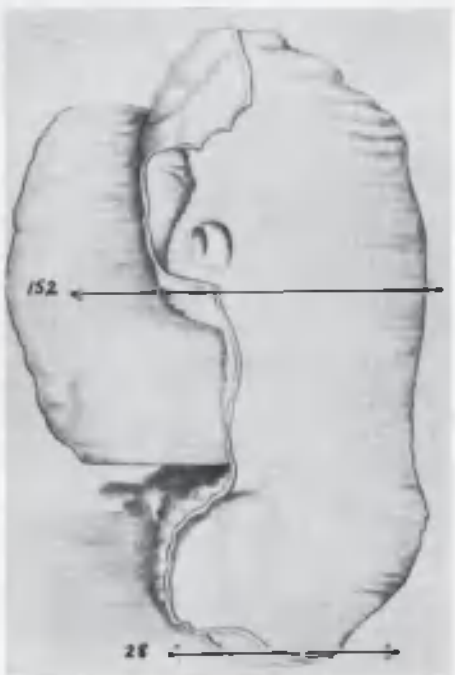


Fig. 12.

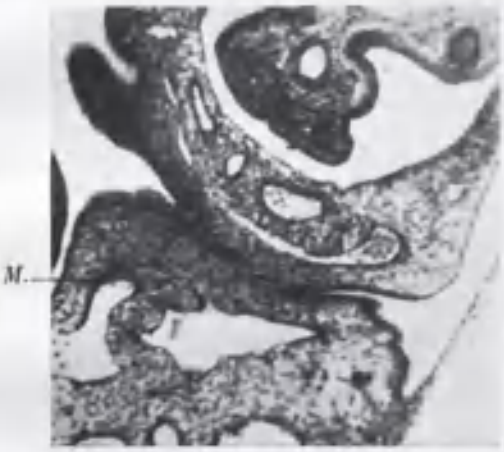


Fig. 13.

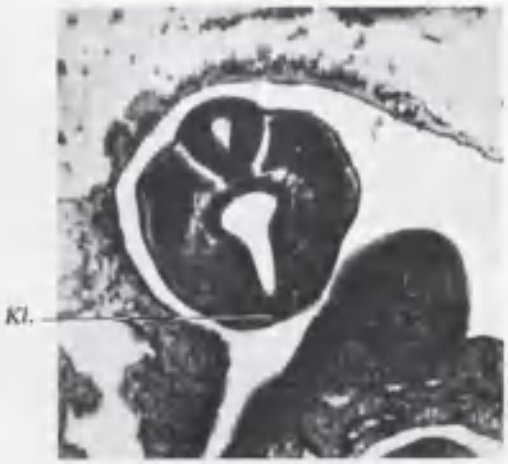


Fig. 14.

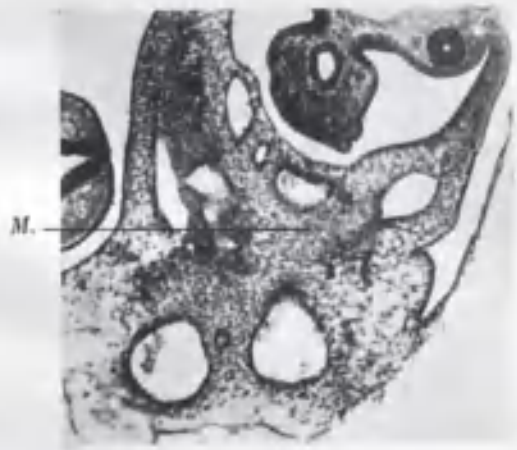


Fig. 15.

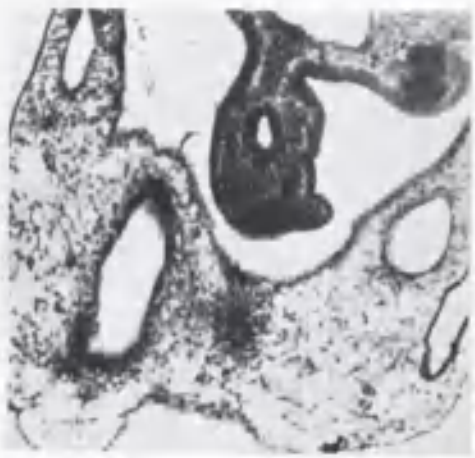


Fig. 16.

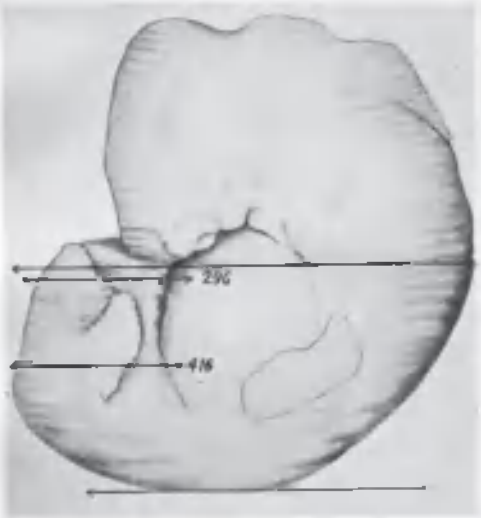


Fig. 17.

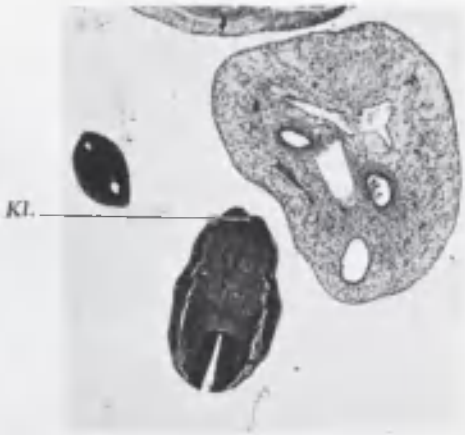


Fig. 18.

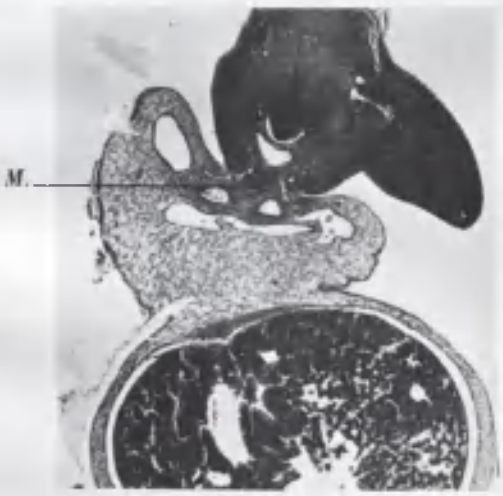


Fig. 19.

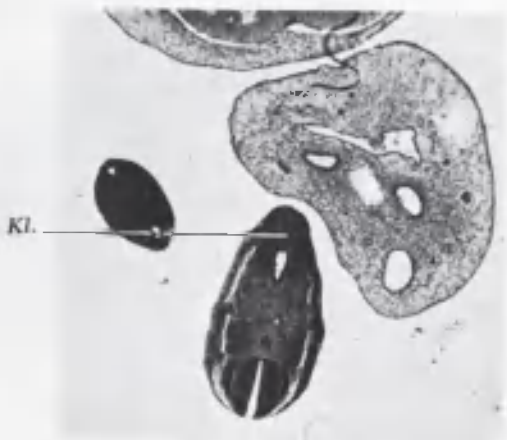


Fig. 20.

Fig. 21.

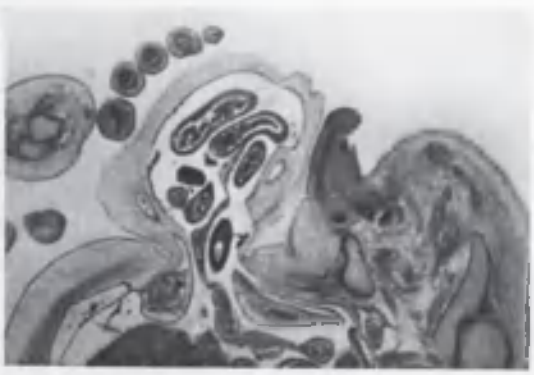


Fig. 22.

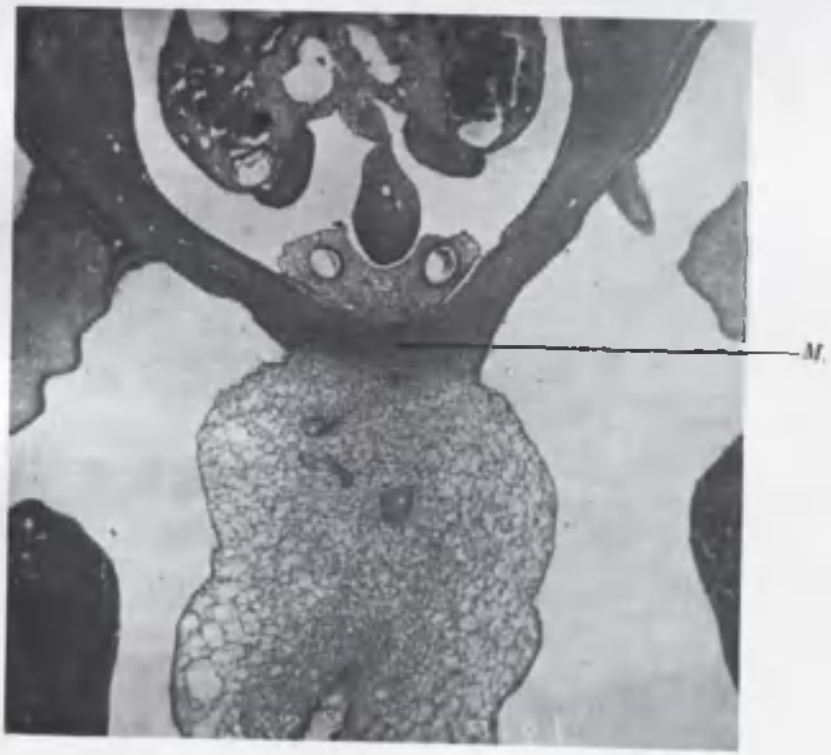


Fig. 23.

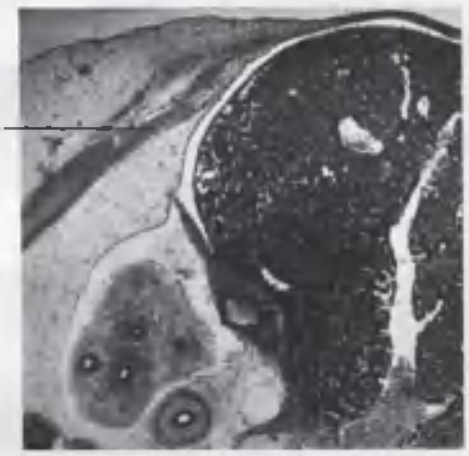


Fig. 24.

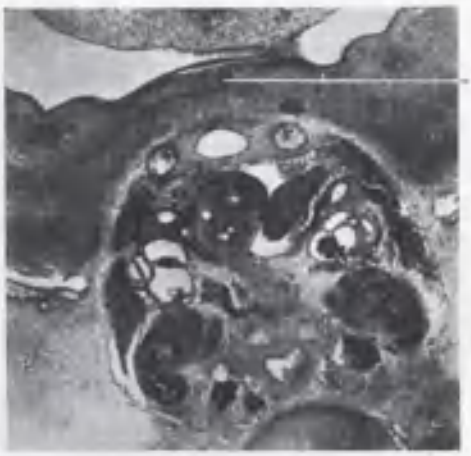


Fig. 25.

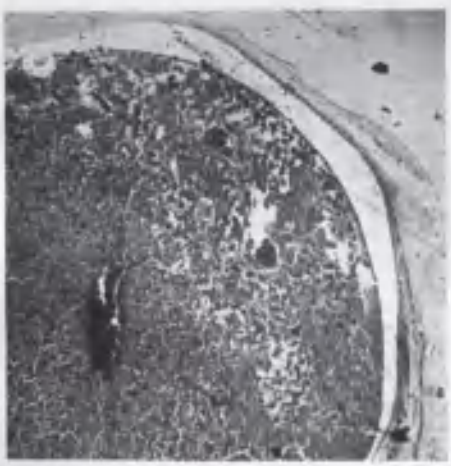


Fig. 26.

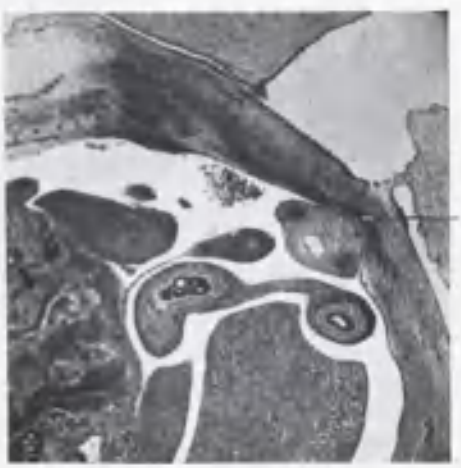


Fig. 27.

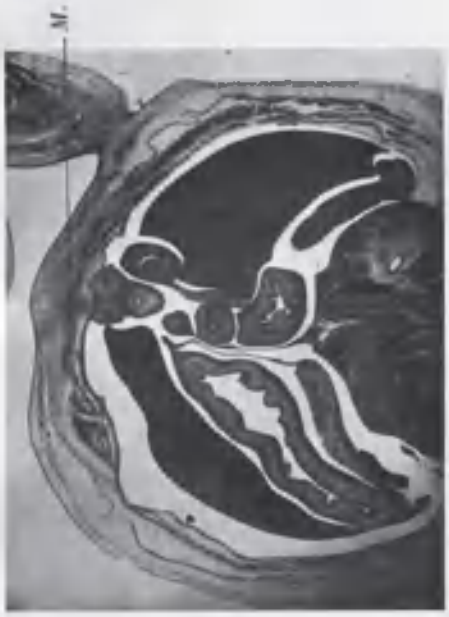


Fig. 29.

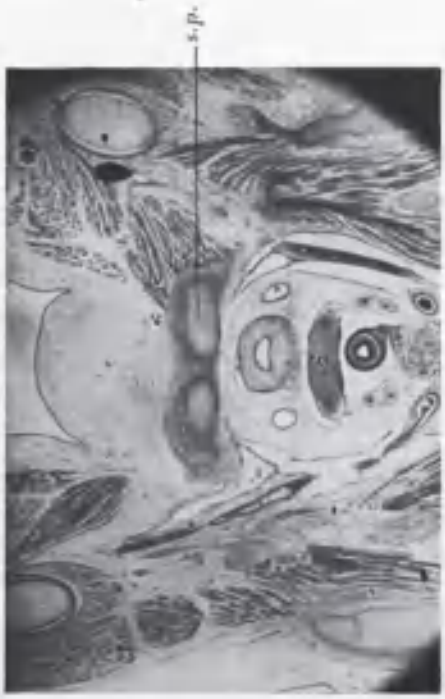


Fig. 31.

Fig. 28.

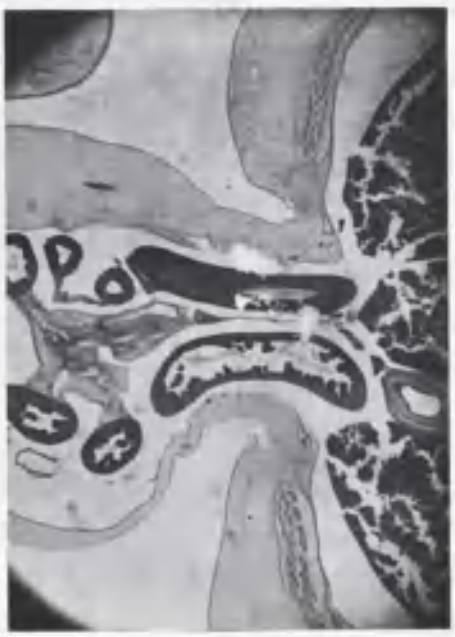


Fig. 30.

PLATE VI

Fig. 21. Photograph of a drawing of a wax plate reconstruction of a 4·5-mm. embryo (McIntyre II). ×*circa* 18. The arrows indicate the plane of the graphic reconstruction (Text-fig. 3 B). The numbers refer to the sections limiting the area reconstructed in the graph.

Fig. 22. Longitudinal section of a 30-mm. embryo. *Photomicrograph* ×*circa* 7.

Fig. 23. Section 864 of 12·5-mm. embryo. Photomicrograph ×*circa* 27. Description in text. *M.* = mesodermal condensation.

PLATE VII

Fig. 24. Section 761 of a 14-mm. embryo. Photomicrograph ×*circa* 17. Description in text. *p.d.* = paraxial myogenic downgrowth.

Fig. 25. Section 1081 of a 14-mm. embryo. Photomicrograph ×*circa* 17. Description in text. *M.* = mesodermal condensation.

Fig. 26. Section 1079 of a 16·1-mm. embryo. Photomicrograph ×*circa* 17. Description in text.

Fig. 27. Section 1278 of a 16·1-mm. embryo. Photomicrograph ×*circa* 17. Description in text. *M.* = mesodermal condensation.

PLATE VIII

Fig. 28. Section 773 of a 23-mm. embryo. Photomicrograph ×*circa* 7. Description in text. *p.d.* = paraxial myogenic downgrowth.

Fig. 29. Section 924 of a 23-mm. embryo. Photomicrograph ×*circa* 7. Description in text. *M.* = mesodermal condensation.

Fig. 30. Section 1216 of a 40-mm. embryo. Photomicrograph ×*circa* 7. Description in text.

Fig. 31. Section 1408 of a 40-mm. embryo. Photomicrograph ×*circa* 7. Description in text. *s.p.* = condensation forming the pubes.

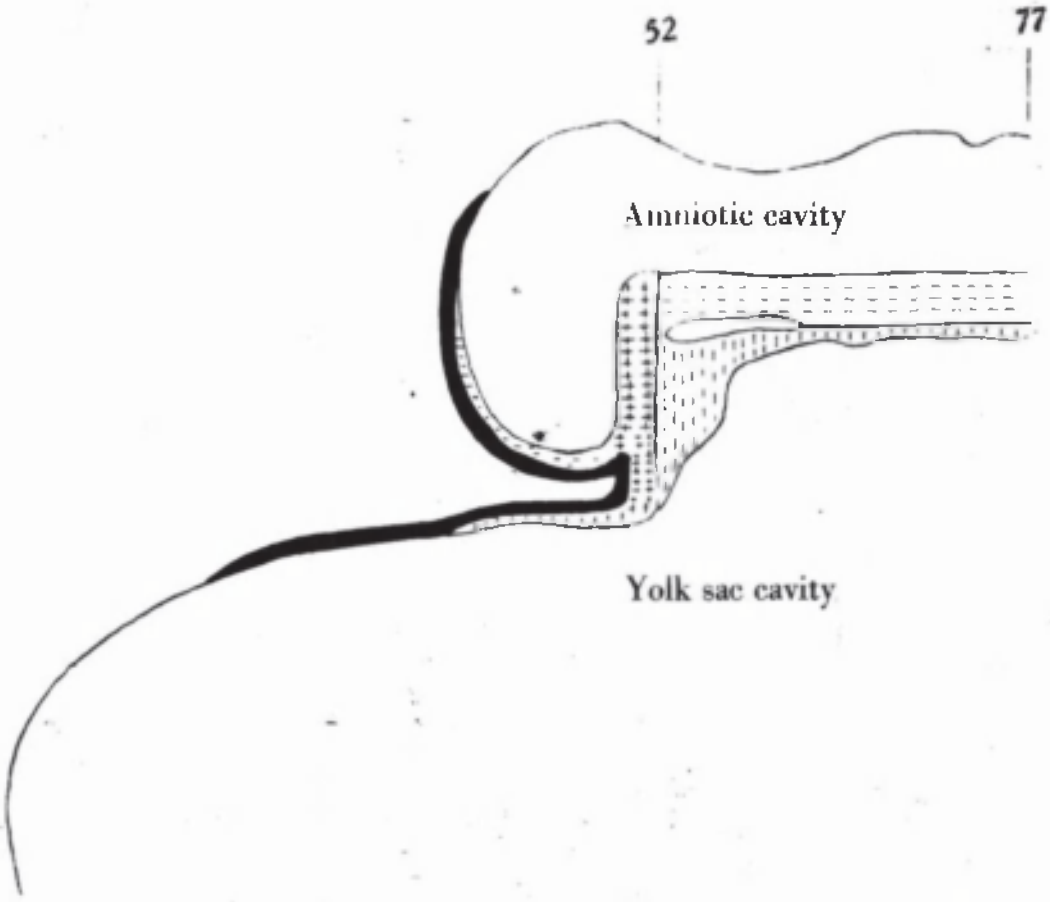
PART II.

THE DEVELOPMENT OF THE SUPRA-UMBILICAL PORTION OF THE ANTERIOR ABDOMINAL WALL.

This work is a continuation of the study of the development of the anterior abdominal wall, the first part of which "The Development of the Infraumbilical portion of the Abdominal Wall, with Remarks on the Aetiology of Ectopia Vesicae" was published in the Journal of Anatomy of January 1937.

The supraumbilical portion of the anterior abdominal wall develops pari passu with the ventral growth of the liver although, as is apparent from cases of eventration, a normally developing liver is not the controlling factor in the completion of this part of the parietes.

Up to and including a 4.5 mm embryo, the umbilical opening, invested by the amnial reflections, has, as its superior limit, the mesodermal mass at the caudal end of the pericardium which more dorsally separates the pericardial from the abdominal coelom. In an embryo measuring 7.5 mm and more emphatically in one of 12.5 mm there is a definite interval between the pericardium and the upper border of the umbilical opening - a supraumbilical wall. The mesodermal basis of this portion of the ventral body wall would seem to be a derivative of the general mass of mesoderm forming a partition between heart and liver, and therefore an endeavour to assess its developmental significance includes an account



Text-Fig. 1A. Embryo McIntyre I. Reconstruction of a median sagittal section. x 200. (See Pl. I, Fig. 1). The numbers refer to the section. Description in text.

Interrupted horizontal lines = ectoderm.
Interrupted vertical lines = Head process and prochordal area.
Crosses = Bucco-pharyngeal membrane.
Black = Mesoderm.

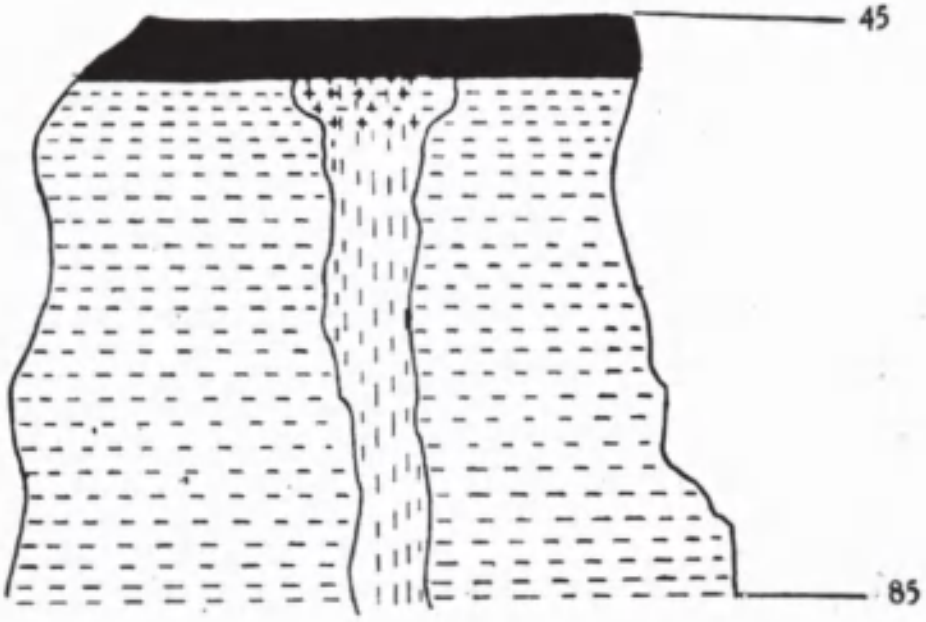
of the origin of the formations known collectively as the septum transversum.

There is some analogy between the two poles of the embryo as represented in later stages by the infra- and supra-umbilical portions of the abdominal wall. Thus relevant to this work are descriptions of the structures laid down at the cranial end of the blastoderm such as the bucco-pharyngeal membrane, the prochordal plate and the head mesoderm.

The Glasgow collection of embryos has again been utilised. The appropriate history of each will be found in the first part of this work. A recent addition to the collection - an embryo of 2.6 mm - is incorporated in the series.

Embryo McIntyre I (1.4 mm).

Observations on this embryo were published by Bryce (1924). Graphic reconstructions of a median sagittal section and the dorsal aspect of the more cranial sections are shown in Text-Figs. 1A and 1B. The area reconstructed is indicated in Pl.I, Fig.1. The head process becomes apparent in section 143 (Pl.I, Fig.2), and the process can be followed to section 63. The floor of the archenteric canal is open towards the yolk sac. In its posterior part it is broad and its margins are in contact with the lateral mesodermal sheets (Pl.I, Fig.3). The mesoderm is uniformly thick and shows no distinction into paraxial and lateral portions, nor is there any variation in texture suggestive of a primary and secondary mesoderm as



Text-Fig. 1B. Embryo McIntyre I. Reconstruction of the dorsal aspect of the cranial end of the embryonic shield. x 200. Area in which the mesoderm crosses the mid line is shown in black. The numbers refer to the section. Des cription in text.

Interrupted horizontal lines = ectoderm.
Interrupted vertical lines = Head process and prochordal area.
Crosses = Bucco-pharyngeal membrane.
Black = Mesoderm.

described by Rossenbeck in embryo Peh-Hochstetter. Further forward the head process becomes narrower; it is recessed and the mesodermal sheets cease to be continuous with it (Pl.I, Fig.4). Cranial to section 62 is probably the domain of the prochordal plate and a short distance in front of this is the anterior bend of the blastoderm, the commencing head fold with the formation of the foregut pit, on the roof of which is the thickened prochordal plate.

The cavities and pocketings in the prochordal region (sections 60-55; Pl.II, Fig.5) are presumably the result of folding of the plate which, as pointed out by Streeter in his studies of the mesoderm in the pig, "shows a strong tendency to the production of clefts opening into the entodermal cavity". There is a definite interval between the endoderm of the embryonic shield and the prochordal plate, the margins of which are continuous on each side with the mesoderm that now shows division into somatopleure and splanchnopleure.

Section 53 (Pl.II,Fig.6) is through the cephalic wall of the foregut pit. The cranial sections are cut obliquely giving considerable thickness and depth of yolk endoderm. Sections 51 and 52 (Pl.II,Fig.7) are at the front end of the disc and through the commencing head fold. The ectoderm and endoderm are here in contact - a bucco-pharyngeal membrane flanked by the mesodermal sheets.

In front of the head fold (Section 50; Pl.II,Fig.8) the ectoderm and endoderm are separated by mesoderm forming

a continuous sheet across the middle line and exhibiting cleavage with the formation of a number of small spaces, precursors of the pericardial coelom. This mesoderm at the anterior end of the disc and in the region of the cranial reflection of the amnion retains its relation to the amnial reflection during subsequent rotation and development, Its position is therefore constant at the anterior boundary of the umbilical opening where it forms the "anterior mesodermal field". It is composed of secondary and primary mesoderm. The secondary element is the fusion, in front of the bucco-pharyngeal membrane, of the mesodermal wings situate on both sides of the axial structures. The primary element is the blending of the amnial and yolk sac mesoderm at the anterior pole of the blastoderm. In its mode of formation the anterior mesodermal field bears comparison with the posterior mesodermal field bounding the umbilical opening caudally where one also finds a fusion of the primary and secondary mesoderm distal to the cloacal membrane.

Further discussion is required regarding (I) the source of the mesoderm forming the secondary element of the anterior mesodermal field and (II) the morphological value of the bucco-pharyngeal membrane as compared to the cloacal membrane.

I. SOURCE OF THE SECONDARY MESODERM.

This tissue may arise (A) direct from the primitive

streak - prostomial mesoderm, (B) indirectly from the streak as part of the process of notogenesis or deuterogenesis - gastral mesoderm, (C) from the prochordal plate if that be regarded as a source of mesoderm.

A. PRIMITIVE STREAK MESODERM.

Streeter in his work on pig embryos shows the primitive streak mesoderm extending forwards as two horn-like processes uniting anteriorly. These processes are present before the advent of the notochordal anlage and the parachordal position of their anterior portion is merely a growth incident. He maintains that the primitive streak is the sole source of mesoderm although reinforced in the later stages by accessions from the prochordal plate. Similarly in the ferret Hamilton finds that there is no mesoderm arising from the head process.

Of the mesoderm in the chick Adelmann states "gastral and peristomal mesoderm are but growth phases in the formation of the definite lateral and paraxial mesoderm, the latter being continually transformed into the former."

On the other hand the concensus of opinion credits the head process with mesodermal production in the human embryo. Hill and Florian in a detailed description of this region in the Dobbin embryo with additional observations on an embryo of Loris conclude that the head process undergoes differentiation in a caudo-cranial direction into a median chorda-canal and two lateral mesodermal bands which they regard as of direct archenteric origin, i.e. gastral mesoderm.

In the description of embryo Wa.17, Grosser describes the head process as consisting of a central core and lateral wings of mesoderm, while in his "Fuhrentwicklung Eihautbildung und Placentation" he states that the primary mesoderm is squeezed out by secondary mesoderm formed from the primitive streak and head process. Stieve classifies mesoderm as firstly that formed before the differentiation of the embryonic knot, secondly from the endoderm, and thirdly from the head process and primitive streak. Sternberg and Waldeyer likewise assume a production of mesoderm from what they term the cranial mesoblastic process (head process) consisting in front of a central core and lateral mesoblastic processes.

It was found impossible to give any definite opinion on the question of mesodermal production from the head process in embryo McIntyre I, the only feature of significance being the breadth of the process in the more posterior sections.

The conception of De Lange that the "phylogenetic acquisition of metamerism is essentially secondary" and his analysis of the vertebrate body as "the primordial unsegmented fundament of the metazoa upon which has been superimposed a segmented dorsal episoma" would seem to favour the view of mesodermal production from the head process.

B. GASTRAL MESODERM.

Deuterogenesis or chordulation would include the formation of the notochord and paraxial mesoderm which however retains its paraxial position in the early stages and is

co-extensive with the notochord. It would not therefore form part of the secondary mesodermal element merging with the anterior mesodermal field.

C. PROCHORDAL PLATE AS A SOURCE OF MESODERM.

The tissue in the region of the cranial termination of the head process has been the subject of much discussion, recondite speculation, and confusion of terms. Prochordal plate is the name given by Hill and Florian in their description of the Dobbin embryo, and will be used here.

There seem to be three main theories regarding its morphological interpretation:-

(1). The prochordal plate represents the anterior end of the head process (Babl).

(2). The prochordal plate is preaxial mesoderm (Adelmann).

(3). The prochordal plate is the thickened endoderm of the roof of the foregut (Bonnet).

The plate is very generally found and is not confined to any single species. It is least well developed in mammals (Adelmann).

Bonnet describes in the dog a thickening of the endoderm in front of the cranial end of the head process which he regards as a source of head mesoderm, and states that in the sheep this thickening is present before the head process, the fusion of the two being secondary.

A similar relationship exists in the ferret - the prochordal plate at one stage is separated by an interval from the head process (Hamilton).

In the pig (Streeter) the plate is an endodermal thickening already present at the time of the beginning of the formation of the notochord. It produces mesoderm which is absorbed into the head region, but is not the entire source of cephalic mesoderm.

The earliest stage of prochordal plate yet described in the human is probably that in embryo Bi(ttmann) 24 (.625 mm) of Florian, and here the cranial end of the head process has already fused with the plate.

From a detailed study of the cranial end in the Dobbin embryo, Hill and Florian conclude that the plate is formed of thickened endoderm overlapped by and fusing with the cranial end of the head process.

Although differing somewhat in their definition of the plate, substantially similar findings are recorded by Rossenbeck (Peh-Hochstetter), Sternberg (4 somites), Payne (7 somites) and Waldeyer (E.Scho), and the position is succinctly summed up by Grosser "Ganz am kranialen Ende des Kopffortsatzes findet sich eine Region, in der die Abgabe von Material aus dem Entoderm an das Mesoderm nicht auszuschlieben ist Protochordal oder Erganzungsplatte."

Adelmann, working with shark and chick embryos, views the prochordal plate from a somewhat different aspect. He suggests that this structure is preaxial mesoderm and is thus "an expression of mesoblastic continuity comparable to a similar preaxial continuity of nervous tissue from side to

side round the anterior end of the blastopore."

On this hypothesis the prochordal plate would be the cranial lip of the blastopore; the axial structures would be formed posterior to it by a fusion of the lip of the blastopore, and as such the plate would maintain its preaxial position. The head process is regarded as dividing the lip into a primitive cranial lip - the prochordal plate - and the so-called dorsal lip at the neurenteric canal.

However attractive or rational this interpretation may seem, the weight of evidence in the human, at any rate, favours the endodermal basis of the prochordal plate.

It is generally admitted that there is some mesodermal production from the prochordal plate. In the human, with the greater preponderance and more dominant role of the primitive mesoderm, this is probably at a minimum.

De Lange has stressed the essentially protogenetic basis of the prochordal plate in accordance with his non-metameric concept of head development. He has shown that the mesoderm cranial to the head process - cephalic mesoderm - is absorbed entirely into the head fold. Such mesoderm as is produced from the prochordal plate exhibits according to Adelmann a phylogenetic urge towards the formation of cavities - well illustrated in sections 60-55 of McIntyre I. In the shark the plate is ultimately represented by the mandibular and premandibular cavities - its median origin betrayed by the cellular connecting cord which later atrophies.

In vertebrates with no head cavities the prochordal mesoderm becomes part of the head mesoderm, and plays no part in the formation of the ventral body wall although the latter is also in the first instance protogenetic. The secondary mesoderm of the anterior mesodermal field thus comes directly from the primitive streak and receives no reinforcements from head process or prochordal plate.

II. BUCCO-PHARYNGEAL MEMBRANE.

The apposition of ectoderm and endoderm anteriorly to form the bucco-pharyngeal membrane of vertebrates is phylogenetically a secondary formation. The more primitive prostomal aperture is divided into anal opening and neurenteric canal. This possibly accounts for the later appearance and more transient nature of the bucco-pharyngeal membrane compared to the cloacal membrane.

In the descriptions and figures of early human blastocysts with an embryonic rudiment there is no mention or semblance of a contact of the two primary germ layers at the head end. Embryo Wo (von Mollendorff), Miller ovum (Streeter), Embryo T.F., Bi.1., Bi.24 (Florian), Wa.17 (Grosser) show in the region in front of the prochordal plate - the proamnion of lower mammals - a layer of cells between the ectoderm and endoderm probably of primitive mesenchymal origin, but as Florian states of the Fetzer embryo, the two layers of the disc are very difficult to distinguish and the presence of mesoderm can only be assumed. In these mammals

where the primitive streak is the main factor in mesodermal production there is at an early stage no intervening tissue between ectoderm and endoderm in the prosmnial area.

Embryo McIntyre 1 is the youngest human embryo in which a bucco-pharyngeal membrane has been described. In sections 52-51 there is ecto-endodermal connection by means of a thick cord of cells - in front of this the layers are separated in the mid line by mesoderm. A bucco-pharyngeal membrane has been described in an embryo of two somites (F. Orts Llorca), in one of four somites (Sternberg) and in the specimen 2-3 somites (Ingalls) there is a membrane .05 mm long lying immediately above the reflection of the somatopleure to form the anterior wall of the pericardium. Older embryos up to 30 somites all have a bucco-pharyngeal membrane with two exceptions, in one of which (Dandy, 7 somites) the damaged tissue at the cranial end would obscure the membrane. About 3 mm (25-30 somites) the membrane becomes ruptured and disappears. Actual perforation of the membrane heralding its ultimate fate is evident in a 20-somite specimen (Davis), and one of 18 somites (Watt).

The contact of ectoderm and endoderm would thus seem to be established at the time of the commencing head fold and the initial formation of the foregut as in McIntyre I; its rupture to follow the completion of pericardial inversion and formation of the stomodaeal depression by the outgrowth of the forebrain and the development of the facial prominences.

Ecto-endodermal contiguity can only be subsequent to the obliteration of intervening mesoderm assuming such to be present between the two layers of the disc from an early stage.

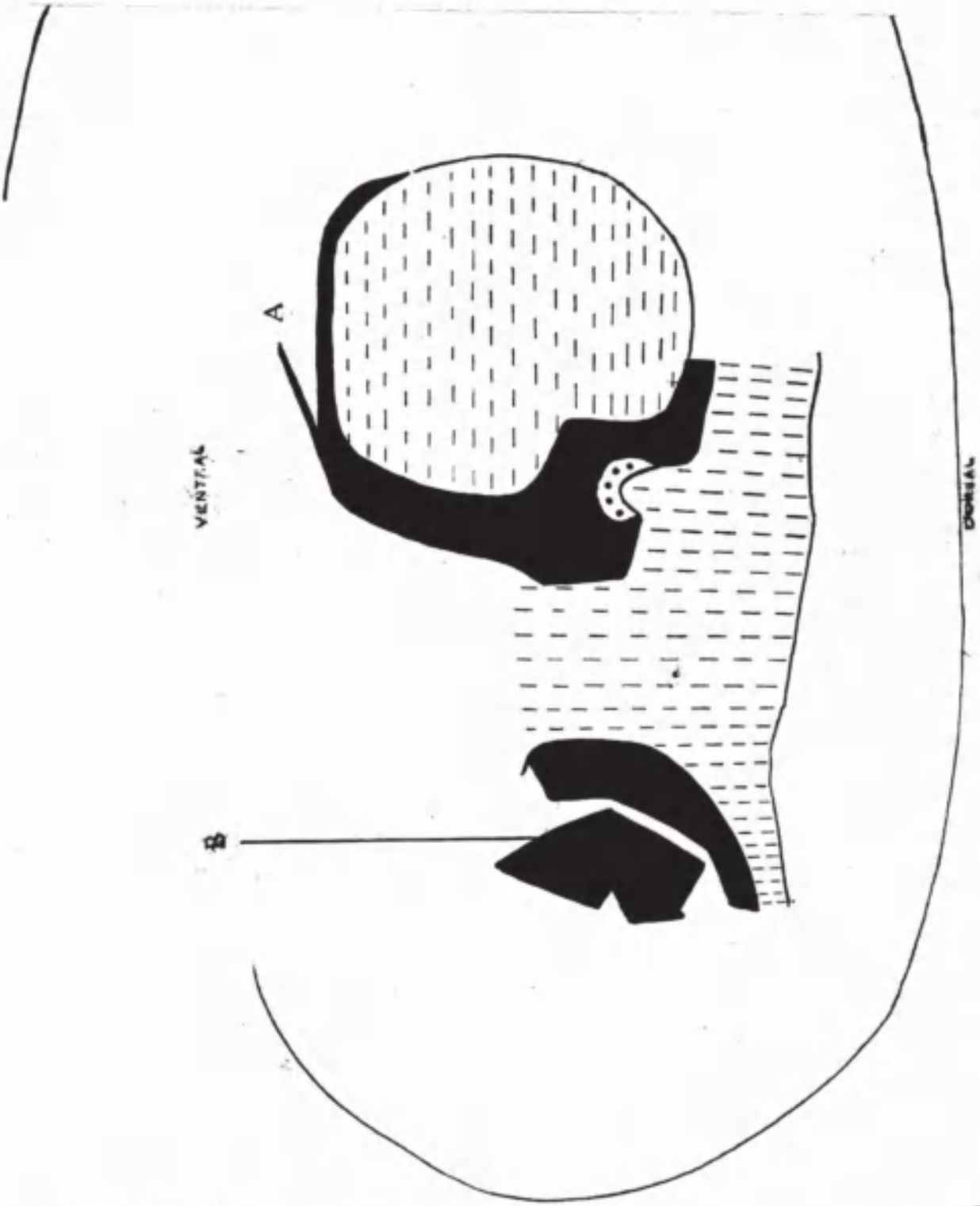
In the dog (Bonnet) the early small anlage of the bucco-pharyngeal membrane receives endoderm from the prochordal plate, while in the ferret (Hamilton) the membrane is formed from the front portion of the plate. In his two-somites human embryo F. Orts Llorca depicts the membrane as a connection between the ectoderm and the prochordal plate, but in view of the difficulty in defining the exact limits of the latter structure it seems inadvisable to dogmatise on its relationship to the bucco-pharyngeal membrane.

From its first appearance this membrane has very constant relations; at the one extremity the prochordal plate and anterior end of head process - chordal end; at the other the pericardium - cardiac end; and like the cloacal membrane it maintains its primary relations during later development and inversion. The head fold arises at the chordal end; similarly the tail fold forms at the chordal end of the cloacal membrane.

At an early stage of the human blastocyst there are areas of ecto-endodermal contact at both poles, each area flanked by wings of primitive streak mesoderm which unite with one another, and the primary mesenchyme, to form the anterior mesodermal field in front and the posterior

Text-Fig. 2. Embryo 2.6 mm. Reconstruction of a median sagittal section. x 100. Description in text. The yolk sac is not shown.

Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Gut.
Large Dots = Liver. Black = Mesoderm. A = Amnion.
B = Body Stalk.



mesodermal field behind; these are the sites of amnial attachment and respectively the anterior and posterior limits of the umbilical opening.

The anterior mesodermal field furnishes the tissue of the supraumbilical abdominal wall which therefore in its development shows an interesting analogy to the origin of the infraumbilical abdominal wall.

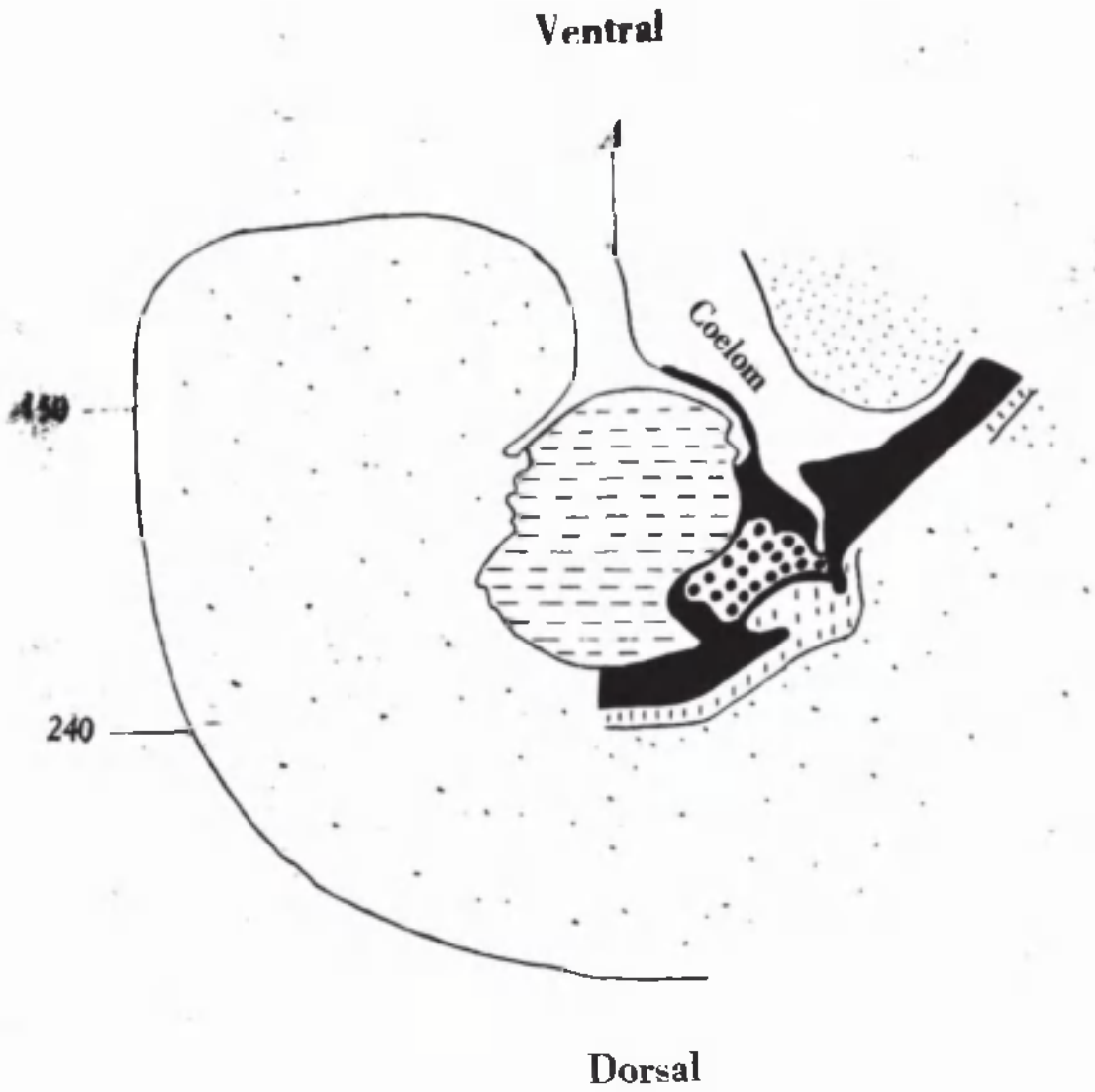
In embryo McIntyre I the pericardial plate is placed ventral to the head fold and cranial to the bucco-pharyngeal membrane. Dorsally it is covered by ectoderm, ventrally by endoderm, and its anterior and lateral boundaries are mesodermal - the anterior mesodermal field. In the cranial portion of the disc there are small mesodermal cavities. In the human embryo it seems more probable that the pericardial cavity is the result of confluence of a number of small mesodermal spaces rather than the fusion of two lateral cavities - a bilateral origin which would predestinate a ventral mesocardium, of the existence of which there is little evidence in the human embryo.

2.6 mm Embryo. History.

This specimen was obtained following laparotomy for a non-ruptured tubal pregnancy. It was fixed in formalin in spite of which, its gross form is normal, although histologically there are imperfections.

Text-Fig. 2 is a graphic reconstruction of a median sagittal section.

Compared with McIntyre I the area of yolk sac



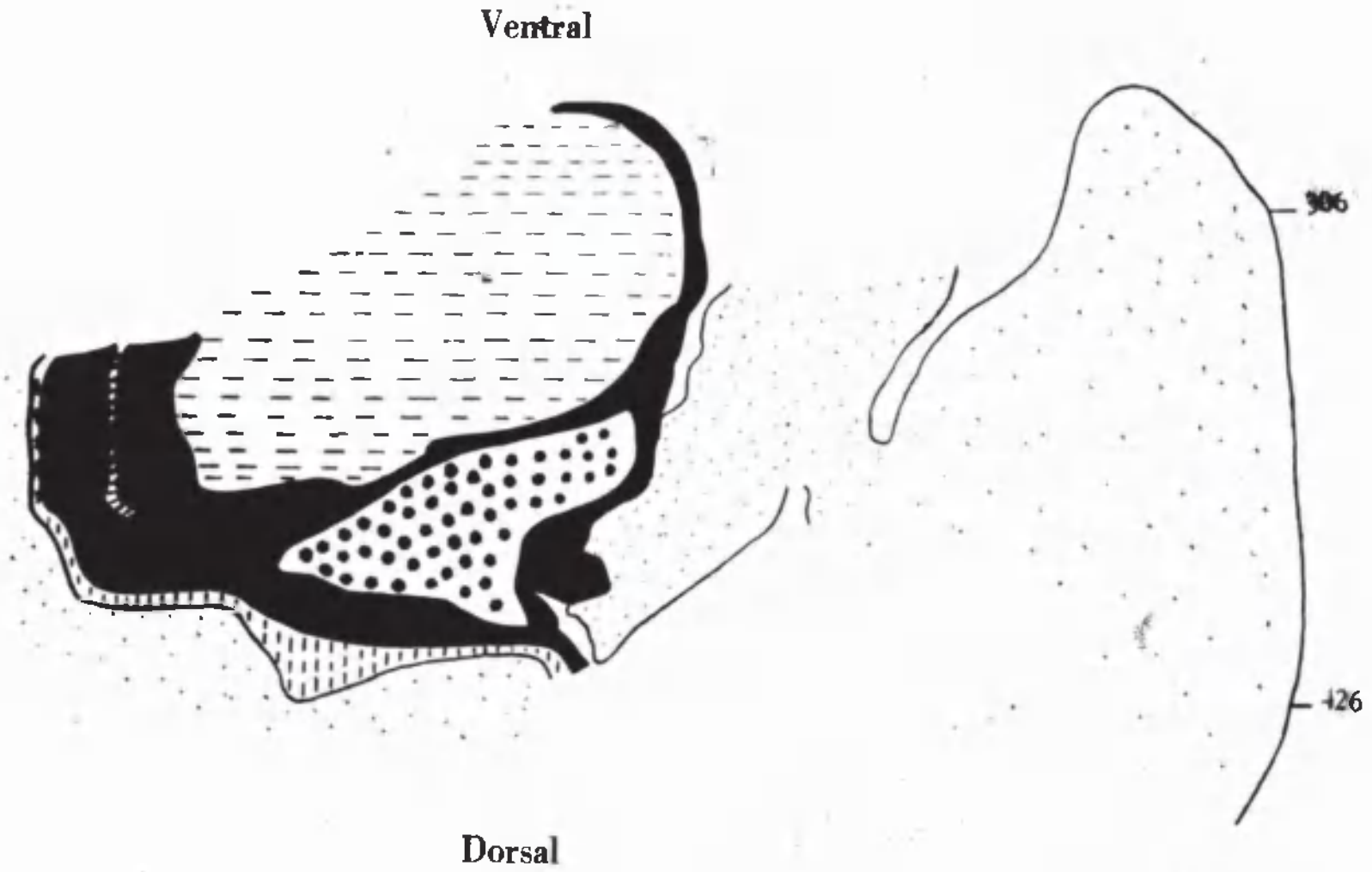
Text-Fig. 3. Embryo 4.5 mm. Reconstruction of a median sagittal section (See Pl. IV, Fig. 13). x 50. The numbers refer to the sections. Description in text. The yolk sac is not shown.

Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Gut.
Large dots = Liver. Black = Mesoderm. A = Amnion.

Into the proliferated mesoderm of the floor of the foregut projects the developing liver - not as a grooved plate or gutter but as a definite hollow outgrowth of the foregut in relation to which the more deeply staining liver cells can be distinguished (Pl. III, Fig.12). A very similar hepatic diverticulum is shown in the reconstruction of the Thompson embryo of 23 paired somites (Keibel and Mall). With the growth of the ectoderm the lateral mesodermal walls of the pericardium are taken into the body of the embryo.

4.5 mm Embryo.

Text-Fig. 3 is a graphic reconstruction of a median sagittal section. The area reconstructed is indicated in Pl. IV, Fig. 13. There has been a further rotation of the pericardium and the cranial attachment of the amnion, carried round from the ventral to the caudal aspect brings with it the region of the anterior mesodermal field. This now definitely forms the caudal boundary of the pericardium and in the mid line is continuous with the splanchnopleure on the floor of the foregut, the two together forming a mass of mesoderm out of which is differentiated a portion of the diaphragm and the supraumbilical abdominal wall. Following the completion of pericardial rotation the amnion becomes the cranial boundary of the umbilical coelom (Pl. IV, Fig.14) cf. Pl. III, Fig. 11. Cords of liver cells invade the dorsal portion of the mesodermal mass (Pl. IV, Fig. 15), and these are broken up by the vitelline veins (Pl. IV, Fig. 16). At



Text-Fig. 4A. Embryo 7 mm. Reconstruction of a median sagittal section (see Pl.V, Fig. 18). x 50. The numbers refer to the sections. Description in text. Interrupted horizontal lines = Pericardial cavity [illegible]. Interrupted vertical lines = gut. Large dots = Liver. Black = Mesoderm. Oblique interrupted lines = trachea.

this stage the liver is confined to the dorsal and dorso-caudal mesoderm and has not yet penetrated the ventral half of the mesoderm on the caudal pericardial wall.

The umbilical veins traverse the mesodermal mass laterally on each side to reach the sinus venosus. They are ventral to the pleuro-pericardial openings and are not broken up by the liver cells (Pl. V, Fig. 17).

In the interest of convenience the familiar term septum transversum will be used here as denoting the general mass of mesoderm, caudal and dorso-caudal to the pericardium, i.e. including the anterior mesodermal field and the proliferated splanchnopleure of the floor of the foregut but not confined to the unsplit cranial pericardial rim - which according to Frazer forms the septum transversum after rotation of the heart.

As this "septum transversum" is but part of the general body mesoderm merging laterally with the somatopleure and in the mid line with the splanchnopleure it is to be regarded as im many ways unfortunate that it has been singled out by a distinctive name. This tends to isolate it as an anatomical entity and causes considerable confusion when any endeavour is made to trace its ultimate fate as such.

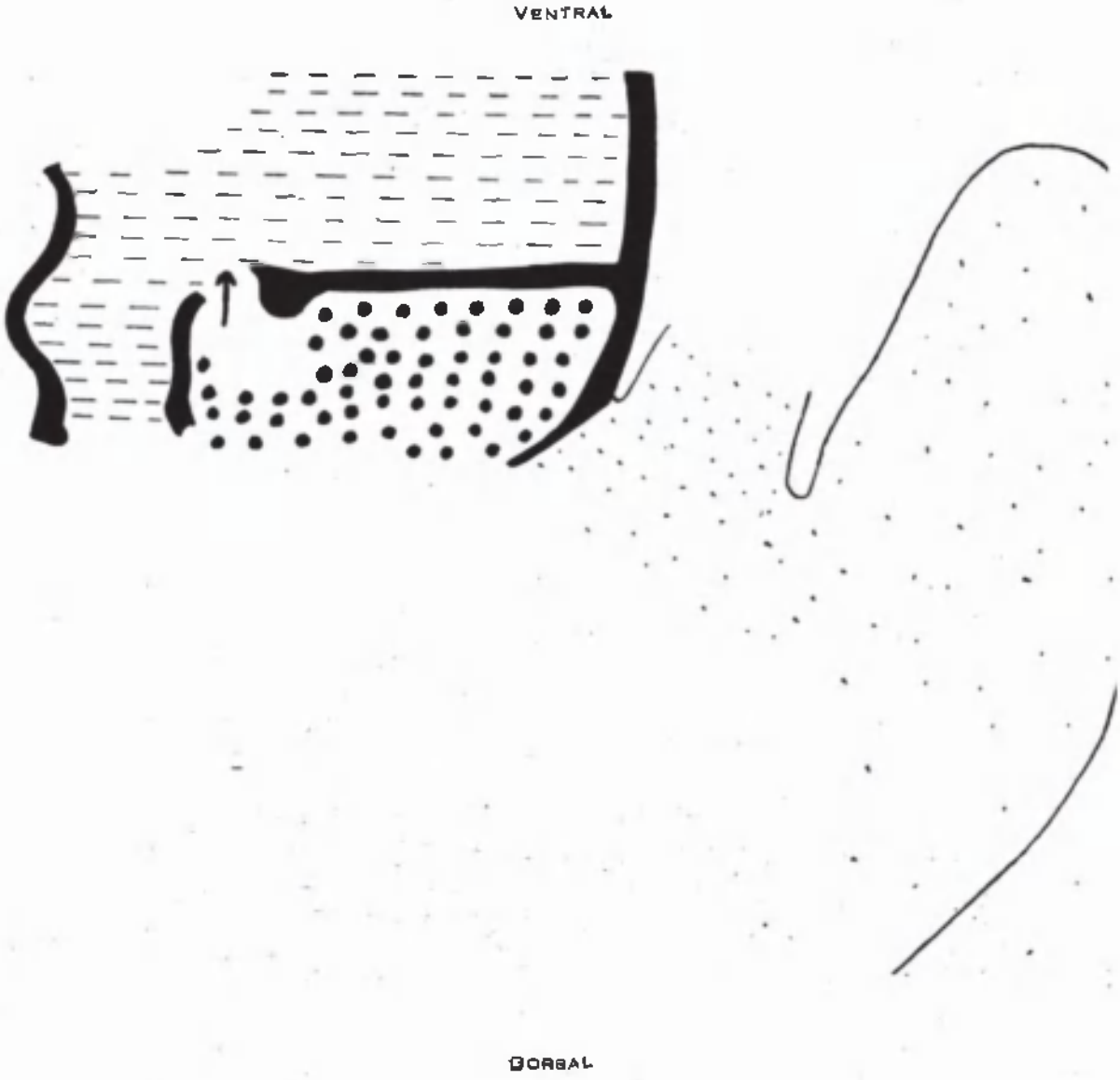
Embryo 7 mm.

Text-Fig. 4A is a graphic reconstruction of a median sagittal section. The area reconstructed is shown in Pl. V, Fig. 18. The liver cells which in the 4.5 mm embryo are confined to the more dorsal part of the septum transversum have now

extended ventrally and invaded the region of the septum on the caudal pericardial wall formed from the anterior mesodermal field. Pl. V, Fig. 19 is a section through the cranial attachment of what is now the umbilical cord and it is evident that this is lying some distance caudal to the pericardium, i.e. there is in this embryo a small interval between the umbilical cord and the pericardium. This specimen is the first of the series in which an umbilical "cord" as such can be said to exist, and with its completed formation there appears a supraumbilical abdominal wall whose mesodermal basis is the ventro-caudal part of the septum transversum, i.e. the anterior mesodermal field pushed caudally and ventrally by the developing liver.

Dorsal to the cranial attachment of the cord the mesoderm of the "septum" blends with the more myxomatous tissue of the cord, the two together forming a partition between the intra and extra umbilical coeloms (Text-Fig. 4A and Pl. V, Fig. 20). The latter figure also shows the left umbilical vein, its course interrupted by the liver cell columns.

At this stage the mesodermal mass of the septum transversum is divided by the invading liver into a cranial portion separating the liver from the pericardium, and a ventro-caudal portion - the mesodermal basis of the supra-umbilical wall. In the midline dorsally is the ventral mesentery of the foregut and on each side of the ventral



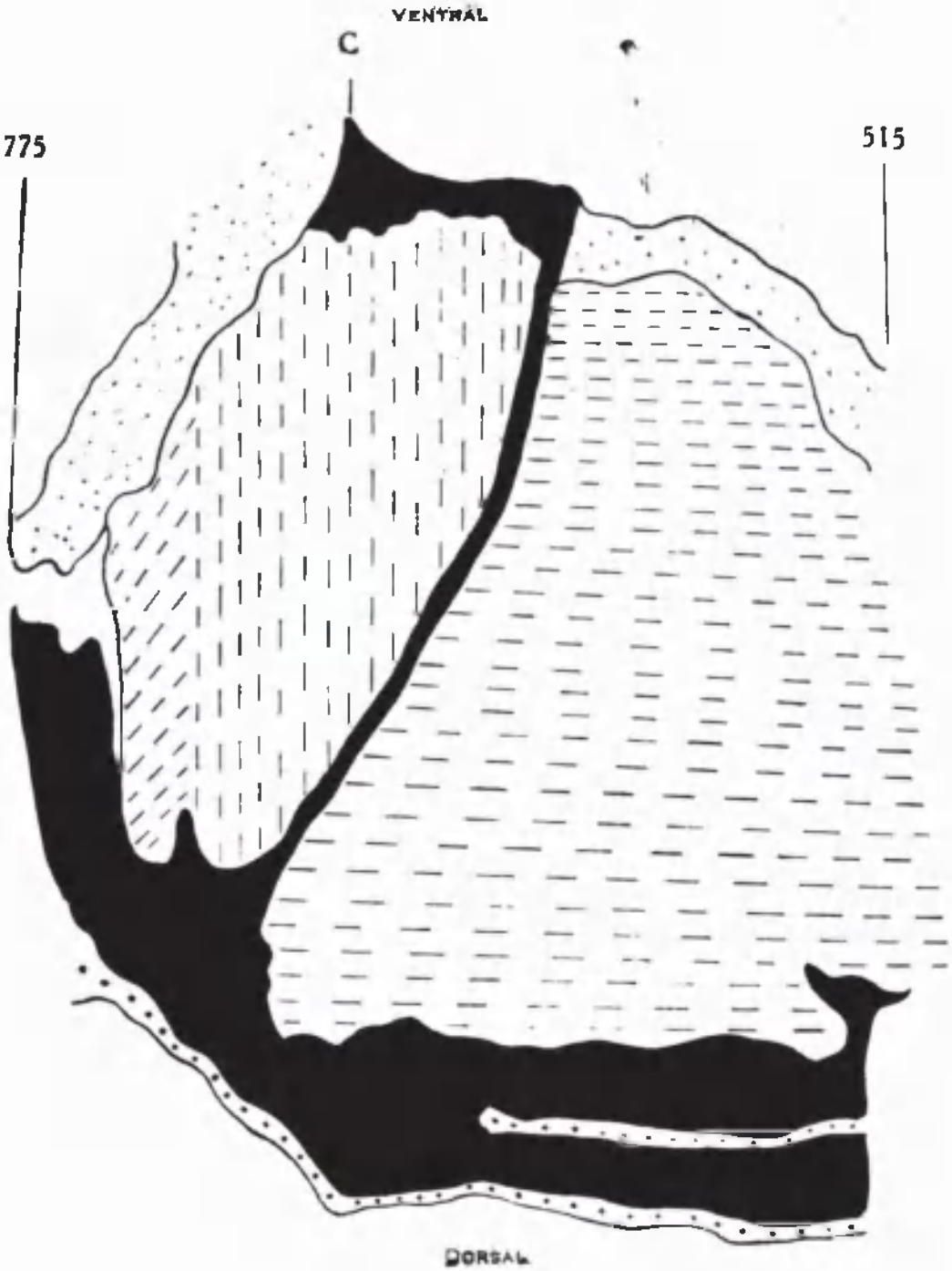
Text-Fig.4B. Embryo 7 mm. Reconstruction of a parasagittal section. x 50. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = pericardial cavity and coelomic passage. Interrupted vertical lines = Gut. Large dots = Liver. Black = Mesoderm. Oblique interrupted lines = Trachea. Arrow indicates the junction of the ductus venosus with the sinus venosus.

mesentery the lung buds occupy the pericardio-peritoneal channels or coelomic tubes whose ventral walls - the dorsal part of the septum transversum - form a pleuro-peritoneal membrane (Pl. VI, Fig. 21).

Pl. VI, Fig. 22 shows the pleuro-peritoneal openings - the section is beyond the dorsal limit of the "septum" and the lung buds are situate actually in the upper part of the abdominal cavity.

There are some additional points of interest in this embryo. With the growth of the liver there is an increase in the circumference of the abdominal cavity with an undermining of the lateral attachment of the "septum" to the somatopleure in the more caudal sections (Pl. VI, Fig. 23), and consequent on this the pleuro-peritoneal opening first appears in the sections as a rupture of the lateral wall of the coelomic tube. This lateral wall of the coelomic tube forms the suspensory ligament of the liver in the lower part of the channel, while caudally where the channel merges into the general body cavity it becomes continuous with the Wolffian mesentery (Pl. V, Fig. 20). It will be appreciated that any attempt to define the limits or extent of a "septum transversum" is fraught with much difficulty.

Text-Fig. 4B is a reconstruction of a para-sagittal section and it can be observed that the pleuro-peritoneal membrane is at this stage the ventral wall of the coelomic tubes. It is, of course, in continuity with the pericardio-



Text-Fig. 5A. Embryo 12.5 mm. Reconstruction of a median sagittal section. x 50. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity. Interrupted vertical lines = Liver. Large dots = Gut and trachea. Black = Mesoderm. C = Cranial attachment of umbilical cord.

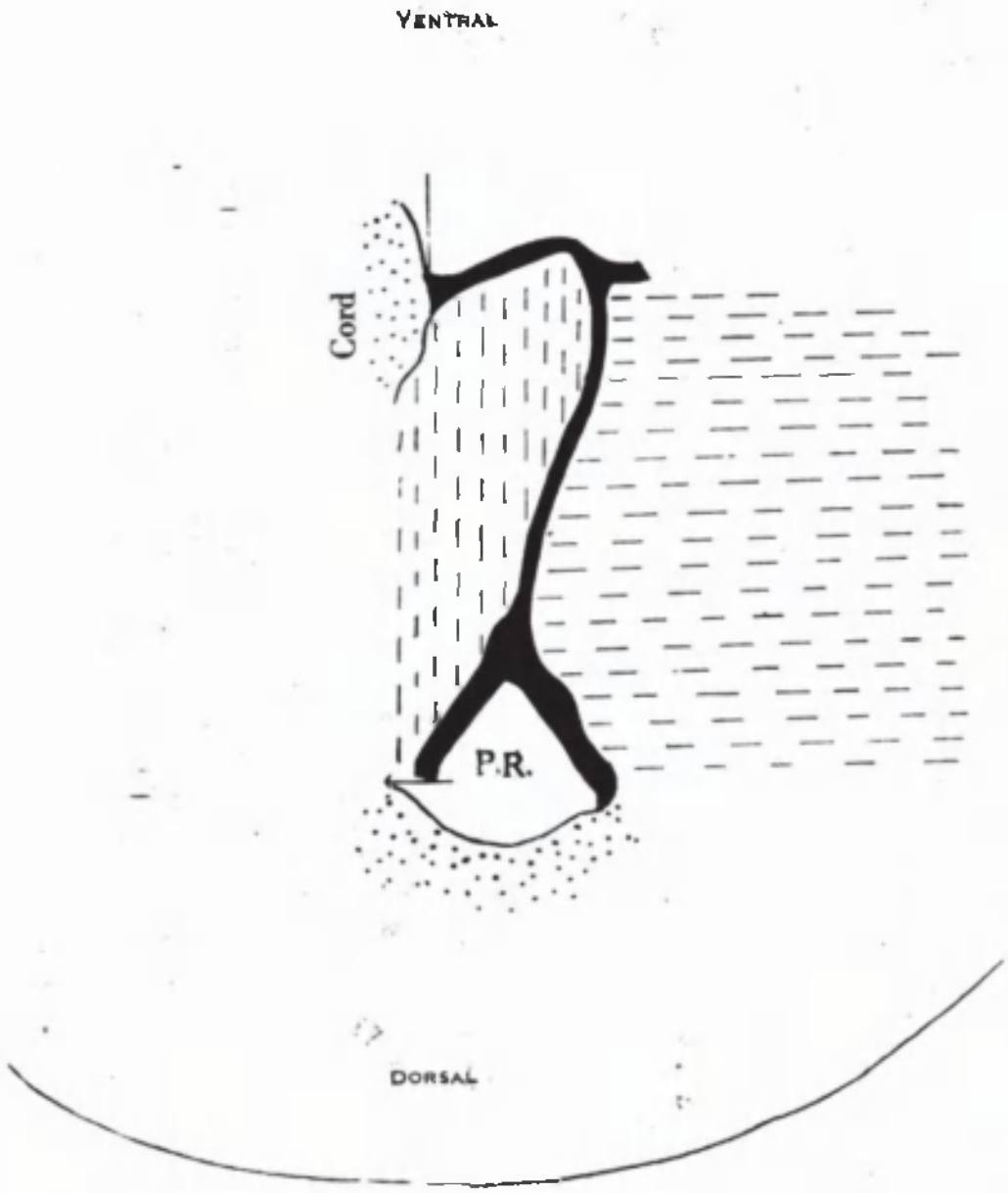
peritoneal membrane; the interruption in the figure is due to the passage of the ductus venosus into the sinus venosus.

Embryo 12.5 mm.

There is a considerable interval between the caudal margin of the pericardium and the cranial attachment of the umbilical cord. This is the supraumbilical wall and measures .6 mm in length. Its mesodermal basis consists for the most part of a narrow band of tissue of loose texture whose dorso-ventral depth increases caudally. In the mid line the mesoderm is denser compared to the more open mesenchymal network of the cord tissue (Pl. VI, Fig. 24).

Along with the increased supraumbilical interval is the marked caudal and ventral growth of the liver carrying with it the tissue of the septum transversum, the mesodermal basis of the supraumbilical wall. In this embryo the "septum transversum" is, in the mid line, represented by the mesoderm of the supraumbilical abdominal wall, the narrow strip of mesoderm (Text-Fig. 5A) between the liver and pericardium which blends in the mid line with the ventral mesentery of the foregut (Pl. VII, Fig. 27), and in the more cranial sections extends the entire width of the body cavity (Pl. VII, Fig. 25) - the pericardio-peritoneal membrane. Followed caudally the pericardio-peritoneal membrane forms only the medial part of the thoraco-abdominal partition (Pl. VII, Fig. 26).

Lateral to the mid line the lung buds are extending into the loose tissue of the parietes carving out the pleural



Text-Fig. 5B. Embryo 12.5 mm. Reconstruction of a parasagittal section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = pericardial cavity. Interrupted vertical lines = Liver. Large dots = Gut and trachea. Black = Mesoderm. C = Cranial attachment of umbilical cord. PR = Pleural cavity. Arrow indicates the pleuro-peritoneal opening.

spaces and fashioning from the somatopleure on each side another mesodermal septum, the cranial part of which becomes the pleuro-pericardial, and the caudal the pleuro-peritoneal membrane (Pl. VII, Fig. 26).

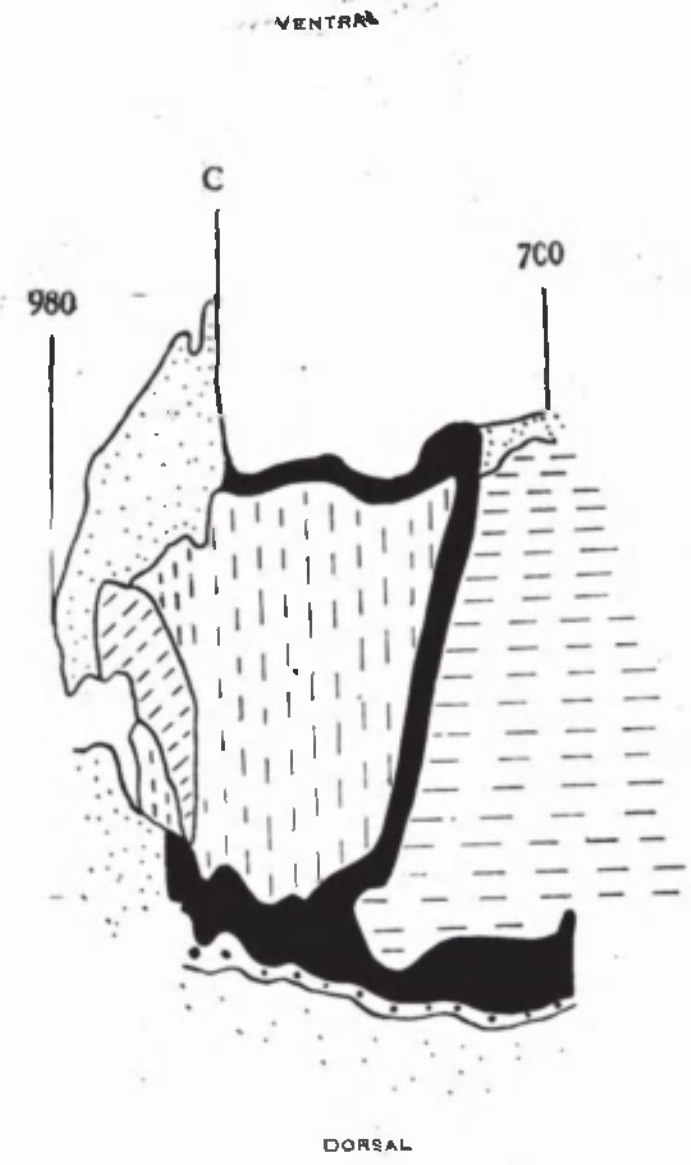
The pleuro-peritoneal membranes caudally form the lateral portions of the thoraco-abdominal partition, the remainder being completed by the pericardio-peritoneal membrane and the ventral mesentery.

Text-Fig. 5B shows the relations and continuity of the three mesodermal membranes, and Pl. VIII, Fig. 29 shows the left pleuro-peritoneal opening and the continuity of pleuro-peritoneal membrane and Wolffian mesentery.

The liver has commenced to separate from its mesodermal bed, the process of peritonealisation, but still maintains a broad connection ventrally where the vitello-umbilical vein enters the liver lateral to the mid line (Pl. VII, Fig. 27), and also dorsally where the ductus venosus enters the sinus (Pl. VII, Fig. 28).

14 mm Embryo.

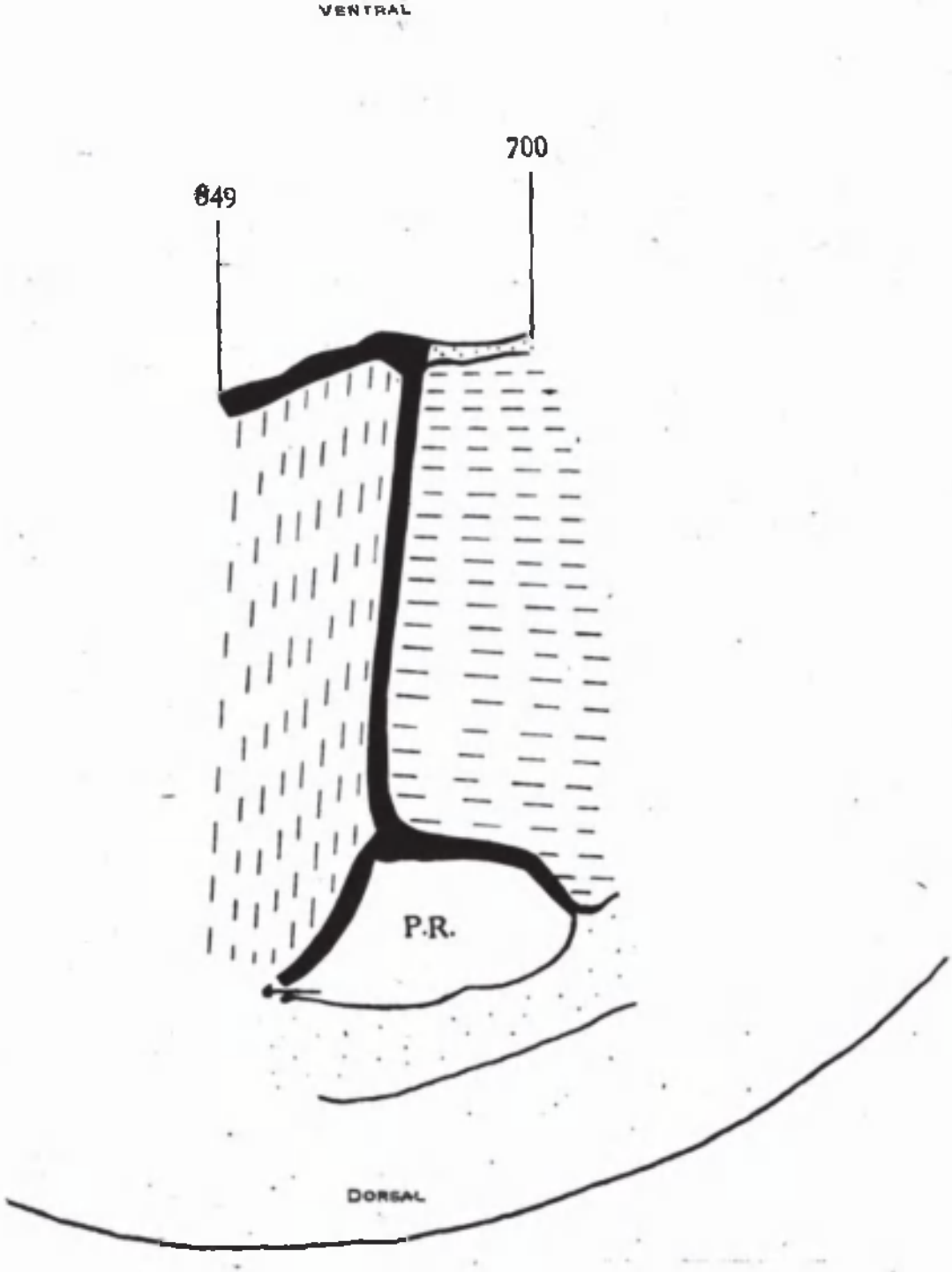
In this embryo the supraumbilical area has increased relatively and absolutely, extending over 128 sections with a total length of 1.28 mm (Text-Fig. 6A). Its mesodermal basis has a greater dorso-ventral depth than the corresponding area in the 12.5 mm embryo (Pl. VIII, Fig. 30), possibly due to an accession of tissue from the paraxial downgrowths although these are not yet well developed.



Text-Fig. 6A. Embryo 14 mm. Reconstruction of a median section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Liver.
Interrupted oblique lines = Vein. Large dots = Gut.
Black = Mesoderm. C = Cranial attachment of the umbilical cord.

With the growth of the pleural cavities which have extended cranially and laterally there is a relative decrease in the area of liver related to pericardium. In the 12.5 mm, and more so in the 7 mm embryo, the lung buds are placed in the coelomic tubes caudo-dorsal to the heart and separated from the liver by a pleuro-peritoneal membrane which in the latter embryo is the mesoderm forming the ventral wall of the coelomic channels - the caudal portion of the pericardio-peritoneal membrane. Consequent on the lateral expansion of the pleural cavities there is a corresponding increase transversely of the pleuro-peritoneal membrane at the expense of the somatopleure. Growth of the lung buds towards the head end brings them into more direct relationship with the dorsal pericardium, and the "cleft part" of the somatopleure in this region forms a mesodermal partition between lungs and heart - the pleuro-pericardial membrane, which is caudally in continuity with the pleuro-peritoneal membrane (Text-Fig. 6B; Pl. VIII, Fig. 31). The latter in turn can be followed to the Wolffian mesentery - the lateral boundary of the pleuro-peritoneal opening (Pl. IX, Fig. 33). These three structures, viz., pleuro-pericardial, pleuro-peritoneal and Wolffian mesentery, form a continuous shelf of mesoderm projecting into the body cavity, the two former serving as a partition between the pleural and pericardial and pleural and abdominal coeloms respectively.

The pleuro-pericardial membrane (Pl. VIII, Fig. 31)



Text-Fig. 6B. Reconstruction of a parasagittal section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Liver.
Interrupted oblique lines = Vein. Large dots = Gut.
Black = Mesoderm. C = Cranial attachment of the umbilical cord. P.R. = Pleural cavity. The arrow indicates the pleuro-peritoneal opening.

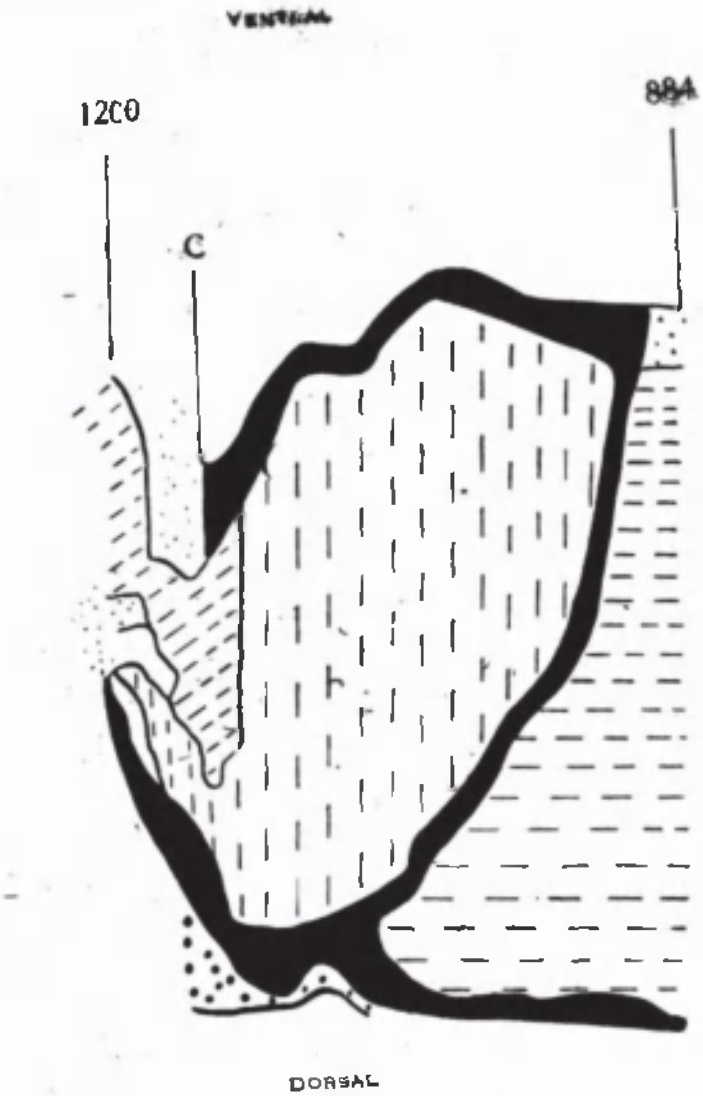
carries with it the duct of Cuvier which comes to lie medial to the pleural cavities (c.f. Pl. V, Fig. 19). Peritonealisation of the liver has increased but it is still attached in the mid line ventrally, and dorsally to the pericardium and foregut mesentery (Pl. VIII, Fig. 32).

16.1 mm Embryo.

The supraumbilical wall is 2 mm in length, protrudes ventrally and has an increased dorso-ventral thickness. In the lower half the paraxial downgrowths extend slightly over half way round the body wall but do not encroach on the mid line (Pl. IX, Fig. 34). The considerable interval between the liver and the parietes laterally and postero-laterally is artificial, due to shrinkage during fixation and there is a slight interval between the liver and the parietes in the midventral line - also an artefact. In the fresh specimen one would expect the two structures to be here in contact. The pleural cavities are still further developed, extending caudally posterior to the suprarenals (Pl. IX, Fig. 35). In this position the pleuro-peritoneal membrane has increased in thickness and appears to derive additional mesoderm from the gut mesentery in the mid line. The muscular element of the diaphragm is first apparent in its dorsal part (Keibel and Mall). The pleuro-peritoneal opening is still present (Pl. IX, Fig. 35).

23 mm Embryo.

The paraxial downgrowths have penetrated into the



Text-Fig. 7A. Embryo 16.1 mm. Reconstruction of a median sagittal section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity. Interrupted vertical lines = Liver. Interrupted oblique lines = Vein. Large dots = Gut. Black = Mesoderm. C = Cranial attachment of umbilical cord.

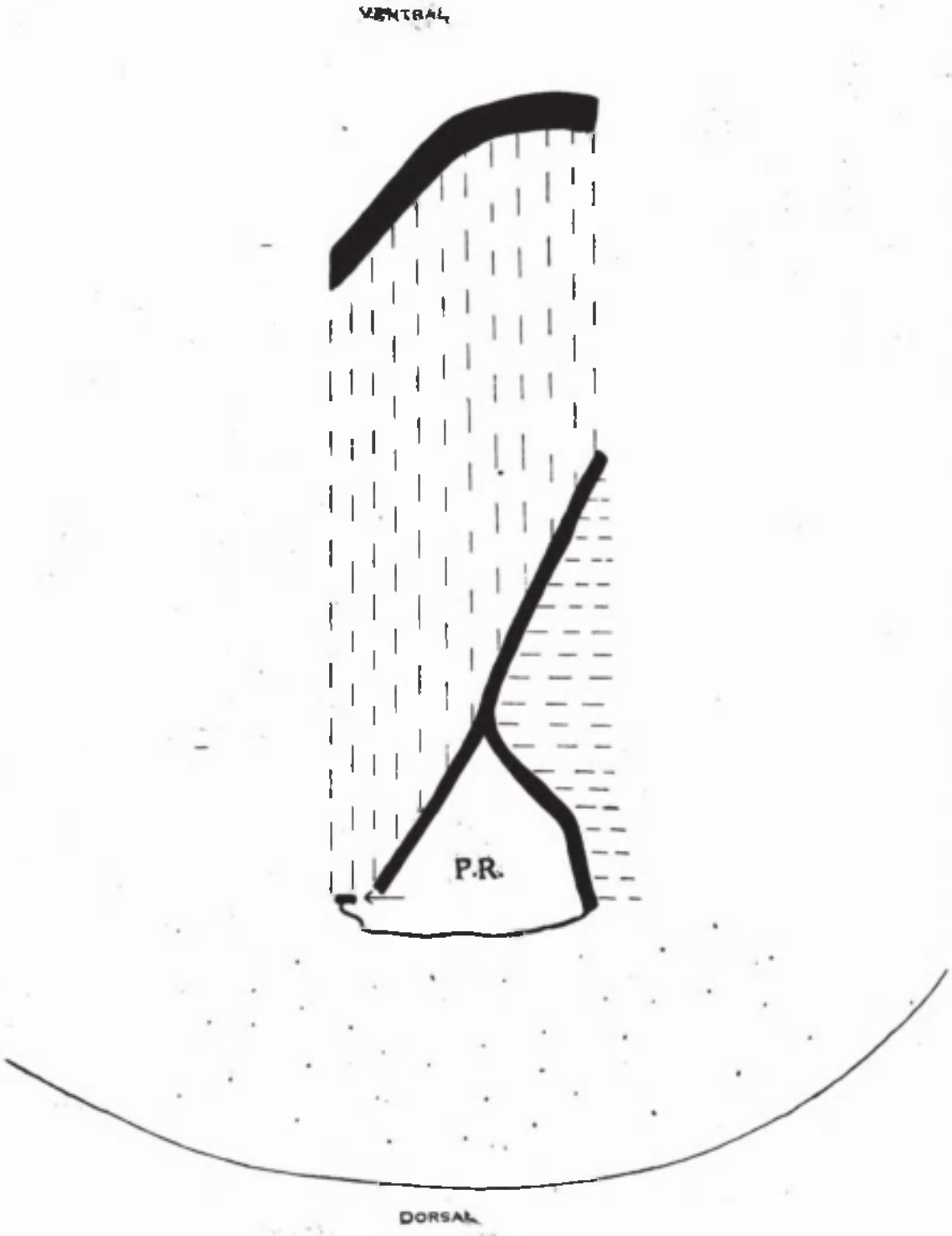
supraumbilical wall. The recti muscles can be seen on each side - situated antero-laterally. The rectus sheaths are prolonged medially and fuse with the tissue of the midventral wall (Pl. IX, Fig. 36). Again in this specimen the wide interval between the liver and parietes is the result of shrinkage. The further development of the pleural cavities with the concomitant increase of pleuro-peritoneal membrane is responsible for a relative decrease in the area of diaphragm formed from the pericardio-peritoneal membrane. Laterally the pleuro-peritoneal membranes on both sides are receiving muscular reinforcements from the paraxial downgrowths (Pl. X, Fig. 37), while medially that portion of the membrane between the pleural cavities and the suprarenals is invaded by muscular tissue arising in the region of the dorsal mesentery and responsible in part for the closure of the pleuro-peritoneal opening (Pl. X, Fig. 38).

30 mm Embryo.

This embryo is cut in an obliquely sagittal plane. Pl. X, Fig. 39 shows the extent of the supraumbilical abdominal wall, and the continuity in a vertical plane of the pericardio-pleural and pleuro-peritoneal membranes and also the extent of the diaphragm which is formed from the pericardio-peritoneal membrane.

40 mm Embryo.

The paraxial downgrowths have penetrated well into the ventral wall. In the more cranial part the ribs reach



Text-Fig. 7B. Embryo 16.1 mm. Reconstruction of a parasagittal section. x 25. The numbers refer to the sections. Description in text.

Interrupted horizontal lines = Pericardial cavity. Interrupted vertical lines = Liver. Interrupted oblique lines = Vein. Large dots = Gut. Black = Mesoderm. C = Cranial attachment of umbilical cord. P.R.= Pleural cavity. The arrow indicates the pleuro-peritoneal opening.

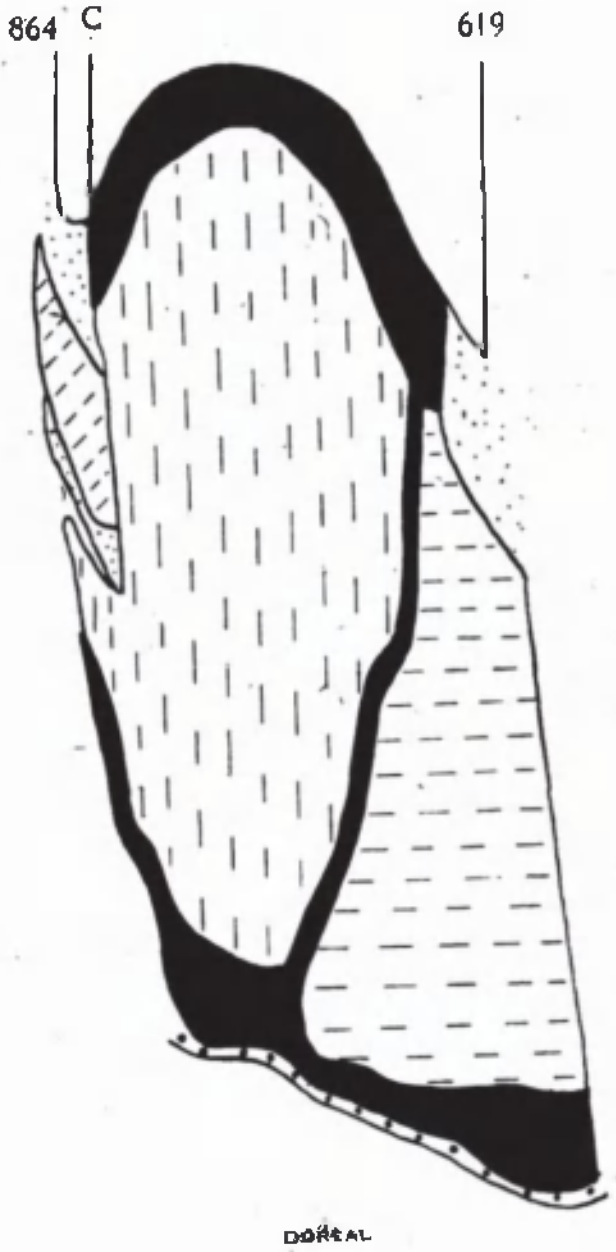
the ventro-lateral aspect. The recti muscles are separated from one another in the midventral line by an interval traversed by the rectus sheaths which by their fusion form a dense central mass of tissue - the linea alba (Pl. XI, Fig. 40). The pericardio-peritoneal portion of the diaphragm now forms a relatively small part of the whole in the midline cranially, while the larger lateral parts - pleuro-peritoneal membranes - have now acquired muscular tissue attached to the deep aspect of the rib processes (Pl. XI, Fig. 41).

In the mid line caudally muscular fibres invade that part of the diaphragm formed from the dorsal mesentery - the contribution from the subvertebral musculature.

The liver has completed its separation from the parietes except in the mid line ventrally and dorsally - the reflection of the future falciform and coronary ligaments.

CONCLUSIONS.

The older embryologists postulated the formation of skin plates in connection with the somites - these passing ventrally with the paraxial muscular downgrowths to complete the ectodermal covering of the ventral body wall. The more modern conception of the expansion of the embryonic body round a relatively fixed rim or circumference - the future umbilical orifice - not only affords an explanation of the formation of head and tail folds, pericardial inversion, and the prevailing dorsal convexity, but is also supported by the constant position of the umbilical vein along the



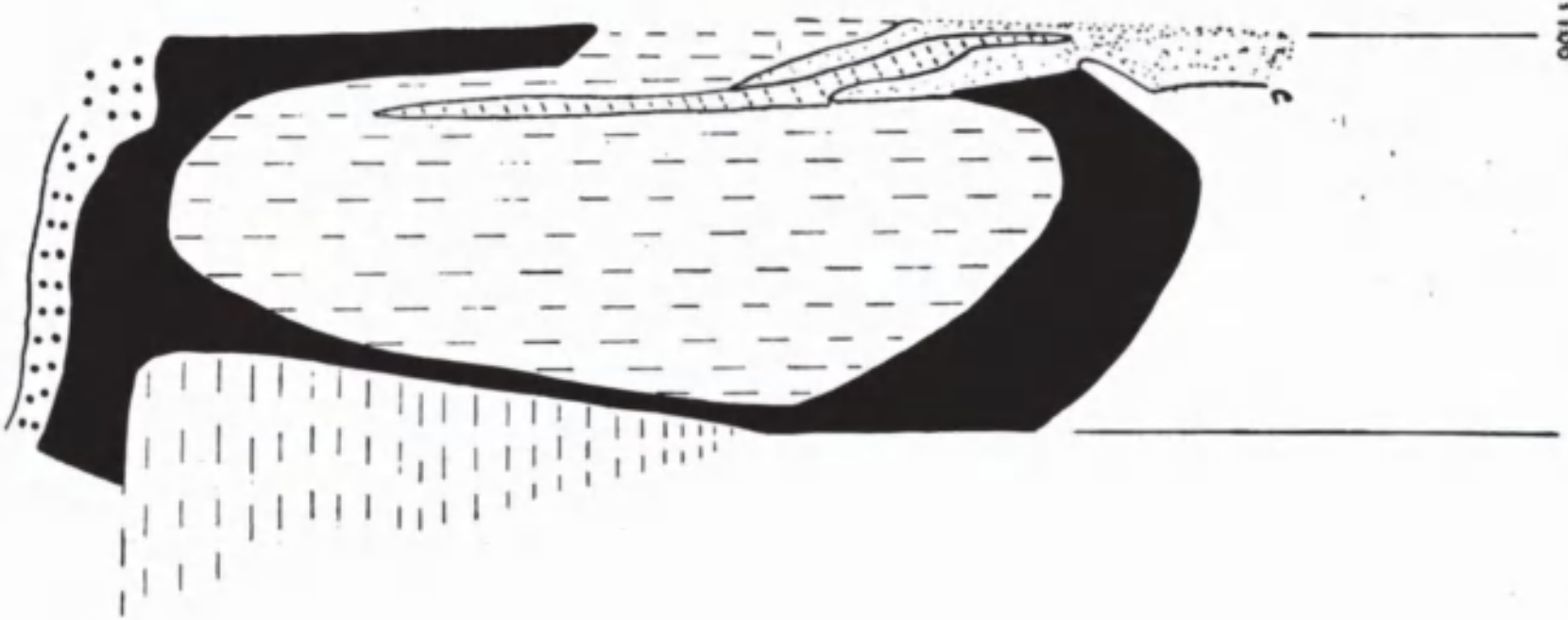
Text-Fig. 8. Embryo 23 mm. A reconstruction of a median sagittal section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Liver.
Interrupted oblique lines = Vein. Large dots = Gut.
Black = Mesoderm. C = Cranial attachment of the umbilical cord.

"rim" and thus in the later stages encroaching on the mid line ventrally.

The mesodermal basis of the lateral portions of the ventral wall is of course, in the first instance, the somatopleure, reinforced later by the muscular sheets of paraxial origin. Above and below the umbilicus are areas of fusion of primary and secondary mesoderm - the anterior and posterior mesodermal fields. The secondary element includes both somatopleure and splanchnopleure, and as has been shown comes directly from the primitive streak.

The mesoderm of the supraumbilical abdominal wall is the ventral portion of the general mass forming a partition between the thoracic and abdominal cavities, and its splanchnopleure becomes the falciform ligament and serous coat of the liver. Into the dorsal part of the mesodermal partition projects the early hepatic bud, while later the liver not only encroaches on the ventral part but in its further growth appears actually to push before it the abdominal parietes.

The appearance of a supraumbilical interval synchronises with the ventral and caudal growth of the liver tissue into the mesoderm of the body wall and one is tempted to assume the interdependence of cause and effect. Certainly the growth of this part of the abdominal wall follows on the enlargement of the liver but only provided other conditions are normal - the cause is not always followed



Text-Fig. 9. Embryo 40 mm. Reconstruction of a median sagittal section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity. Interrupted vertical lines = Liver. Interrupted oblique lines = Vein. Large dots = Gut. Black = Mesoderm. C = Cranial attachment of umbilical cord.

by the effect.

In congenital abnormalities involving deficiency, partial or complete, of the supraumbilical wall - for example, abdominal fissure or eventration - there may be a liver normal in size and shape.

The development of the abdominal coverings would therefore seem to some extent to be independent of the viscera and influenced by factors mechanical or otherwise which do not necessarily affect visceral growth.

EVENTRATION. *

Complete absence of the upper abdominal wall - eventration - is a comparatively rare congenital defect; Schwalbe quotes 1 in 5000 as the relative frequency.

In the Hunterian Collection (Glasgow) there are five specimens of this condition, three of which have in addition a spina bifida. In all of them there is marked retroflexion of the body wall with, in one case, a scoliosis.

Specimen No. 50.115 (Pl. XI, Figs. 42 and 43). Female child about nine months with non-closure of the abdomen. The viscera are prolapsed into a large membranous bag which has been cut away. The lower half of the body and lower limbs are flexed backwards and to the left. There is a small spina bifida in the sacral region.

Specimen No. 50.116. Twin fellow of the preceding with the

* Small abdominal herniae as distinct from umbilical herniae will be more appropriately discussed in connection with the development of the umbilical portion of the abdominal wall.

same deficiency of parietes; a large spina bifida and retroflexion.

Specimen No. 50.117. There is deficiency of abdominal parietes and the viscera are enclosed in a membranous sac; an extreme degree of retroflexion, a large spina bifida and double talipes equina.

Specimen No. 50.114. The spleen and almost the whole intestines are outside the abdominal cavity. The head is bent back between the shoulders. There is anencephaly and amyelia.

Specimen No. 50.119. Extreme degree of non-formation of the abdominal wall with retroflexion.

Schwalbe in his considerable series remarks on the almost invariable presence of curvature of the vertebral column. This fact, coupled with the presence of retroflexion in each of the above examples makes it difficult to dismiss it as a mere coincidence. Either the condition is a concomitant defect - the two having a common casual value or alternatively the one follows as a consequence of the other. Bryce describing a foetus, the subject of ectopia viscerum, spina bifida, dorsal retroflexion and other abnormalities, considers the dorsal curvature is primary and expresses the maintenance of a very early attitude.

Some retroflexion may be normal at an early stage. Ingalls suggests that such curvature is the inevitable result of the lifting up of the head by the developing pericardium and accentuated by the precocious development of the forebrain.

But its persistence in a marked degree is definitely abnormal. The His embryos Lg and Sc.H. both show sharp dorsal concavities which Ingalls inclines to regard as abnormal. It is conceivable, taking the retroflexion as the primary condition, that such curvature would seriously interfere with the direction of growth forces.

The embryonic rim or umbilical orifice instead of remaining relatively fixed would tend to become "pulled out" in both the transverse and cranio-caudal axis, interfering with the normal growth of the ventral somatopleure which in turn would of course retard the forward extension of the muscle ingrowths.

The unusual "set" of the sclerotome resulting from a persistent retroflexion would favour a tendency to non-closure of the neural arch over the affected segment.

Amnial adhesions at an early stage might be the cause of the abnormal retroflexion and this in turn occasion the deficiency of the abdominal parietes, or again, amnial fusion could be the common aetiological factor responsible for both defects.

Schwalbe's contribution to the genesis of the condition assumes the presence of "skin plates" growing forwards to unite in the mid ventral line and complete the closure of the abdominal cavity.

SEPTUM TRANSVERSUM.

Most accounts of the development of the diaphragm

centre round the "septum transversum" and much of the difficulty in the ultimate analysis of the adult structure is due to conflicting opinions as to what constitutes the "septum".

Politzer and Sternberg regard the septum transversum as the proliferation of the endodermal mesoderm of the floor of the gut. Frazer's conception, already mentioned, includes the region of the anterior mesodermal field.

Keith shows the septum transversum cleft into a pericardial and diaphragmatic lamina by the lung buds, an interpretation which would include the dorsal pericardial wall as part of the septum; this could also be regarded as somatopleure.

In the 7 mm embryo (Pl. VI, Fig. 21) the pleural cavities are separated from the liver by mesoderm - a pleuro-peritoneal membrane which is the ventral wall of the coelomic passages. In the later stage (12.5 mm) the pleuro-peritoneal membrane is increased from the lateral somatopleure. Should this also be regarded as part of the septum transversum?

After the inversion of the heart region there is a mass of mesoderm between the pericardial and abdominal coeloms which in the mid line is continuous with the foregut mesentery and so with the dorsal pericardial wall. Posteriorly on each side the partition is incomplete and the coelomic passages are bounded laterally by the somatopleure which is also continuous with the central mesodermal mass. As the pleural

cavities develop there is a corresponding increase in the mesodermal partition effected at the expense of the somatopleure. This borrowing of somatopleure mesoderm is a concomitant of thoracic expansion and the mesodermal partition is enlarging almost day by day. It is clearly impossible at any given stage to delimit an original "septum transversum".

The invasion by the pleural cavities is also occurring dorsally where the somatopleure forms the posterior pericardial wall and the "stripped mesoderm" in this position forms a septum between heart and lungs - pleuro-pericardial membrane.

From the study of this series of embryos one is of the opinion that the name septum transversum, if it must be utilised, should have a much wider and more generous interpretation than it enjoys at present. The only justifiable embryological division of the diaphragm is on the basis of its muscular morphology, and any attempt to map out in the adult structure an area derived from an early septum transversum only invites controversy and makes for subsequent confusion.

S U M M A R Y.

1. The development of the supraumbilical abdominal wall has been studied in a series of embryos ranging from 1.4 mm to 12.5 mm.
2. The ventral portion of the mesodermal partition between the thoraco-abdominal cavities furnishes the basis of the

supraumbilical wall.

3. This ventral part of the thoraco-abdominal partition is itself derived from the anterior mesodermal field subsequent to pericardial inversion.
4. The anterior mesodermal field is composed of primary and secondary mesoderm - the secondary element is formed from the fusion of processes of primitive streak mesoderm passing round the bucco-pharyngeal membrane.
5. There is a developmental analogy between the anterior and posterior poles of the blastoderm - the future supra and infraumbilical regions respectively.
6. Eventration with deficiency of the supraumbilical wall is commonly associated with retroflexion, and it is suggested that there is some aetiological relationship.
7. The term "septum transversum" is criticised as being misleading and the cause of much confusion in the embryological interpretation of the diaphragm.

---o---oOo---o---

I have to record my indebtedness to my chief, Professor Blair, for his supervision of the work.

R E F E R E N C E S.

ADELMANN, H.R. (1922). The Significance of the Prochordal Plate. Amer. Jour. Anat., vol. 31.

BONNET, R. (1901). Beitrage zur Embryologie des Hunds. Anat. Hefte. Bd. 16.

BRYCE, T.H. (1895). Description of a Foetus the subject of Retroflexion of the Trunk - Ectopia Viscerum and Spina Bifida; with a discussion as to the cause of these Associated Abnormalities. Jour. Anat. and Physiol., vol. XXIX.

Do. Do. (1924). Observations on the Early Development of the Human Embryo. Trans. Roy. Soc. Edin., vol. LIII, pt. iii, No.26.

DANDY, W.E. (1910). A Human Embryo with Seven pairs of Somites. Amer. Jour. Anat., vol. 10.

DAVIS, C.L. (1924). The Description of a Human Embryo having Twenty Paired Somites. Carneg. Instn. Publ., No. 332; Contr. Embryol. No. 72.

FETZER, M. and FLORIAN, J. (1930). Der Embryo 'Fetzer' mit beginnender Axialmesodermbildung und bereits angelegter Kloakenmembran. Z. mikr.-anat. Forsch., Bd. XXI.

FLORIAN, J. (1928). Ein junges menschliches Ei in situ (Embryo T.F. mit Primitivstreifen, ohne Kopffortsatz). Z. mikr.-anat. Forsch. Bd. XIII.

Do. Do. (1934). Ein Schema der Entwicklung der Axialgebilde des menschlichen Embryos bis in das Stadium von 10 Urwirbelpaaren. Biol. gen. Bd. X, Lief 2.

FRAZER, E. (1931). Manual of Embryology. London, Bailliere, Tindall & Cox.

GROSSER, O. (1927). Fruhentwicklung, Eihautbildung und Placentation. Munich.

Do. Do. (1931). Primitivstreifen und Kopffortsatz beim Menschen. Anat. Anz., Bd. LXXI.

HAMILTON, W.J. (1937). The Early Stages in the Development of the Ferret: The Formation of the Mesoblast and Notochord. Trans. Roy. Soc. Edin., vol. LIX, Pt.i.

HILL, J.P. and FLORIAN, J. (1931). A Young Human Embryo (Embryo Dobbin) with Head Process and Prochordal Plate. Phil. Trans., B., vol. CCXIX.

INGALLS, N.W. (1920). A Human Embryo at the beginning of Segmentation. Carneg. Instn. Publ., No. 274; Contr. Embryol., No. 52.

KEITH, A. (1921). Manual of Embryology and Morphology. 4th ed.

KEIBEL, F. and MALL, F.P. (1912). Manual of Human Embryology. vol. II.

LANGE, D. de. (1936). The Head Problem in Chordates. Jour. Anat., vol. LXX.

LLORCA, F.Orts. (1934). Beschreibung eines menschlichen Embryo mit 4 Urwirbelpaaren. Z. ges. Anat. 1. Z.Anat.EntwGesch. Bd. CIII, Heft 6.

MOLLENDORFF, vom. (1925). Das menschliche Ei. Wo(lfring) Implantation. Verschluss der Implantationsoffnung und Keimesentwicklung beim Menschen vor Bildung des Primitivstreifens. Z. ges. Anat. 1. Z. Anat. EntwGesch. Bd. 76.

PAYNE, F. (1925). General description of a seven somite human embryo. Carneg. Instn. Publ., No. 361; Contr. Embryol. No. 81.

POLITZER, G. and STERNBERG, H. (1930). Uber die Entwicklung der ventralen Korperwand und des Nabelstranges beim Menschen. Z. f. Anat. u. EntwGesch. Bd. XCII, Heft 4.

RABL, C. (1899). Theorie des Mesoderm. Morph. Jahrb., Bd. XV.

ROSSENBECK, H. (1923). Ein junges menschliches Ei, Ovum Humanum Peh-Hochstebber. Z. ges. Anat. 1. Z. Anat. EntwGesch., Bd. LXVIII.

SCHWALBE, E. (1909). Die Morphologie der Missbildungen des Menschen und der Tiere.

STERNBERG, H. (1927). Beschreibung eines menschlichen Embryos mit vier besegmentpaaren. Z. ges. Anat. 1. Z. Anat. EntwGesch. Bd. LXXXII.

STIEVE, H. (1926). Ein 13½-Tage altes, in der Gebarmutter erhaltenes und durch Eingriff gewonnenes menschliches Ei. Z. mikr.-anat. Forsch. Bd. VII.

STREETER, G.L. (1927). Development of the mesoblast and notochord in pig embryos. Carneg. Instn. Publ., No. 380; Contr. Embryol. No. 19.

Do. Do. (1927). The Miller ovum. Carneg. Instn. Publ., No. 363; Contr. Embryol. No. 92.

WALDEYER, H. (1929). Ein junges menschlichen Ei in situ (scho(nholz). Z. ges. Anat. 1. Z. Anat. EntwGesch. Bd. XC.

WATT, J.C. (1915). Description of two young twin human embryos with 17-19 paired somites. Carneg. Instn. Publ., No. 222; Contr. Embryol. No. 2.

PART III.

THE FORMATION OF THE UMBILICAL CORD AND THE UMBILICAL REGION OF THE ANTERIOR ABDOMINAL WALL.

I N T R O D U C T I O N.

"It is a characteristic of many vertebrates that, associated with the provision of special arrangements for nourishing the young individual, the time of commencing an independent existence on its own account is greatly delayed. In such cases where a considerable proportion of the whole development takes place within the shelter of the egg shell or parental body we have to do with what is known as embryonic in contradistinction to larval development." (Graham Kerr).

The young larvae of the holoblastic Anamnia such as the frog quickly learn to fend for themselves and therefore have a very small store of nourishment easily housed within the ventral wall of the gut.

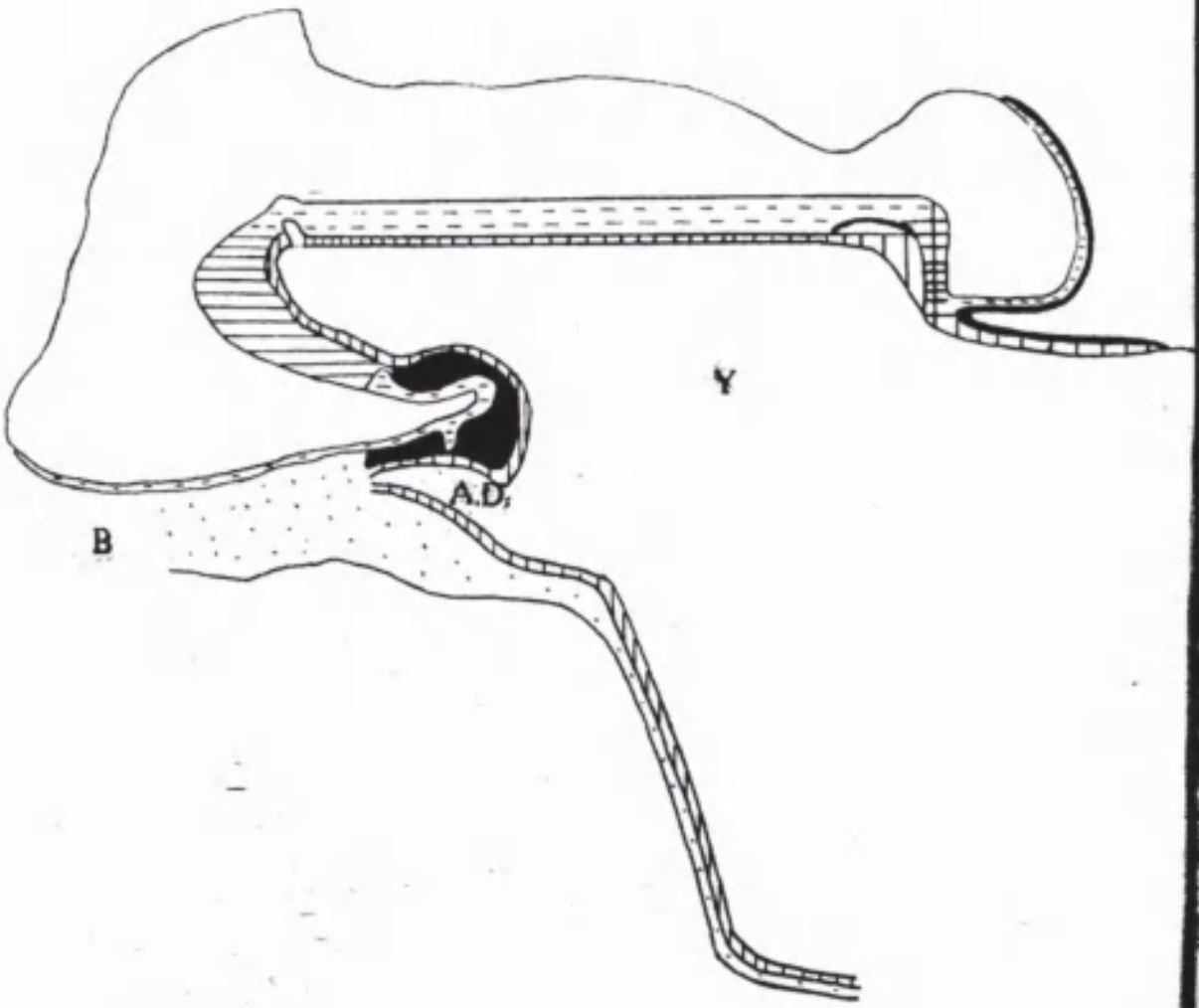
In the meroblastic Elasmobranchs there is a considerable store of nourishment to tide the developing young over the much longer period preceding the acquisition of independence. The larger yolk mass is for a time extraembryonic. It is encircled by the endodermal cells, forming a primitive gut or enteron, and later enclosed by the extra-embryonic blastoderm. The yolk sac then becomes

connected to the embryo by a constricted narrow part - the yolk duct; this in turn has its covering of mesoderm and ectoderm, and constitutes the somatic stalk. In the final stages the yolk sac is drawn into the body and the somatic stalk is incorporated in the body wall.

The umbilical cord of the Amniota constitutes the pathway for the transit of substances to and from the embryo. In birds and reptiles the extra-embryonic blastoderm (false amnion and endoderm) grows round and encloses the large yolk mass carrying with it an extension of the coelom between the somatopleure and splanchnopleure. In Amniota the allantois issues from the hind gut on the caudal and ventral aspect of the embryo. The true amnion, attached round the embryonic "rim", forms the boundaries of the somatic stalk which thus includes the yolk stalk, a portion of the exocoelom and more caudally the allantoic stalk.

The somatic stalk or umbilical cord of placental mammals is essentially of a similar nature to that described above, although the now increased functional importance of the allantoic element overshadows that of the yolk stalk.

This work consists of a study of the umbilical cord in the series of human embryos already utilised in parts I and II, with the addition of an embryo of 8.5 mm, one of 42 mm, and one of 60 mm. Sections were also made of rabbit embryos in which the gut had returned into the



Text-Fig. 10. Embryo McIntyre I. Reconstruction of a median sagittal section. x 100. Description in text.
Horizontal lines = Primitive streak.
Interrupted horizontal lines = Ectoderm.
Vertical lines = Endoderm, head process and prochordal area.
Black = Mesoderm.
Y = Yolk sac.
A.D.= Allantoic diverticulum.
B = Body stalk.

abdominal cavity, but as these show no features of peculiar interest they are not described in detail.

The method of graphic reconstruction is again adopted where possible, as it affords a ready appreciation of the relations in any given embryo, and obviates much tedious description of individual sections.

From the observations on the individual embryos one suggests the method of formation of the umbilical cord, completed in human embryos somewhere between the 5 and 7 mm stage - of the formation and expansion of the umbilical cord coelom which attains its maximum size between the 30 and 40 mm stage, and of the final obliteration of the cord coelom and closure of the umbilical ring subsequent to the return of the gut into the abdominal cavity. No great attention has been paid to the relations and fate of the contents of the umbilical cord such as the yolk duct and vitelline vessels, as these have been recounted with much thoroughness by Politzer and Sternberg in their comprehensive paper "Uber die Entwicklung der ventralen korperwand und des Nabelstranges beim Menschen" to which frequent reference is made throughout.

DESCRIPTION OF EMBRYOS.

Embryo McIntyre I. (1.4 mm). (Text-Fig. 10).

This embryo has already commenced to fold off from the yolk sac and there is a small foregut and larger hindgut diverticulum. The ventral aspect consists mainly of the

yolk sac which shows a slight lateral furrowing indicating the site of later constriction. Cranially the anterior mesodermal field forms the anterior and lateral boundaries of the pericardial plate where the mesoderm exhibits cleavage. Elsewhere there is as yet no intra-embryonic coelom.

With the formation of the tail fold the embryonic attachment of the body stalk comes to lie on the ventral aspect. This region has already been described in Part I, where it was suggested that the stalk mesoderm was not only derived from primitive chorionic mesenchyme, but received accessions from the caudal margin of the embryonic disc.

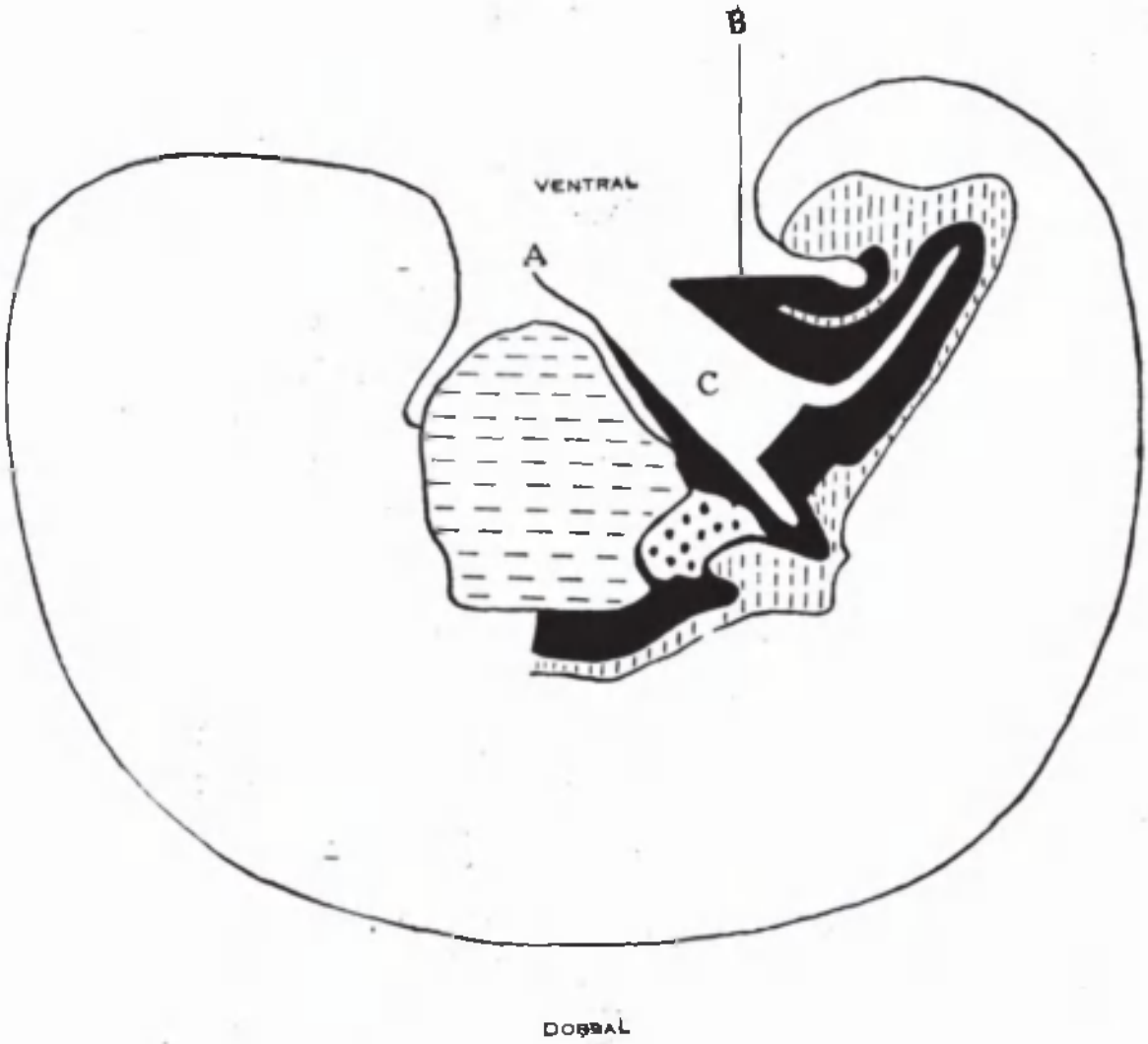
Embryo McIntyre I differs from the four-somite embryo of Sternberg in the absence of any extensive connection of amnion and chorion, i.e. a "primary amnio-chorionic field". There is no amnio-embryonic stalk as described by Florian in presomite embryos. In this respect it can be compared to Embryo Bi.XI (Florian) of ten somites to which it has also some external resemblance.

Embryo 2.6 mm. (Text-Fig. 2).

Following the pronounced involution of the embryonic body the ectodermal surface of the pericardium forms the cranial part of the ventral aspect. There is still a broad yolk sac connection which however in comparison to the 1.4 mm embryo has a marked "waisting" at the junction with the mid gut.

Between the attachment of the amnion and the cranial aspect of the yolk sac connection is a broad band of mesoderm, the anterior mesodermal field, which is continuous dorsally with the splanchnopleure on the floor of the gut. A prolongation of the coelom - the posterior coelomic portal - separates the body stalk from the mesoderm on the caudal side of the yolk sac connection. As the tail fold develops this coelomic portal is taken still further into the embryonic body to form the pelvic cavity. The most caudal structure in the somatic stalk is the allantoic or body stalk. This has an oblique attachment, being directed to the left while the yolk sac is to the right (Pl. XII, Fig. 45). In consequence of this deviation of the body stalk the amnion clothes the greater portion of its left lateral aspect (Pl. XII, Fig. 44), and much of the right side is extra-amniotic.

As has already been noted the cranial aspect of the yolk sac connection is lying against the anterior mesodermal field. There is now a body cavity which has a relatively extensive communication with the extra-embryonic coelom on each side of the yolk sac connection, i.e. where the ventral wall remains "open". Each intercoelomic communication is bounded medially by the yolk sac connection and laterally by the body wall with the amnial reflection. At the rim or point of amnial reflection are the umbilical veins, the left larger than the right. Here



Text-Fig. 11. Embryo 4.5 mm. Reconstruction of a median sagittal section. x 50. Description in text. Yolk sac is not shown.

Interrupted horizontal lines = Pericardium.
Interrupted vertical lines = Gut.
Black = Mesoderm. Large dots = Liver.
C = Coelom.
A = Amnion.
B = Body Stalk.

the somatopleure of the lateral body wall becomes continuous with the mesoderm of the amnion. There is a marked increase of mesoderm at the site of amnial reflection (Pl. XII, Fig.46).

Embryo 4.5 mm. (Text-Fig. 11).

The further folding of the head and tail ends is responsible for the relative decrease in the extent of the "open" ventral aspect and the increased dorsi-ventral convexity for the greater depth of intra-embryonic coelom. Moreover a part of the extra-embryonic coelom has been taken into the body anteriorly as well as posteriorly, and now a coelomic prolongation separates the proximal end of the yolk duct from the anterior mesodermal field and septum transversum (Pl. XIII, Fig. 50). The connection of the intestine to the yolk sac has become narrowed to a tube-like communication which at this stage could be called the vitelline duct.

The open ventral aspect is limited cranially by the amnion reflected on to the caudal wall of the completely rotated pericardium, and caudally by the allantoic stalk* which in this embryo has a more or less median position.

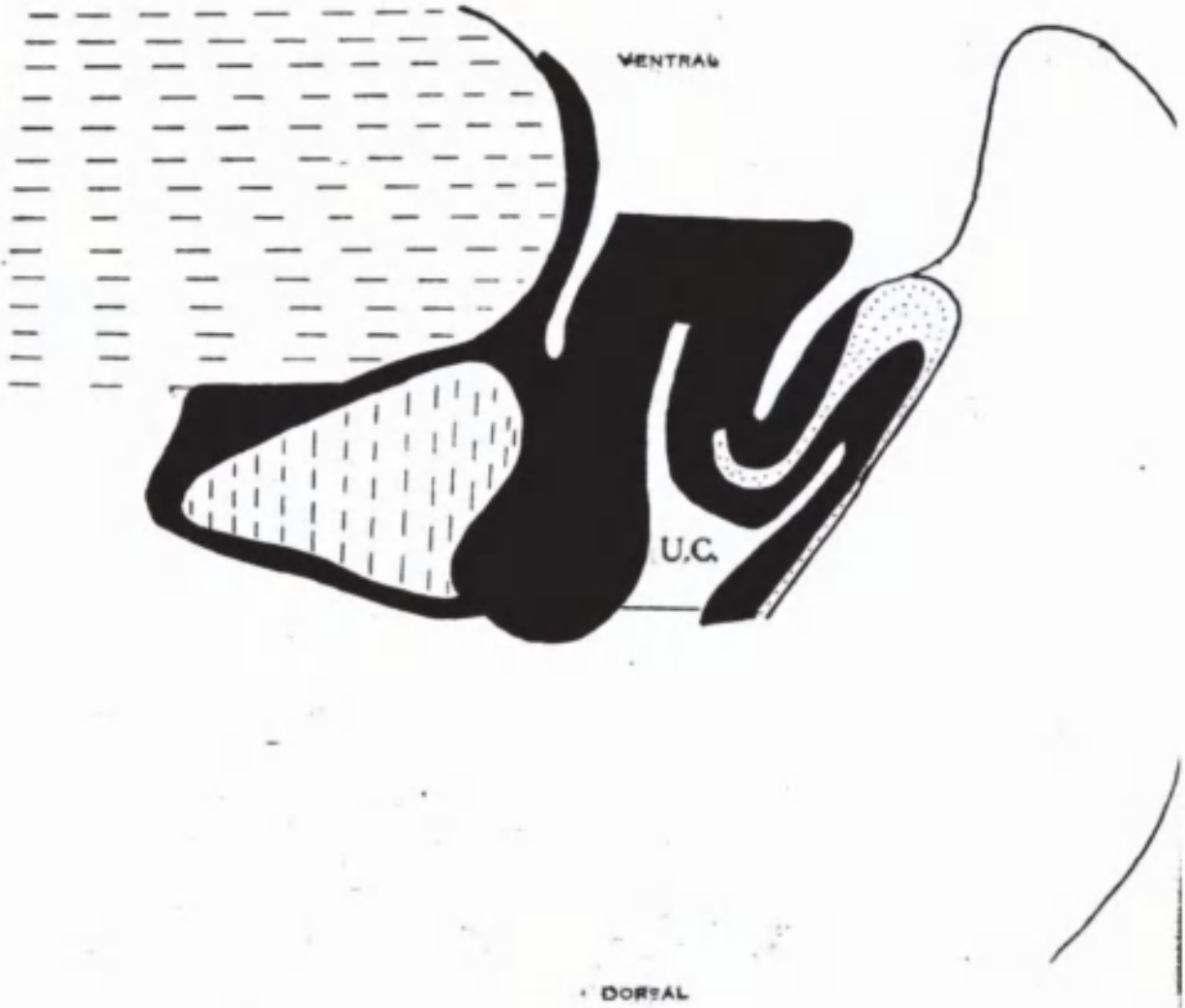
The lateral boundaries are the somatopleure of the body wall and more ventrally the thickened mesoderm on the inner aspect of the amnion. This thickening of the amnial mesoderm is much more apparent than in the

* From now on the allantoic stalk will be referred to as "stalk".

2.6 mm embryo. In its forward growth it carries with it the reflection of the amnion on each side and forms lateral tissue plates* which extend from the "stalk" to the septum transversum (Pl. XIII, Fig. 49). There is therefore in this embryo a part of the extra-embryonic coelom enclosed between the stalk, the cranial reflection of the amnion and the lateral tissue plates, i.e. there is a short umbilical cord.

The earlier site of lateral amnial reflection is indicated by the position of the umbilical veins, each of which runs in a ridge of tissue projecting from the internal aspect of the somatopleure. This is also the junction of the lateral body wall with the lateral tissue plates and of the exocoelom with the body cavity. The lateral tissue plates consist externally of amnial ectoderm, internally of endothelium from the amnial mesoderm and a thick middle coat of proliferated embryonic connective tissue. This young connective tissue may result from migration of somatopleure cells but more probably is a derivative of the amnial mesoderm. The lateral tissue plates are deeper caudally and "taper" towards the septum transversum so that in the wax reconstruction they have the appearance of cranial extensions or pillars of the stalk.

* The term "lateral tissue plate" shall be used to denote the amnion with its thickened mesoderm ventral to the umbilical veins.



Text-Fig. 12. Embryo 7 mm. Reconstruction of a median sagittal section. x 50. Description in text.
Interrupted horizontal lines = Pericardium.
Interrupted vertical lines = Liver.
Small dots = Gut and allantoic diverticulum.
U.C.= Umbilical cord coelom.
Black line indicates the plane of the umbilical veins.

The smooth mesothelium of the cranial aspect of the stalk forms the caudal lining of the enclosed exocoelom. An umbilical loop of intestine is not yet formed.

The amnion covers the posterior aspect and sides of the proximal portion of the "stalk" (Pl. XIII, Fig. 48) - the posterior aspect of the middle portion, while the distal part is entirely extra-amniotic (Pl. XII, Fig. 47).

Embryo 7 mm. (Text-Fig. 12).

This is the youngest embryo of the series to possess a formed umbilical cord. Coincident with this is the first appearance of a short supra-umbilical abdominal wall, and thus the cranial attachment of the cord is a little distance caudal to the pericardium.

Comparison of Text-Figs. 11 and 12 gives some indication of the changes by which the "open" ventral wall of the embryo is now the site of attachment of the umbilical cord.

The lateral tissue plates whose formation had commenced in the 4.5 mm embryo undergo further growth by proliferation of their connective tissue and in their ventral extension carry with them the amnial reflection. There is also proliferation of the mesoderm at the cranial reflection of the amnion. Therefore the amnion at its embryonic attachment will at this stage enclose a circular band of embryonic connective tissue made up of the "stalk" caudally, the lateral tissue plates on each side, and

side round the anterior end of the blastopore."

On this hypothesis the prochordal plate would be the cranial lip of the blastopore; the axial structures would be formed posterior to it by a fusion of the lip of the blastopore, and as such the plate would maintain its preaxial position. The head process is regarded as dividing the lip into a primitive cranial lip - the prochordal plate - and the so-called dorsal lip at the neurenteric canal.

However attractive or rational this interpretation may seem, the weight of evidence in the human, at any rate, favours the endodermal basis of the prochordal plate.

It is generally admitted that there is some mesodermal production from the prochordal plate. In the human, with the greater preponderence and more dominant role of the primitive mesoderm, this is probably at a minimum.

De Lange has stressed the essentially protogenetic basis of the prochordal plate in accordance with his non-metameric concept of head development. He has shown that the mesoderm cranial to the head process - cephalic mesoderm - is absorbed entirely into the head fold. Such mesoderm as is produced from the prochordal plate exhibits according to Adelmann a phylogenetic urge towards the formation of cavities - well illustrated in sections 60-55 of McIntyre I. In the shark the plate is ultimately represented by the mandibular and premandibular cavities - its median origin betrayed by the cellular connecting cord which later atrophies.

In vertebrates with no head cavities the prochordal mesoderm becomes part of the head mesoderm, and plays no part in the formation of the ventral body wall although the latter is also in the first instance protogenetic. The secondary mesoderm of the anterior mesodermal field thus comes directly from the primitive streak and receives no reinforcements from head process or prochordal plate.

II. BUCCO-PHARYNGEAL MEMBRANE.

The apposition of ectoderm and endoderm anteriorly to form the bucco-pharyngeal membrane of vertebrates is phylogenetically a secondary formation. The more primitive prostomal aperture is divided into anal opening and neurenteric canal. This possibly accounts for the later appearance and more transient nature of the bucco-pharyngeal membrane compared to the cloacal membrane.

In the descriptions and figures of early human blastocysts with an embryonic rudiment there is no mention or semblance of a contact of the two primary germ layers at the head end. Embryo Wo (von Mollendorff), Miller ovum (Streeter), Embryo T.F., Bi.1., Bi.24 (Florian), Wa.17 (Grosser) show in the region in front of the prochordal plate - the proamnion of lower mammals - a layer of cells between the ectoderm and endoderm probably of primitive mesenchymal origin, but as Florian states of the Fetzer embryo, the two layers of the disc are very difficult to distinguish and the presence of mesoderm can only be assumed. In these mammals

where the primitive streak is the main factor in mesodermal production there is at an early stage no intervening tissue between ectoderm and endoderm in the proamnial area.

Embryo McIntyre 1 is the youngest human embryo in which a bucco-pharyngeal membrane has been described. In sections 52-51 there is ecto-endodermal connection by means of a thick cord of cells - in front of this the layers are separated in the mid line by mesoderm. A bucco-pharyngeal membrane has been described in an embryo of two somites (F. Orts Llorca), in one of four somites (Sternberg) and in the specimen 2-3 somites (Ingalls) there is a membrane .05 mm long lying immediately above the reflection of the somatopleure to form the anterior wall of the pericardium. Older embryos up to 30 somites all have a bucco-pharyngeal membrane with two exceptions, in one of which (Dandy, 7 somites) the damaged tissue at the cranial end would obscure the membrane. About 3 mm (25-30 somites) the membrane becomes ruptured and disappears. Actual perforation of the membrane heralding its ultimate fate is evident in a 20-somite specimen (Davis), and one of 18 somites (Watt).

The contact of ectoderm and endoderm would thus seem to be established at the time of the commencing head fold and the initial formation of the foregut as in McIntyre I; its rupture to follow the completion of pericardial inversion and formation of the stomodaeal depression by the outgrowth of the forebrain and the development of the facial prominences.

Ecto-endodermal contiguity can only be subsequent to the obliteration of intervening mesoderm assuming such to be present between the two layers of the disc from an early stage.

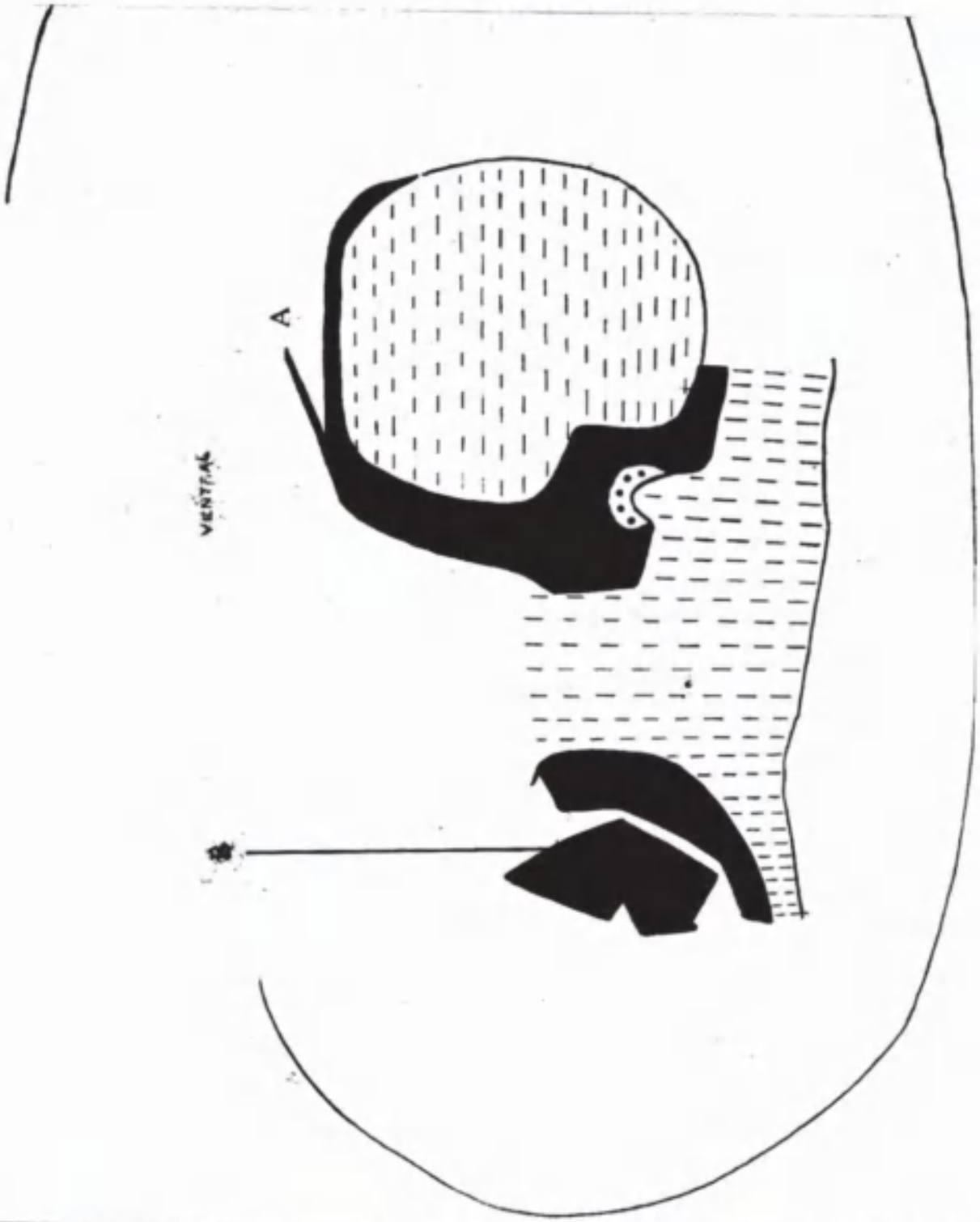
In the dog (Bonnet) the early small anlage of the bucco-pharyngeal membrane receives endoderm from the prochordal plate, while in the ferret (Hamilton) the membrane is formed from the front portion of the plate. In his two-somites human embryo F. Orts Llorca depicts the membrane as a connection between the ectoderm and the prochordal plate, but in view of the difficulty in defining the exact limits of the latter structure it seems inadvisable to dogmatise on its relationship to the bucco-pharyngeal membrane.

From its first appearance this membrane has very constant relations; at the one extremity the prochordal plate and anterior end of head process - chordal end; at the other the pericardium - cardiac end; and like the cloacal membrane it maintains its primary relations during later development and inversion. The head fold arises at the chordal end; similarly the tail fold forms at the chordal end of the cloacal membrane.

At an early stage of the human blastocyst there are areas of ecto-endodermal contact at both poles, each area flanked by wings of primitive streak mesoderm which unite with one another, and the primary mesenchyme, to form the anterior mesodermal field in front and the posterior

Text-Fig. 2. Embryo 2.6 mm. Reconstruction of a median sagittal section. x 100. Description in text. The yolk sac is not shown.

Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Gut.
Large Dots = Liver. Black = Mesoderm. A = Amnion.
B = Body Stalk.



mesodermal field behind; these are the sites of amnial attachment and respectively the anterior and posterior limits of the umbilical opening.

The anterior mesodermal field furnishes the tissue of the supraumbilical abdominal wall which therefore in its development shows an interesting analogy to the origin of the infraumbilical abdominal wall.

In embryo McIntyre I the pericardial plate is placed ventral to the head fold and cranial to the bucco-pharyngeal membrane. Dorsally it is covered by ectoderm, ventrally by endoderm, and its anterior and lateral boundaries are mesodermal - the anterior mesodermal field. In the cranial portion of the disc there are small mesodermal cavities. In the human embryo it seems more probable that the pericardial cavity is the result of confluence of a number of small mesodermal spaces rather than the fusion of two lateral cavities - a bilateral origin which would predestinate a ventral mesocardium, of the existence of which there is little evidence in the human embryo.

2.6 mm Embryo. History.

This specimen was obtained following laparotomy for a non-ruptured tubal pregnancy. It was fixed in formalin in spite of which, its gross form is normal, although histologically there are imperfections.

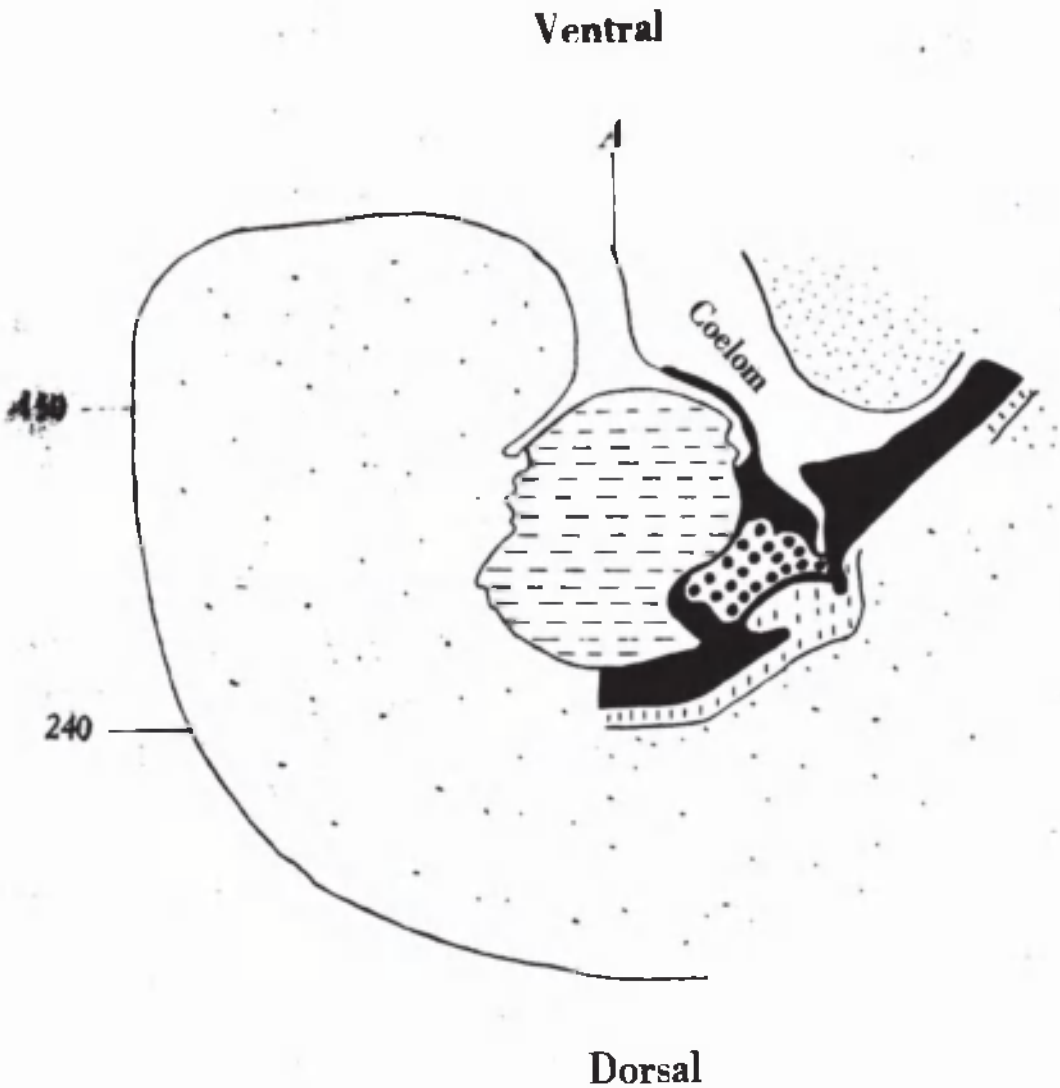
Text-Fig. 2 is a graphic reconstruction of a median sagittal section.

Compared with McIntyre I the area of yolk sac

connection is reduced to the relatively small gut portal with on each side the communication of intra and extra embryonic coeloms. This is to a great extent the result of the expansion of the embryonic disc and formation of head and tail folds coupled with the increased transverse convexity.

Inversion of the pericardium is in progress and it has rotated round a transverse axis to slightly over 90 degrees. The ectodermal covering now occupies the anterior and antero-ventral aspects while the endodermal boundary - the floor of the foregut - is dorso-caudal but separated from the dorsal wall of the pericardium in the median plane by a considerable thickness of embryonal mesenchyme. There has been proliferation of this tissue, i.e. the splanchnopleural mesoderm on the floor of the gut (Pl.III, Fig.9). The mesodermal field, at an early stage forming the anterior pericardial wall, is situated ventro-caudally so that in this embryo the pericardium is covered on the dorso-caudal and caudal half of the ventral aspect by mesoderm forming a continuous sheet in the midline. Laterally this mesoderm forms the ventral wall of the coelomic tubes - communication between pericardial and abdominal coeloms (Pl. III, Fig.10).

From the graphic reconstruction it is evident that the tissue of the mesodermal field lies between the amnial attachment and the wide communication with the yolk sac (Pl.III, Fig.11) and forms the cranial wall of the umbilical opening. The vitelline and umbilical veins run into this mesodermal mass.



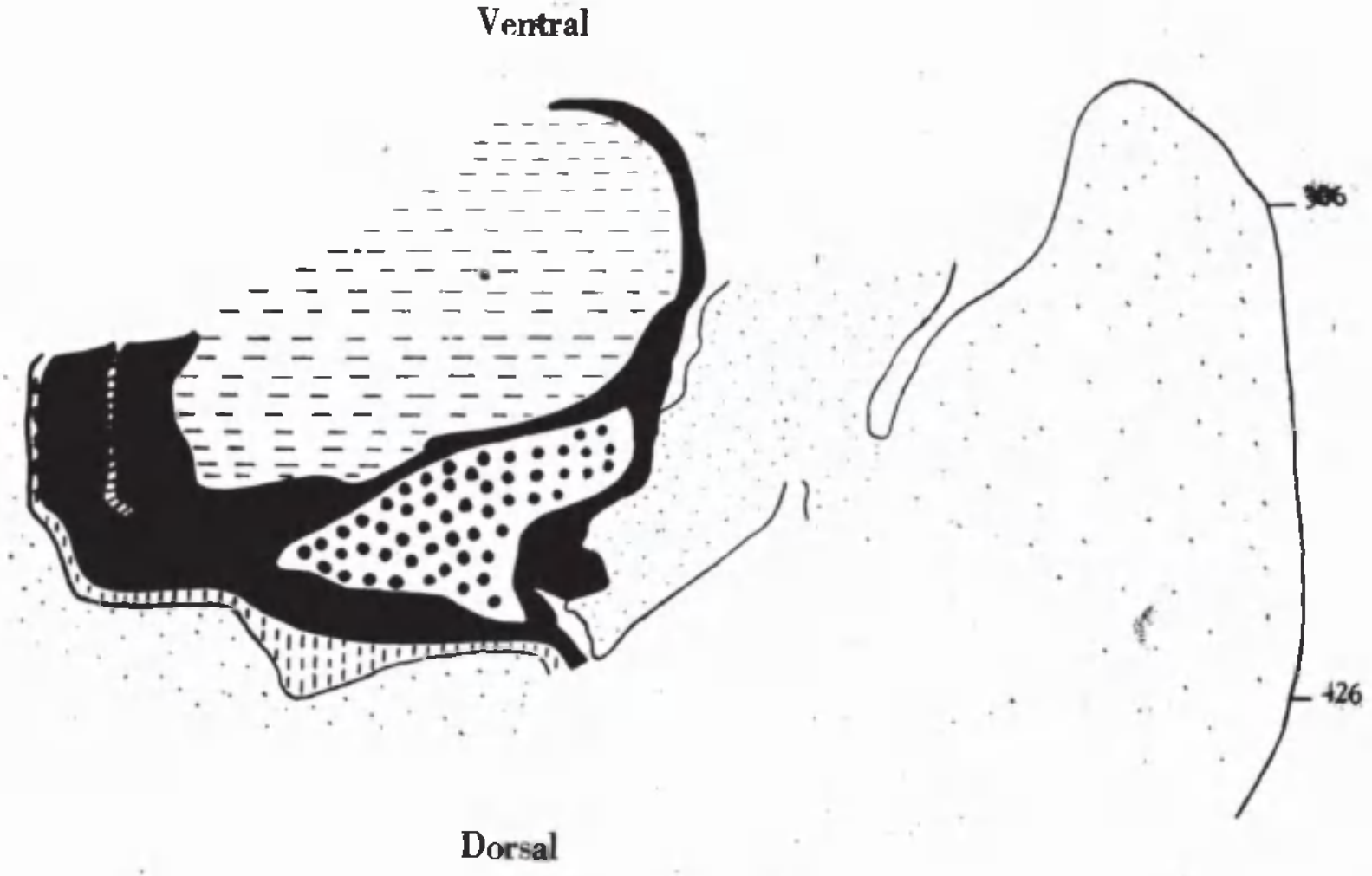
Text-Fig. 3. Embryo 4.5 mm. Reconstruction of a median sagittal section (See Pl. IV, Fig. 13). x 50. The numbers refer to the sections. Description in text. The yolk sac is not shown.

Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Gut.
Large dots = Liver. Black = Mesoderm. A = Amnion.

Into the proliferated mesoderm of the floor of the foregut projects the developing liver - not as a grooved plate or gutter but as a definite hollow outgrowth of the foregut in relation to which the more deeply staining liver cells can be distinguished (Pl. III, Fig.12). A very similar hepatic diverticulum is shown in the reconstruction of the Thompson embryo of 23 paired somites (Keibel and Mall). With the growth of the ectoderm the lateral mesodermal walls of the pericardium are taken into the body of the embryo.

4.5 mm Embryo.

Text-Fig. 3 is a graphic reconstruction of a median sagittal section. The area reconstructed is indicated in Pl. IV, Fig. 13. There has been a further rotation of the pericardium and the cranial attachment of the amnion, carried round from the ventral to the caudal aspect brings with it the region of the anterior mesodermal field. This now definitely forms the caudal boundary of the pericardium and in the mid line is continuous with the splanchnopleure on the floor of the foregut, the two together forming a mass of mesoderm out of which is differentiated a portion of the diaphragm and the supraumbilical abdominal wall. Following the completion of pericardial rotation the amnion becomes the cranial boundary of the umbilical coelom (Pl. IV, Fig.14) cf. Pl. III, Fig. 11. Cords of liver cells invade the dorsal portion of the mesodermal mass (Pl. IV, Fig. 15), and these are broken up by the vitelline veins (l. IV, Fig. 16). At



Text-Fig. 4A. Embryo 7 mm. Reconstruction of a median sagittal section (see Pl.V, Fig. 1B). x 50. The numbers refer to the sections. Description in text. Interrupted horizontal lines = Pericardial cavity and coelomic passage. Interrupted vertical lines = gut. Large dots = Liver. Black = Mesoderm. Oblique interrupted lines = trachea.

this stage the liver is confined to the dorsal and dorso-caudal mesoderm and has not yet penetrated the ventral half of the mesoderm on the caudal pericardial wall.

The umbilical veins traverse the mesodermal mass laterally on each side to reach the sinus venosus. They are ventral to the pleuro-pericardial openings and are not broken up by the liver cells (Pl. V, Fig. 17).

In the interest of convenience the familiar term septum transversum will be used here as denoting the general mass of mesoderm, caudal and dorso-caudal to the pericardium, i.e. including the anterior mesodermal field and the proliferated splanchnopleure of the floor of the foregut but not confined to the unsplit cranial pericardial rim - which according to Frazer forms the septum transversum after rotation of the heart.

As this "septum transversum" is but part of the general body mesoderm merging laterally with the somatopleure and in the mid line with the splanchnopleure it is to be regarded as im many ways unfortunate that it has been singled out by a distinctive name. This tends to isolate it as an anatomical entity and causes considerable confusion when any endeavour is made to trace its ultimate fate as such.

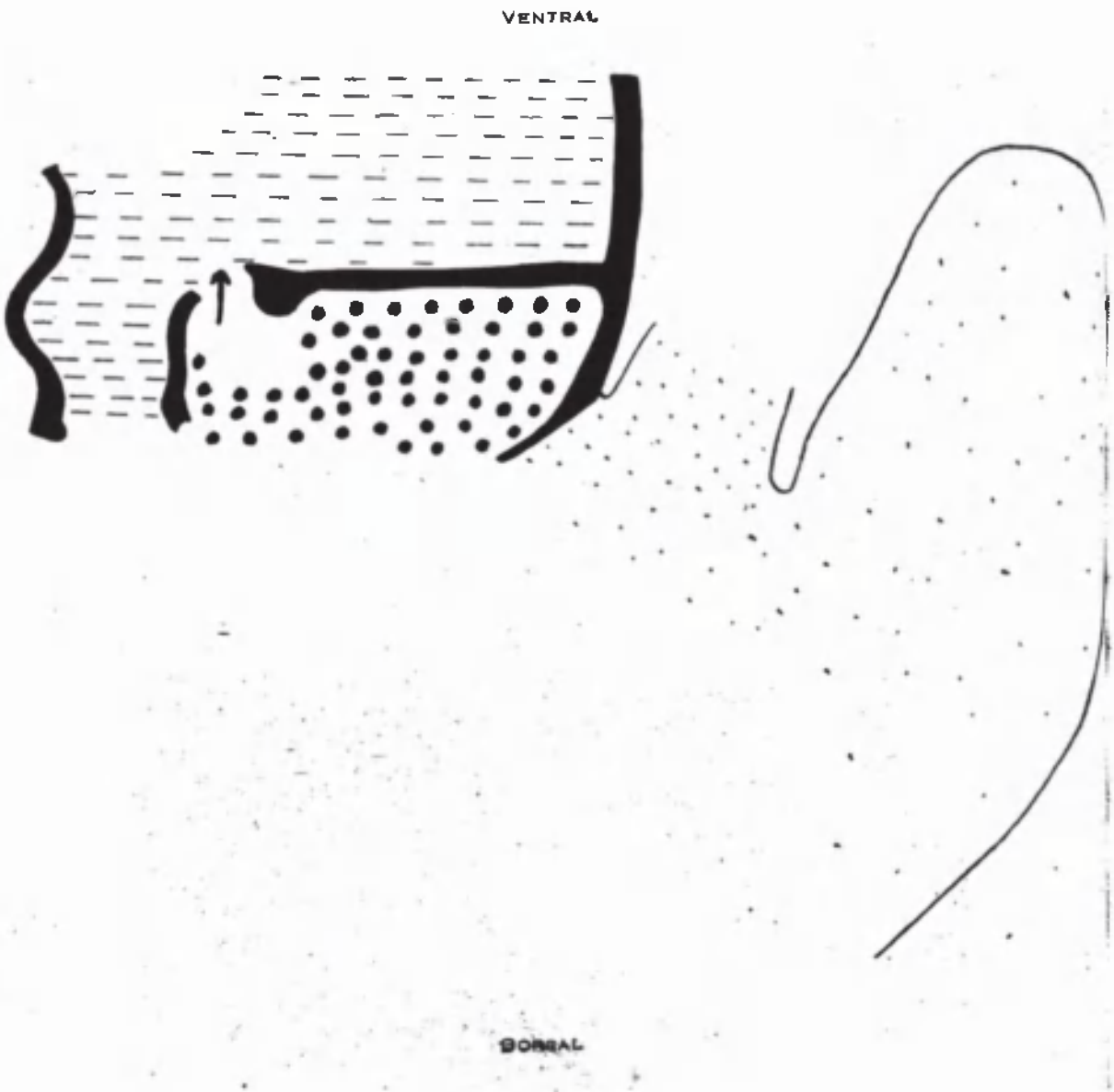
Embryo 7 mm.

Text-Fig. 4A is a graphic reconstruction of a median sagittal section. The area reconstructed is shown in Pl. V, Fig. 18. The liver cells which in the 4.5 mm embryo are confined to the more dorsal part of the septum transversum have now

extended ventrally and invaded the region of the septum on the caudal pericardial wall formed from the anterior mesodermal field. Pl. V, Fig. 19 is a section through the cranial attachment of what is now the umbilical cord and it is evident that this is lying some distance caudal to the pericardium, i.e. there is in this embryo a small interval between the umbilical cord and the pericardium. This specimen is the first of the series in which an umbilical "cord" as such can be said to exist, and with its completed formation there appears a supraumbilical abdominal wall whose mesodermal basis is the ventro-caudal part of the septum transversum, i.e. the anterior mesodermal field pushed caudally and ventrally by the developing liver.

Dorsal to the cranial attachment of the cord the mesoderm of the "septum" blends with the more myxomatous tissue of the cord, the two together forming a partition between the intra and extra umbilical coeloms (Text-Fig. 4A and Pl. V, Fig. 20). The latter figure also shows the left umbilical vein, its course interrupted by the liver cell columns.

At this stage the mesodermal mass of the septum transversum is divided by the invading liver into a cranial portion separating the liver from the pericardium, and a ventro-caudal portion - the mesodermal basis of the supra-umbilical wall. In the midline dorsally is the ventral mesentery of the foregut and on each side of the ventral



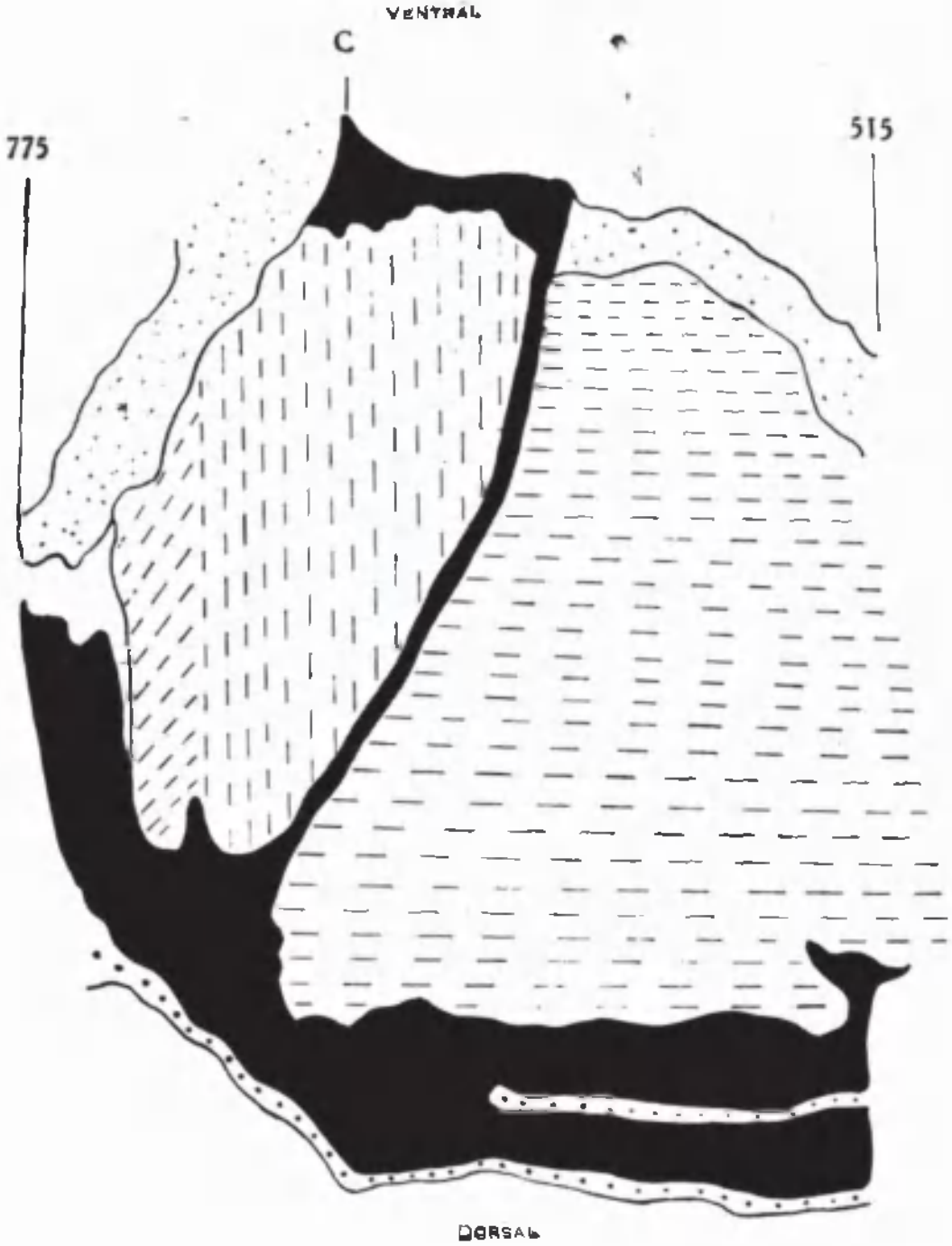
Text-Fig.4B. Embryo 7 mm. Reconstruction of a parasagittal section. x 50. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = pericardial cavity and coelomic passage. Interrupted vertical lines = Gut. Large dots = Liver. Black = Mesoderm. Oblique interrupted lines = Trachea. Arrow indicates the junction of the ductus venosus with the sinus venosus.

mesentery the lung buds occupy the pericardio-peritoneal channels or coelomic tubes whose ventral walls - the dorsal part of the septum transversum - form a pleuro-peritoneal membrane (Pl. VI, Fig. 21).

Pl. VI, Fig. 22 shows the pleuro-peritoneal openings - the section is beyond the dorsal limit of the "septum" and the lung buds are situate actually in the upper part of the abdominal cavity.

There are some additional points of interest in this embryo. With the growth of the liver there is an increase in the circumference of the abdominal cavity with an undermining of the lateral attachment of the "septum" to the somatopleure in the more caudal sections (Pl. VI, Fig. 23), and consequent on this the pleuro-peritoneal opening first appears in the sections as a rupture of the lateral wall of the coelomic tube. This lateral wall of the coelomic tube forms the suspensory ligament of the liver in the lower part of the channel, while caudally where the channel merges into the general body cavity it becomes continuous with the Wolffian mesentery (Pl. V, Fig. 20). It will be appreciated that any attempt to define the limits or extent of a "septum transversum" is fraught with much difficulty.

Text-Fig. 4B is a reconstruction of a para-sagittal section and it can be observed that the pleuro-peritoneal membrane is at this stage the ventral wall of the coelomic tubes. It is, of course, in continuity with the pericardio-



Text-Fig. 5A. Embryo 12.5 mm. Reconstruction of a median sagittal section. x 50. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity. Interrupted vertical lines = Liver. Large dots = Gut and trachea. Black = Mesoderm. C = Cranial attachment of umbilical cord.

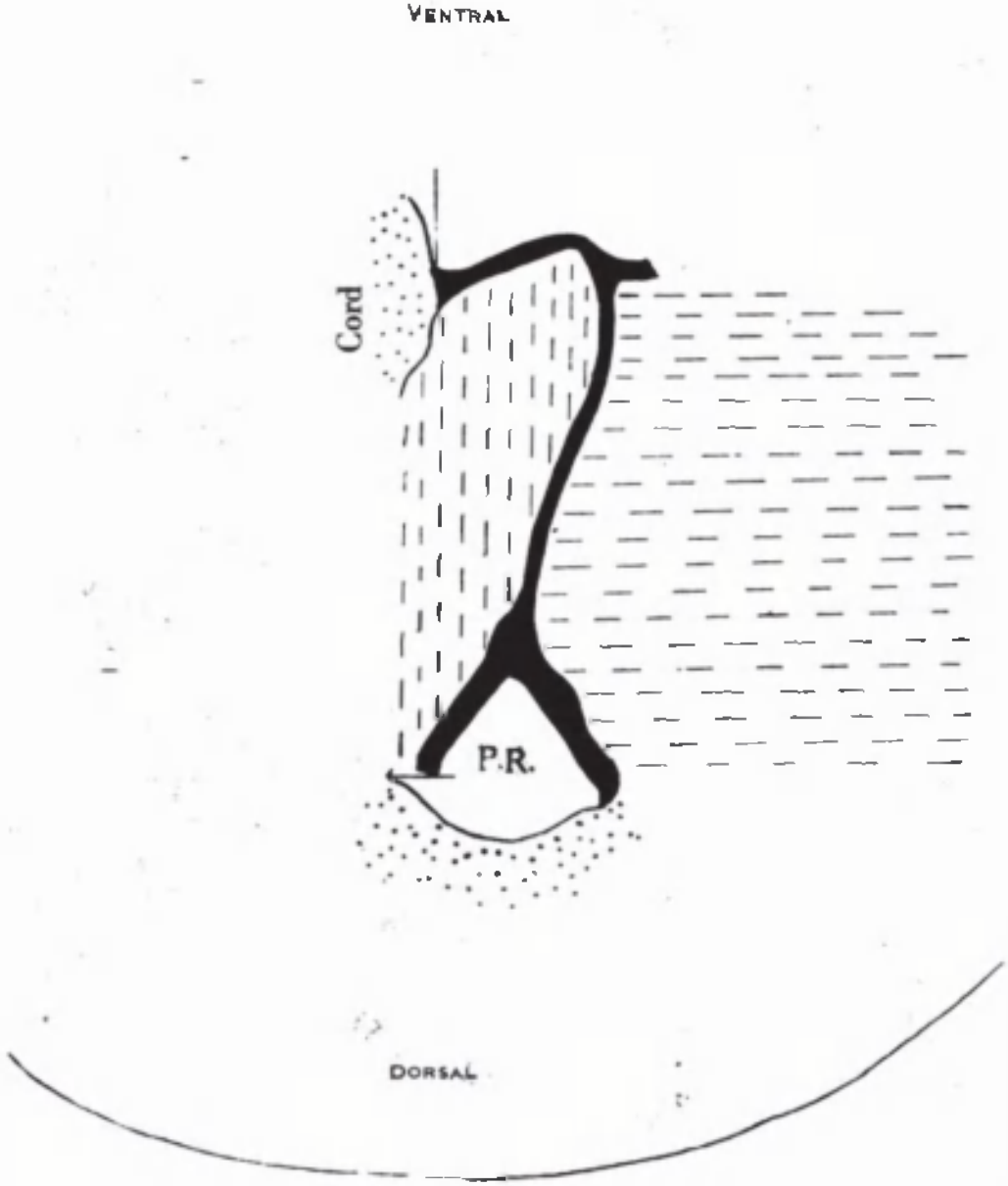
peritoneal membrane; the interruption in the figure is due to the passage of the ductus venosus into the sinus venosus.

Embryo 12.5 mm.

There is a considerable interval between the caudal margin of the pericardium and the cranial attachment of the umbilical cord. This is the supraumbilical wall and measures .6 mm in length. Its mesodermal basis consists for the most part of a narrow band of tissue of loose texture whose dorso-ventral depth increases caudally. In the mid line the mesoderm is denser compared to the more open mesenchymal network of the cord tissue (Pl. VI, Fig. 24).

Along with the increased supraumbilical interval is the marked caudal and ventral growth of the liver carrying with it the tissue of the septum transversum, the mesodermal basis of the supraumbilical wall. In this embryo the "septum transversum" is, in the mid line, represented by the mesoderm of the supraumbilical abdominal wall, the narrow strip of mesoderm (Text-Fig. 5A) between the liver and pericardium which blends in the mid line with the ventral mesentery of the foregut (Pl. VII, Fig. 27), and in the more cranial sections extends the entire width of the body cavity (Pl. VII, Fig. 25) - the pericardio-peritoneal membrane. Followed caudally the pericardio-peritoneal membrane forms only the medial part of the thoraco-abdominal partition (Pl. VII, Fig. 26).

Lateral to the mid line the lung buds are extending into the loose tissue of the parietes carving out the pleural



Text-Fig. 5B. Embryo 12.5 mm. Reconstruction of a parasagittal section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = pericardial cavity. Interrupted vertical lines = Liver. Large dots = Gut and trachea. Black = Mesoderm. C = Cranial attachment of umbilical cord. PR = Pleural cavity. Arrow indicates the pleuro-peritoneal opening.

spaces and fashioning from the somatopleure on each side another mesodermal septum, the cranial part of which becomes the pleuro-pericardial, and the caudal the pleuro-peritoneal membrane (Pl. VII, Fig. 26).

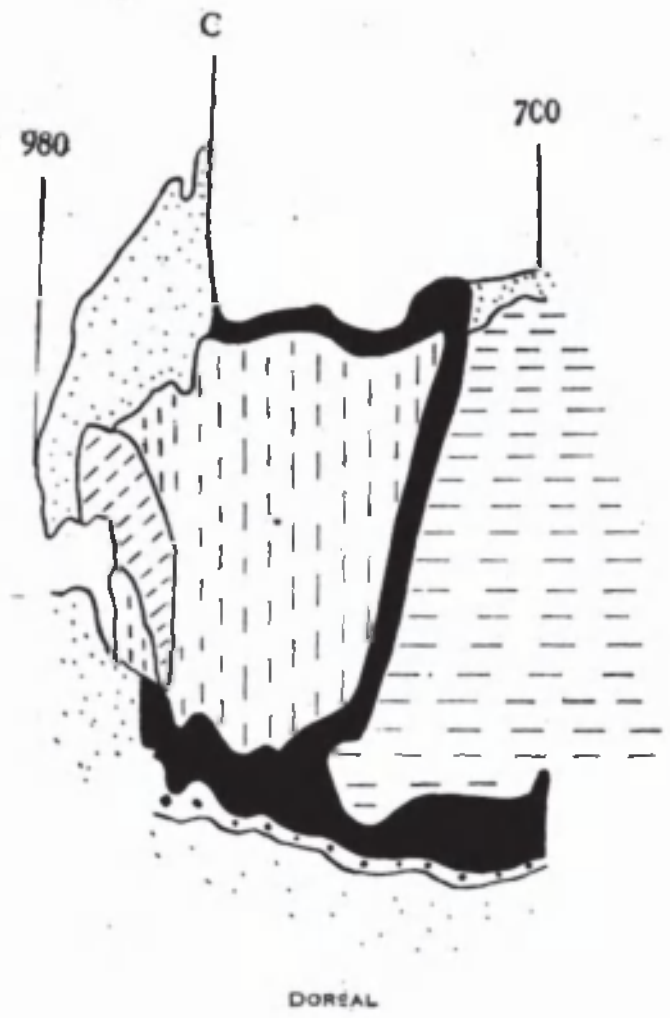
The pleuro-peritoneal membranes caudally form the lateral portions of the thoraco-abdominal partition, the remainder being completed by the pericardio-peritoneal membrane and the ventral mesentery.

Text-Fig. 5B shows the relations and continuity of the three mesodermal membranes, and Pl. VIII, Fig. 29 shows the left pleuro-peritoneal opening and the continuity of pleuro-peritoneal membrane and Wolffian mesentery.

The liver has commenced to separate from its mesodermal bed, the process of peritonealisation, but still maintains a broad connection ventrally where the vitello-umbilical vein enters the liver lateral to the mid line (Pl. VII, Fig. 27), and also dorsally where the ductus venosus enters the sinus (Pl. VII, Fig. 28).

14 mm Embryo.

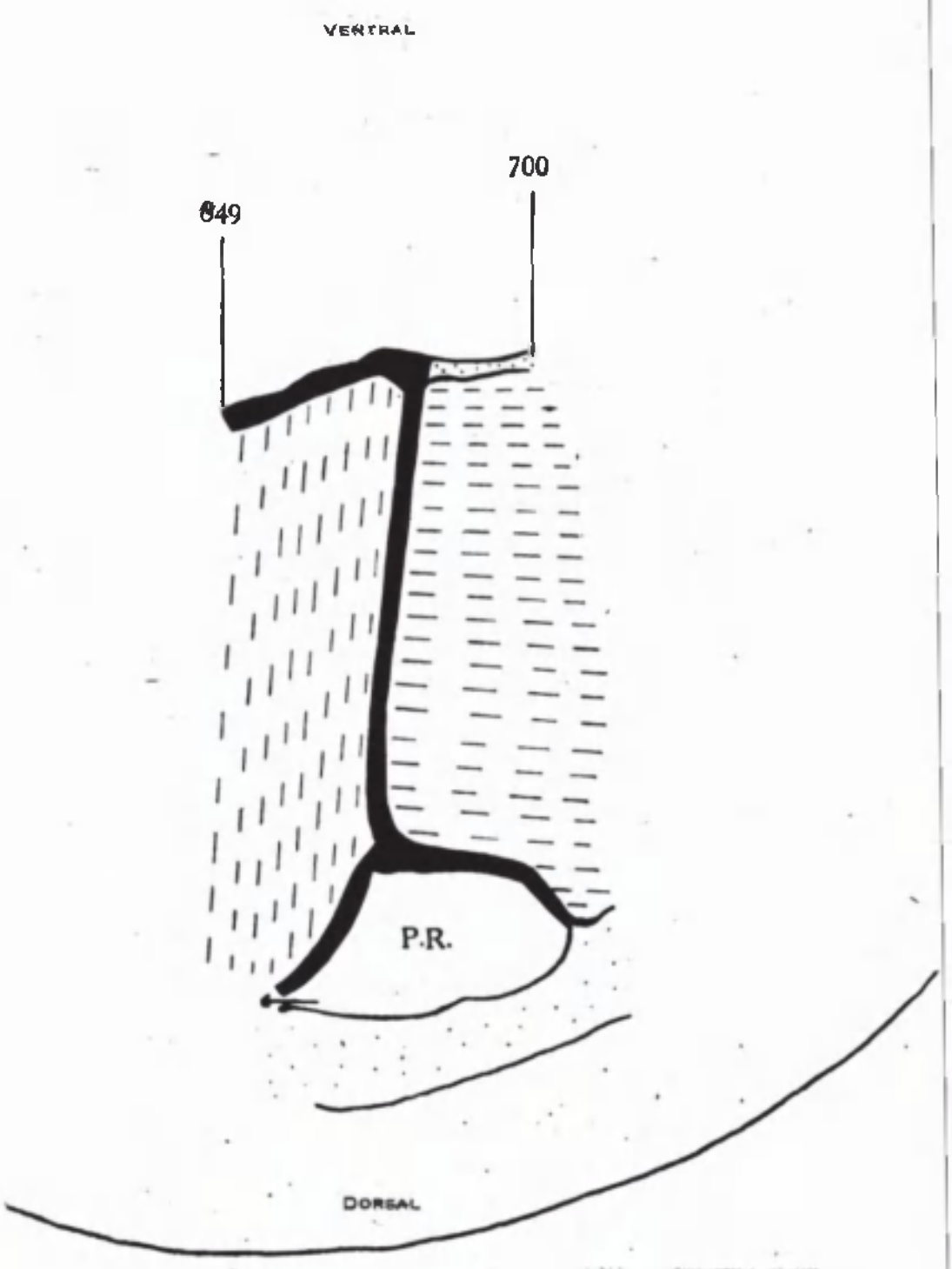
In this embryo the supraumbilical area has increased relatively and absolutely, extending over 128 sections with a total length of 1.28 mm (Text-Fig. 6A). Its mesodermal basis has a greater dorso-ventral depth than the corresponding area in the 12.5 mm embryo (Pl. VIII, Fig. 30), possibly due to an accession of tissue from the paraxial downgrowths although these are not yet well developed.



Text-Fig. 6A. Embryo 14 mm. Reconstruction of a median section. x 35. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Liver.
Interrupted oblique lines = Vein. Large dots = Gut.
Black = Mesoderm. C = Cranial attachment of the umbilical cord.

With the growth of the pleural cavities which have extended cranially and laterally there is a relative decrease in the area of liver related to pericardium. In the 12.5 mm, and more so in the 7 mm embryo, the lung buds are placed in the coelomic tubes caudo-dorsal to the heart and separated from the liver by a pleuro-peritoneal membrane which in the latter embryo is the mesoderm forming the ventral wall of the coelomic channels - the caudal portion of the pericardio-peritoneal membrane. Consequent on the lateral expansion of the pleural cavities there is a corresponding increase transversely of the pleuro-peritoneal membrane at the expense of the somatopleure. Growth of the lung buds towards the head end brings them into more direct relationship with the dorsal pericardium, and the "cleft part" of the somatopleure in this region forms a mesodermal partition between lungs and heart - the pleuro-pericardial membrane, which is caudally in continuity with the pleuro-peritoneal membrane (Text-Fig. 6B; Pl. VIII, Fig. 31). The latter in turn can be followed to the Wolffian mesentery - the lateral boundary of the pleuro-peritoneal opening (Pl. IX, Fig. 33). These three structures, viz., pleuro-pericardial, pleuro-peritoneal and Wolffian mesentery, form a continuous shelf of mesoderm projecting into the body cavity, the two former serving as a partition between the pleural and pericardial and pleural and abdominal coeloms respectively.

The pleuro-pericardial membrane (Pl. VIII, Fig. 31)



Text-Fig. 6B. Reconstruction of a parasagittal section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Liver.
Interrupted oblique lines = Vein. Large dots = Gut.
Black = Mesoderm. C = Cranial attachment of the umbilical cord. P.R. = Pleural cavity. The arrow indicates the pleuro-peritoneal opening.

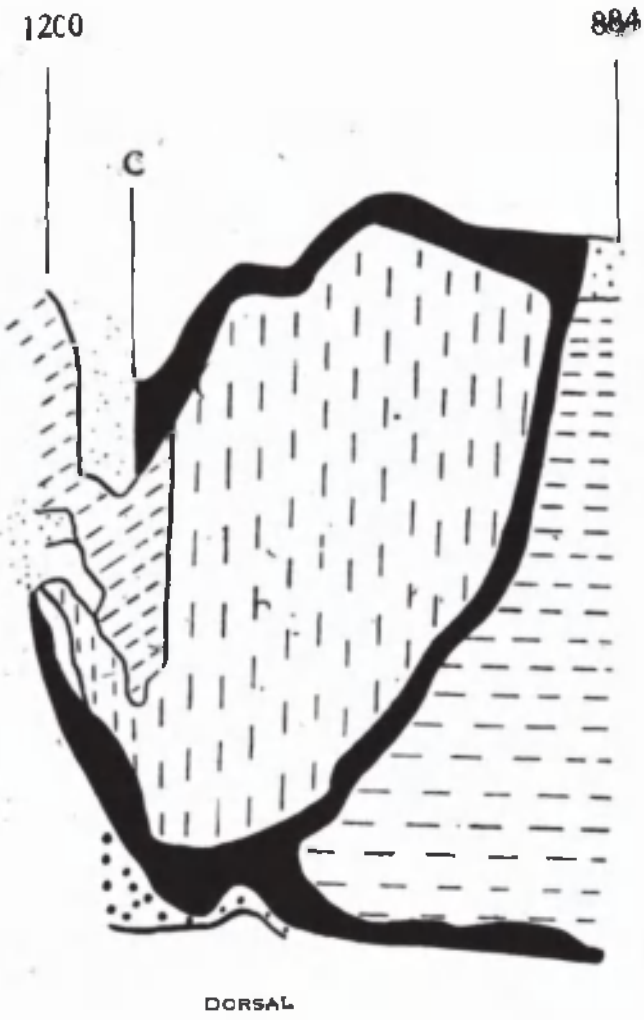
carries with it the duct of Cuvier which comes to lie medial to the pleural cavities (c.f. Pl. V, Fig. 19). Peritonealisation of the liver has increased but it is still attached in the mid line ventrally, and dorsally to the pericardium and foregut mesentery (Pl. VIII, Fig. 32).

16.1 mm Embryo.

The supraumbilical wall is 2 mm in length, protrudes ventrally and has an increased dorso-ventral thickness. In the lower half the paraxial downgrowths extend slightly over half way round the body wall but do not encroach on the mid line (Pl. IX, Fig. 34). The considerable interval between the liver and the parietes laterally and postero-laterally is artificial, due to shrinkage during fixation and there is a slight interval between the liver and the parietes in the midventral line - also an artefact. In the fresh specimen one would expect the two structures to be here in contact. The pleural cavities are still further developed, extending caudally posterior to the suprarenals (Pl. IX, Fig. 35). In this position the pleuro-peritoneal membrane has increased in thickness and appears to derive additional mesoderm from the gut mesentery in the mid line. The muscular element of the diaphragm is first apparent in its dorsal part (Keibel and Mall). The pleuro-peritoneal opening is still present (Pl. IX, Fig. 35).

23 mm Embryo.

The paraxial downgrowths have penetrated into the



Text-Fig. 7A. Embryo 16.1 mm. Reconstruction of a median sagittal section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity. Interrupted vertical lines = Liver. Interrupted oblique lines = Vein. Large dots = Gut. Black = Mesoderm. C = Cranial attachment of umbilical cord.

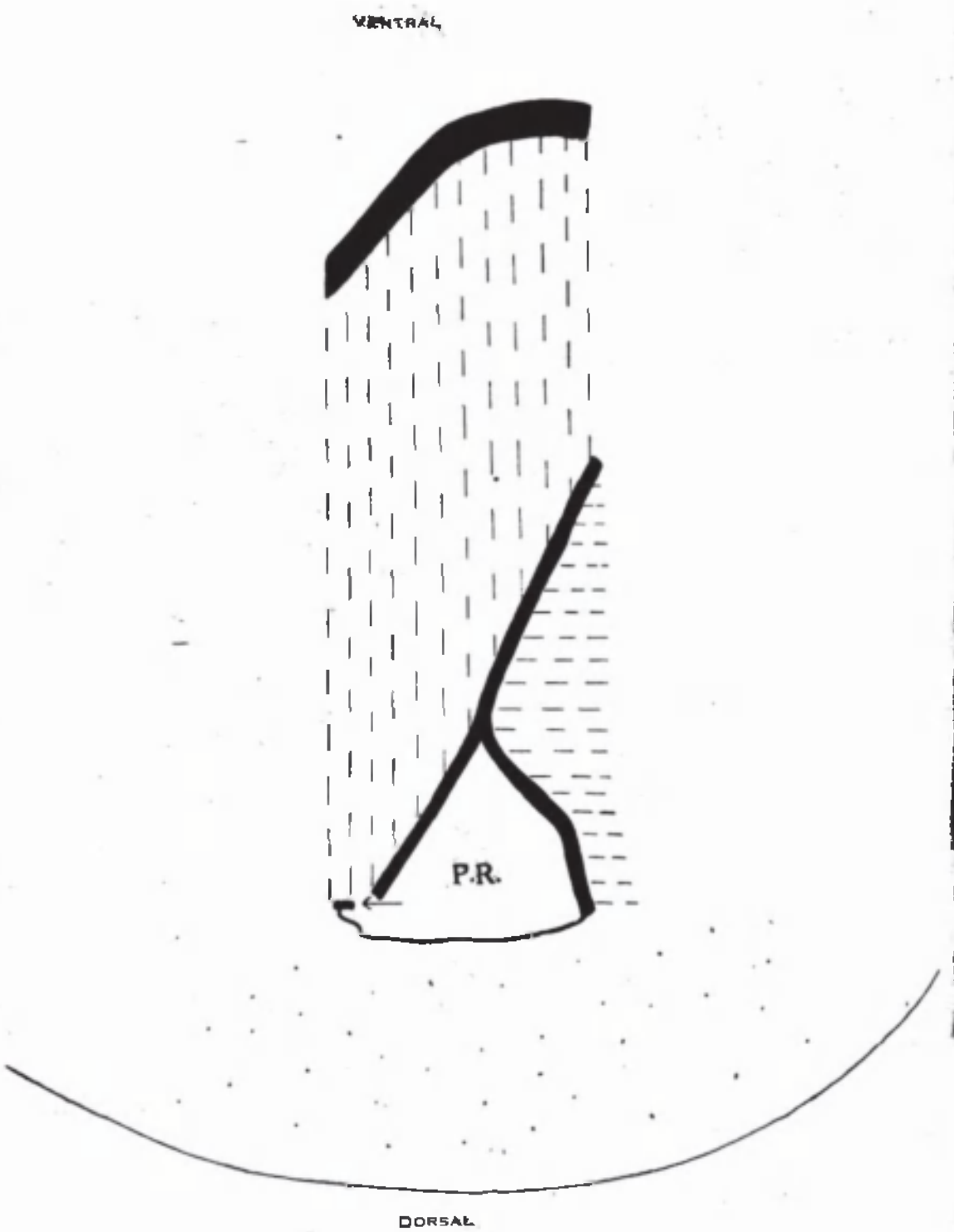
supraumbilical wall. The recti muscles can be seen on each side - situated antero-laterally. The rectus sheaths are prolonged medially and fuse with the tissue of the midventral wall (Pl. IX, Fig. 36). Again in this specimen the wide interval between the liver and parietes is the result of shrinkage. The further development of the pleural cavities with the concomitant increase of pleuro-peritoneal membrane is responsible for a relative decrease in the area of diaphragm formed from the pericardio-peritoneal membrane. Laterally the pleuro-peritoneal membranes on both sides are receiving muscular reinforcements from the paraxial downgrowths (Pl. X, Fig. 37), while medially that portion of the membrane between the pleural cavities and the suprarenals is invaded by muscular tissue arising in the region of the dorsal mesentery and responsible in part for the closure of the pleuro-peritoneal opening (Pl. X, Fig. 38).

30 mm Embryo.

This embryo is cut in an obliquely sagittal plane. Pl. X, Fig. 39 shows the extent of the supraumbilical abdominal wall, and the continuity in a vertical plane of the pericardio-pleural and pleuro-peritoneal membranes and also the extent of the diaphragm which is formed from the pericardio-peritoneal membrane.

40 mm Embryo.

The paraxial downgrowths have penetrated well into the ventral wall. In the more cranial part the ribs reach



Text-Fig. 7B. Embryo 16.1 mm. Reconstruction of a parasagittal section. x 25. The numbers refer to the sections. Description in text.

Interrupted horizontal lines = Pericardial cavity. Interrupted vertical lines = Liver. Interrupted oblique lines = Vein. Large dots = Gut. Black = Mesoderm. C = Cranial attachment of umbilical cord. P.R.= Pleural cavity. The arrow indicates the pleuro-peritoneal opening.

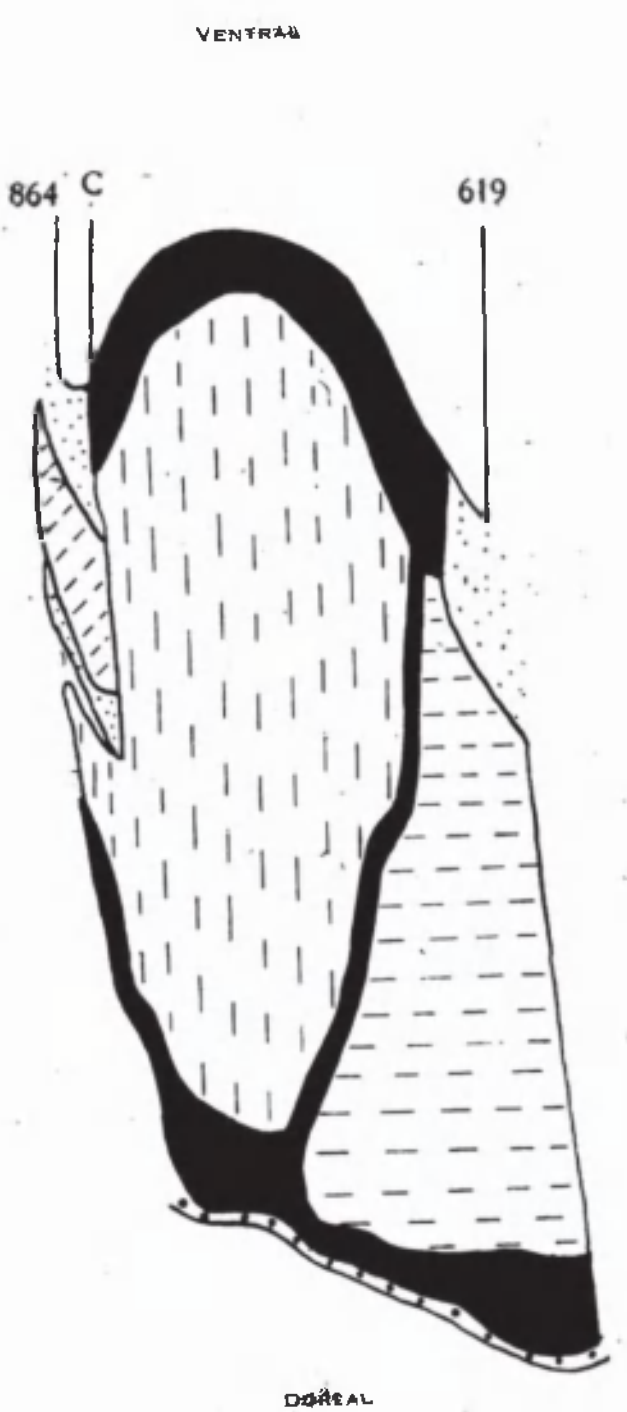
the ventro-lateral aspect. The recti muscles are separated from one another in the midventral line by an interval traversed by the rectus sheaths which by their fusion form a dense central mass of tissue - the linea alba (Pl. XI, Fig. 40). The pericardio-peritoneal portion of the diaphragm now forms a relatively small part of the whole in the midline cranially, while the larger lateral parts - pleuro-peritoneal membranes - have now acquired muscular tissue attached to the deep aspect of the rib processes (Pl. XI, Fig. 41).

In the mid line caudally muscular fibres invade that part of the diaphragm formed from the dorsal mesentery - the contribution from the subvertebral musculature.

The liver has completed its separation from the parietes except in the mid line ventrally and dorsally - the reflection of the future falciform and coronary ligaments.

CONCLUSIONS.

The older embryologists postulated the formation of skin plates in connection with the somites - these passing ventrally with the paraxial muscular downgrowths to complete the ectodermal covering of the ventral body wall. The more modern conception of the expansion of the embryonic body round a relatively fixed rim or circumference - the future umbilical orifice - not only affords an explanation of the formation of head and tail folds, pericardial inversion, and the prevailing dorsal convexity, but is also supported by the constant position of the umbilical vein along the



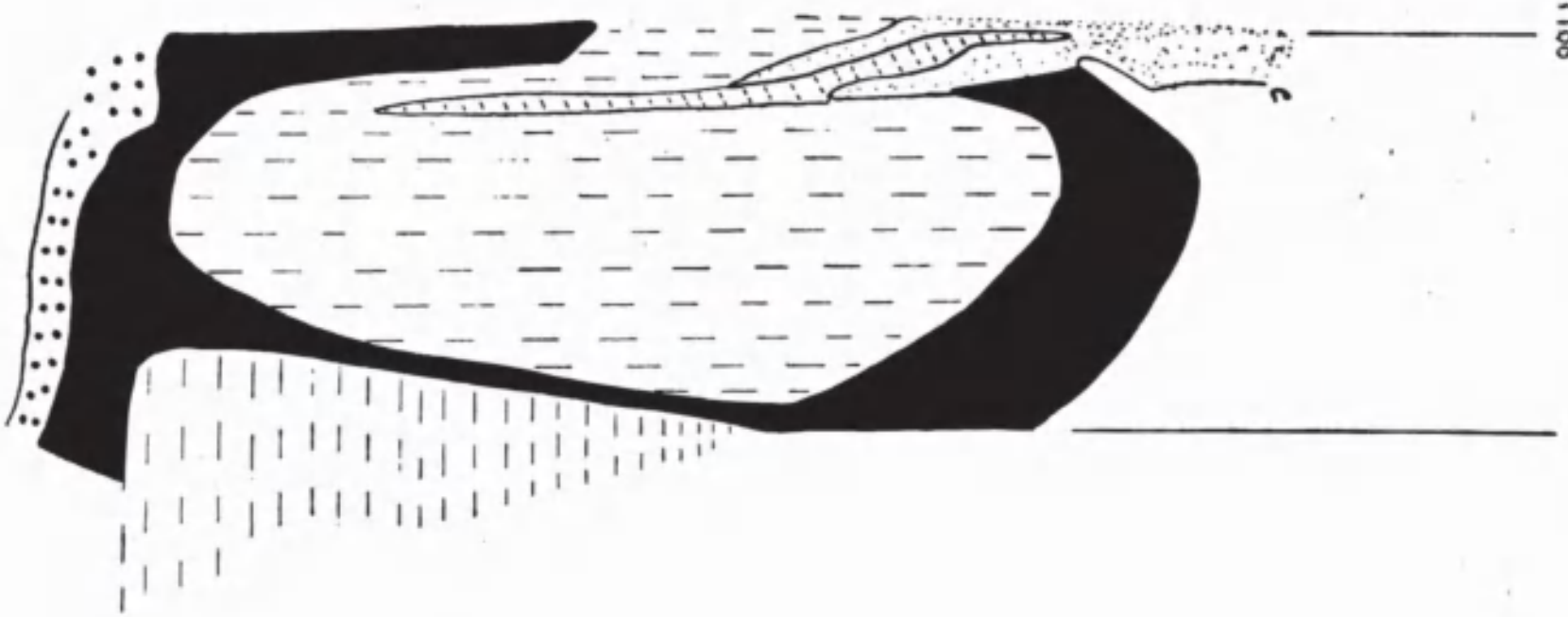
Text-Fig. 8. Embryo 23 mm. A reconstruction of a median sagittal section. x 25. The numbers refer to the sections. Description in text.
Interrupted horizontal lines = Pericardial cavity.
Interrupted vertical lines = Liver.
Interrupted oblique lines = Vein. Large dots = Gut.
Black = Mesoderm. C = Cranial attachment of the umbilical cord.

"rim" and thus in the later stages encroaching on the mid line ventrally.

The mesodermal basis of the lateral portions of the ventral wall is of course, in the first instance, the somatopleure, reinforced later by the muscular sheets of paraxial origin. Above and below the umbilicus are areas of fusion of primary and secondary mesoderm - the anterior and posterior mesodermal fields. The secondary element includes both somatopleure and splanchnopleure, and as has been shown comes directly from the primitive streak.

The mesoderm of the supraumbilical abdominal wall is the ventral portion of the general mass forming a partition between the thoracic and abdominal cavities, and its splanchnopleure becomes the falciform ligament and serous coat of the liver. Into the dorsal part of the mesodermal partition projects the early hepatic bud, while later the liver not only encroaches on the ventral part but in its further growth appears actually to push before it the abdominal parietes.

The appearance of a supraumbilical interval synchronises with the ventral and caudal growth of the liver tissue into the mesoderm of the body wall and one is tempted to assume the interdependence of cause and effect. Certainly the growth of this part of the abdominal wall follows on the enlargement of the liver but only provided other conditions are normal - the cause is not always followed



Text-Fig. 9. Embryo 40 mm. Reconstruction of a median sagittal section. x 25. The numbers refer to the sections. Description in text. Interrupted horizontal lines = Pericardial cavity. Interrupted vertical lines = Liver. Interrupted oblique lines = Vein. Large dots = Gut. Black = Mesoderm. C = Cranial attachment of umbilical cord.

by the effect.

In congenital abnormalities involving deficiency, partial or complete, of the supraumbilical wall - for example, abdominal fissure or eventration - there may be a liver normal in size and shape.

The development of the abdominal coverings would therefore seem to some extent to be independent of the viscera and influenced by factors mechanical or otherwise which do not necessarily affect visceral growth.

EVENTRATION. *

Complete absence of the upper abdominal wall - eventration - is a comparatively rare congenital defect; Schwalbe quotes 1 in 5000 as the relative frequency.

In the Hunterian Collection (Glasgow) there are five specimens of this condition, three of which have in addition a spina bifida. In all of them there is marked retroflexion of the body wall with, in one case, a scoliosis.

Specimen No. 50.115 (Pl. XI, Figs. 42 and 43). Female child about nine months with non-closure of the abdomen. The viscera are prolapsed into a large membranous bag which has been cut away. The lower half of the body and lower limbs are flexed backwards and to the left. There is a small spina bifida in the sacral region.

Specimen No. 50.116. Twin fellow of the preceding with the

* Small abdominal herniae as distinct from umbilical herniae will be more appropriately discussed in connection with the development of the umbilical portion of the abdominal wall.

same deficiency of parietes; a large spina bifida and retroflexion.

Specimen No. 50.117. There is deficiency of abdominal parietes and the viscera are enclosed in a membranous sac; an extreme degree of retroflexion, a large spina bifida and double talipes equina.

Specimen No. 50.114. The spleen and almost the whole intestines are outside the abdominal cavity. The head is bent back between the shoulders. There is anencephaly and amyelia.

Specimen No. 50.119. Extreme degree of non-formation of the abdominal wall with retroflexion.

Schwalbe in his considerable series remarks on the almost invariable presence of curvature of the vertebral column. This fact, coupled with the presence of retroflexion in each of the above examples makes it difficult to dismiss it as a mere coincidence. Either the condition is a concomitant defect - the two having a common casual value or alternatively the one follows as a consequence of the other. Bryce describing a foetus, the subject of ectopia viscerum, spina bifida, dorsal retroflexion and other abnormalities, considers the dorsal curvature is primary and expresses the maintenance of a very early attitude.

Some retroflexion may be normal at an early stage. Ingalls suggests that such curvature is the inevitable result of the lifting up of the head by the developing pericardium and accentuated by the precocious development of the forebrain.

But its persistence in a marked degree is definitely abnormal. The His embryos Lg and Sc.H. both show sharp dorsal concavities which Ingalls inclines to regard as abnormal. It is conceivable, taking the retroflexion as the primary condition, that such curvature would seriously interfere with the direction of growth forces.

The embryonic rim or umbilical orifice instead of remaining relatively fixed would tend to become "pulled out" in both the transverse and cranio-caudal axis, interfering with the normal growth of the ventral somatopleure which in turn would of course retard the forward extension of the muscle ingrowths.

The unusual "set" of the sclerotome resulting from a persistent retroflexion would favour a tendency to non-closure of the neural arch over the affected segment.

Amnial adhesions at an early stage might be the cause of the abnormal retroflexion and this in turn occasion the deficiency of the abdominal parietes, or again, amnial fusion could be the common aetiological factor responsible for both defects.

Schwalbe's contribution to the genesis of the condition assumes the presence of "skin plates" growing forwards to unite in the mid ventral line and complete the closure of the abdominal cavity.

SEPTUM TRANSVERSUM.

Most accounts of the development of the diaphragm

centre round the "septum transversum" and much of the difficulty in the ultimate analysis of the adult structure is due to conflicting opinions as to what constitutes the "septum".

Politzer and Sternberg regard the septum transversum as the proliferation of the endodermal mesoderm of the floor of the gut. Frazer's conception, already mentioned, includes the region of the anterior mesodermal field.

Keith shows the septum transversum cleft into a pericardial and diaphragmatic lamina by the lung buds, an interpretation which would include the dorsal pericardial wall as part of the septum: this could also be regarded as somatopleure.

In the 7 mm embryo (Pl. VI, Fig. 21) the pleural cavities are separated from the liver by mesoderm - a pleuro-peritoneal membrane which is the ventral wall of the coelomic passages. In the later stage (12.5 mm) the pleuro-peritoneal membrane is increased from the lateral somatopleure. Should this also be regarded as part of the septum transversum?

After the inversion of the heart region there is a mass of mesoderm between the pericardial and abdominal coeloms which in the mid line is continuous with the foregut mesentery and so with the dorsal pericardial wall. Posteriorly on each side the partition is incomplete and the coelomic passages are bounded laterally by the somatopleure which is also continuous with the central mesodermal mass. As the pleural

cavities develop there is a corresponding increase in the mesodermal partition effected at the expense of the somatopleure. This borrowing of somatopleure mesoderm is a concomitant of thoracic expansion and the mesodermal partition is enlarging almost day by day. It is clearly impossible at any given stage to delimit an original "septum transversum".

The invasion by the pleural cavities is also occurring dorsally where the somatopleure forms the posterior pericardial wall and the "stripped mesoderm" in this position forms a septum between heart and lungs - pleuro-pericardial membrane.

From the study of this series of embryos one is of the opinion that the name septum transversum, if it must be utilised, should have a much wider and more generous interpretation than it enjoys at present. The only justifiable embryological division of the diaphragm is on the basis of its muscular morphology, and any attempt to map out in the adult structure an area derived from an early septum transversum only invites controversy and makes for subsequent confusion.

S U M M A R Y.

1. The development of the supraumbilical abdominal wall has been studied in a series of embryos ranging from 1.4 mm to 12.5 mm.
2. The ventral portion of the mesodermal partition between the thoraco-abdominal cavities furnishes the basis of the

supraumbilical wall.

3. This ventral part of the thoraco-abdominal partition is itself derived from the anterior mesodermal field subsequent to pericardial inversion.
4. The anterior mesodermal field is composed of primary and secondary mesoderm - the secondary element is formed from the fusion of processes of primitive streak mesoderm passing round the bucco-pharyngeal membrane.
5. There is a developmental analogy between the anterior and posterior poles of the blastoderm - the future supra and infraumbilical regions respectively.
6. Eventration with deficiency of the supraumbilical wall is commonly associated with retroflexion, and it is suggested that there is some aetiological relationship.
7. The term "septum transversum" is criticised as being misleading and the cause of much confusion in the embryological interpretation of the diaphragm.

---o---ooo---o---

I have to record my indebtedness to my chief, Professor Blair, for his supervision of the work.

R E F E R E N C E S.

ADELMANN, H.R. (1922). The Significance of the Prochordal Plate. Amer. Jour. Anat., vol. 31.

BONNET, R. (1901). Beitrage zur Embryologie des Hunds. Anat. Hefte. Bd. 16.

BRYCE, T.H. (1895). Description of a Foetus the subject of Retroflexion of the Trunk - Ectopia Viscerum and Spina Bifida; with a discussion as to the cause of these Associated Abnormalities. Jour. Anat. and Physiol., vol. XXIX.

Do. Do. (1924). Observations on the Early Development of the Human Embryo. Trams. Roy. Soc. Edin., vol. LIII, pt. iii, No.26.

DANDY, W.E. (1910). A Human Embryo with Seven pairs of Somites. Amer. Jour. Anat., vol. 10.

DAVIS, C.L. (1924). The Description of a Human Embryo having Twenty Paired Somites. Carneg. Instn. Publ., No. 332; Contr. Embryol. No. 72.

FETZER, M. and FLORIAN, J. (1930). Der Embryo 'Fetzer' mit beginnender Axialmesodermbildung und bereits angelegter Kloakenmembran. Z. mikr.-anat. Forsch., Bd. XXI.

FLORIAN, J. (1928). Ein junges menschliches Ei in situ (Embryo T.F. mit Primitivstreifen, ohne Kopffortsatz). Z. mikr.-anat. Forsch. Bd. XIII.

Do. Do. (1934). Ein Schema der Entwicklung der Axialgebilde des menschlichen Embryos bis in das Stadium von 10 Urwirbelpaaren. Biol. gen. Bd. X, Lief 2.

FRAZER, E. (1931). Manual of Embryology. London, Bailliere, Tindall & Cox.

GROSSER, O. (1927). Fruhentwicklung, Eihautbildung und Placentation. Munich.

Do. Do. (1931). Primitivstreifen und Kopffortsatz beim Menschen. Anat. Anz., Bd. LXXI.

HAMILTON, W.J. (1937). The Early Stages in the Development of the Ferret: The Formation of the Mesoblast and Notochord. Trans. Roy. Soc. Edin., vol. LIX, Pt.1.

HILL, J.P. and FLORIAN, J. (1931). A Young Human Embryo (Embryo Dobbin) with Head Process and Prochordal Plate. Phil. Trans., B., vol. CCXIX.

INGALLS, N.W. (1920). A Human Embryo at the beginning of Segmentation. Carneg. Instn. Publ., No. 274; Contr. Embryol., No. 52.

KEITH, A. (1921). Manual of Embryology and Morphology. 4th ed.

KEIBEL, F. and MALL, F.P. (1912). Manual of Human Embryology. vol. II.

LANGE, D. de. (1936). The Head Problem in Chordates. Jour. Anat., vol. LXX.

LLORCA, F.Orts. (1934). Beschreibung eines menschlichen Embryo mit 4 Urwirbelpaaren. Z. ges. Anat. 1. Z.Anat.EntwGesch. Bd. CIII, Heft 6.

MOLLENDORFF, vom. (1925). Das menschliche Ei. Wo(lfring) Implantation. Verschluss der Implantationsoffnung und Keimesentwicklung beim Menschen vor Bildung des Primitivstreifens. Z. ges. Anat. 1. Z. Anat. EntwGesch. Bd. 76.

PAYNE, F. (1925). General description of a seven somite human embryo. Carneg. Instn. Publ., No. 361; Contr. Embryol. No. 81.

POLITZER, G. and STERNBERG, H. (1930). Uber die Entwicklung der ventralen Korperwand und des Nabelstranges beim Menschen. Z. f. Anat. u. EntwGesch. Bd. XCII, Heft 4.

RABL, C. (1899). Theorie des Mesoderm. Morph. Jahrb., Bd. XV.

ROSSENBECK, H. (1923). Ein junges menschliches Ei, Ovum Humanum Peh-Hochstetter. Z. ges. Anat. 1. Z. Anat. EntwGesch., Bd. LXVIII.

SCHWALBE, E. (1909). Die Morphologie der Missbildungen des Menschen und der Tiere.

STERNBERG, H. (1927). Beschreibung eines menschlichen Embryos mit vier Ursegmentpaaren. Z. ges. Anat. 1. Z. Anat. EntwGesch. Bd. LXXXII.

STIEVE, H. (1926). Ein 13½-Tage altes, in der Gebarmutter erhaltenes und durch Eingriff gewonnenes menschliches Ei. Z. mikr.-anat. Forsch. Bd. VII.

STREETER, G.L. (1927). Development of the mesoblast and notochord in pig embryos. Carneg. Instn. Publ., No. 380; Contr. Embryol. No. 19.

Do. Do. (1927). The Miller ovum. Carneg. Instn. Publ., No. 363; Contr. Embryol. No. 92.

WALDEYER, H. (1929). Ein junges menschlichen Ei in situ (scho(nholz). Z. ges. Anat. 1. Z. Anat. EntwGesch. Bd. XC.

WATT, J.C. (1915). Description of two young twin human embryos with 17-19 paired somites. Carneg. Instn. Publ., No. 222; Contr. Embryol. No. 2.

PART III.

THE FORMATION OF THE UMBILICAL CORD AND THE UMBILICAL REGION OF THE ANTERIOR ABDOMINAL WALL.

I N T R O D U C T I O N.

"It is a characteristic of many vertebrates that, associated with the provision of special arrangements for nourishing the young individual, the time of commencing an independent existence on its own account is greatly delayed. In such cases where a considerable proportion of the whole development takes place within the shelter of the egg shell or parental body we have to do with what is known as embryonic in contradistinction to larval development." (Graham Kerr).

The young larvae of the holoblastic Anamnia such as the frog quickly learn to fend for themselves and therefore have a very small store of nourishment easily housed within the ventral wall of the gut.

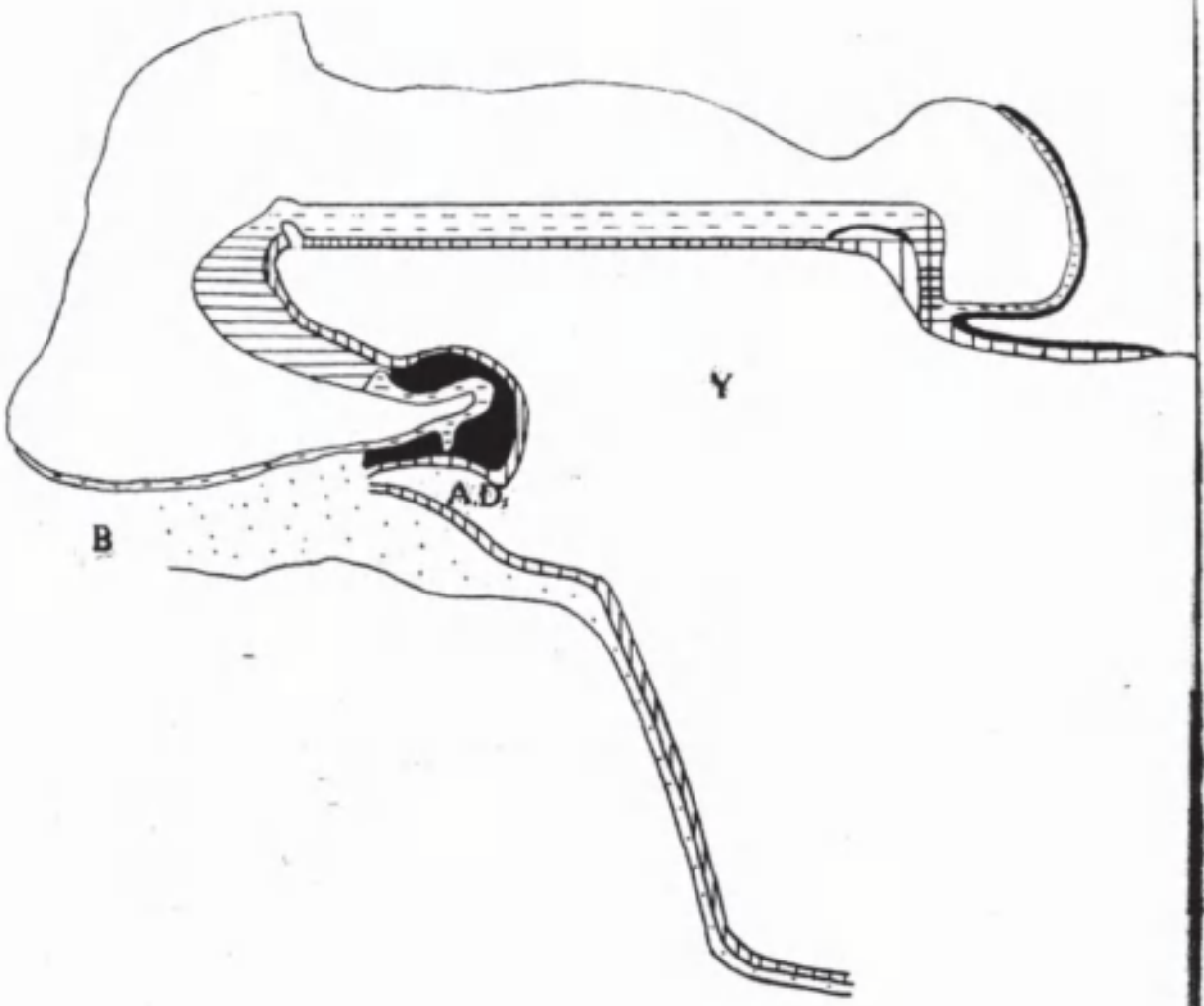
In the meroblastic Elasmobranchs there is a considerable store of nourishment to tide the developing young over the much longer period preceding the acquisition of independence. The larger yolk mass is for a time extraembryonic. It is encircled by the endodermal cells, forming a primitive gut or enteron, and later enclosed by the extra-embryonic blastoderm. The yolk sac then becomes

connected to the embryo by a constricted narrow part - the yolk duct; this in turn has its covering of mesoderm and ectoderm, and constitutes the somatic stalk. In the final stages the yolk sac is drawn into the body and the somatic stalk is incorporated in the body wall.

The umbilical cord of the Amniota constitutes the pathway for the transit of substances to and from the embryo. In birds and reptiles the extra-embryonic blastoderm (false amnion and endoderm) grows round and encloses the large yolk mass carrying with it an extension of the coelom between the somatopleure and splanchnopleure. In Amniota the allantois issues from the hind gut on the caudal and ventral aspect of the embryo. The true amnion, attached round the embryonic "rim", forms the boundaries of the somatic stalk which thus includes the yolk stalk, a portion of the exocoelom and more caudally the allantoic stalk.

The somatic stalk or umbilical cord of placental mammals is essentially of a similar nature to that described above, although the now increased functional importance of the allantoic element overshadows that of the yolk stalk.

This work consists of a study of the umbilical cord in the series of human embryos already utilised in parts I and II, with the addition of an embryo of 8.5 mm, one of 42 mm, and one of 60 mm. Sections were also made of rabbit embryos in which the gut had returned into the



Text-Fig. 10. Embryo McIntyre I. Reconstruction of a median sagittal section. x 100. Description in text.
Horizontal lines = Primitive streak.
Interrupted horizontal lines = Ectoderm.
Vertical lines = Endoderm, head process and prochordal area.
Black = Mesoderm.
Y = Yolk sac.
A.D.= Allantoic diverticulum.
B = Body stalk.

abdominal cavity, but as these show no features of peculiar interest they are not described in detail.

The method of graphic reconstruction is again adopted where possible, as it affords a ready appreciation of the relations in any given embryo, and obviates much tedious description of individual sections.

From the observations on the individual embryos one suggests the method of formation of the umbilical cord, completed in human embryos somewhere between the 5 and 7 mm stage - of the formation and expansion of the umbilical cord coelom which attains its maximum size between the 30 and 40 mm stage, and of the final obliteration of the cord coelom and closure of the umbilical ring subsequent to the return of the gut into the abdominal cavity. No great attention has been paid to the relations and fate of the contents of the umbilical cord such as the yolk duct and vitelline vessels, as these have been recounted with much thoroughness by Politzer and Sternberg in their comprehensive paper "Uber die Entwicklung der ventralen korperwand und des Nabelstranges beim Menschen" to which frequent reference is made throughout.

DESCRIPTION OF EMBRYOS.

Embryo McIntyre I. (1.4 mm). (Text-Fig. 10).

This embryo has already commenced to fold off from the yolk sac and there is a small foregut and larger hindgut diverticulum. The ventral aspect consists mainly of the

yolk sac which shows a slight lateral furrowing indicating the site of later constriction. Cranially the anterior mesodermal field forms the anterior and lateral boundaries of the pericardial plate where the mesoderm exhibits cleavage. Elsewhere there is as yet no intra-embryonic coelom.

With the formation of the tail fold the embryonic attachment of the body stalk comes to lie on the ventral aspect. This region has already been described in Part I, where it was suggested that the stalk mesoderm was not only derived from primitive chorionic mesenchyme, but received accessions from the caudal margin of the embryonic disc.

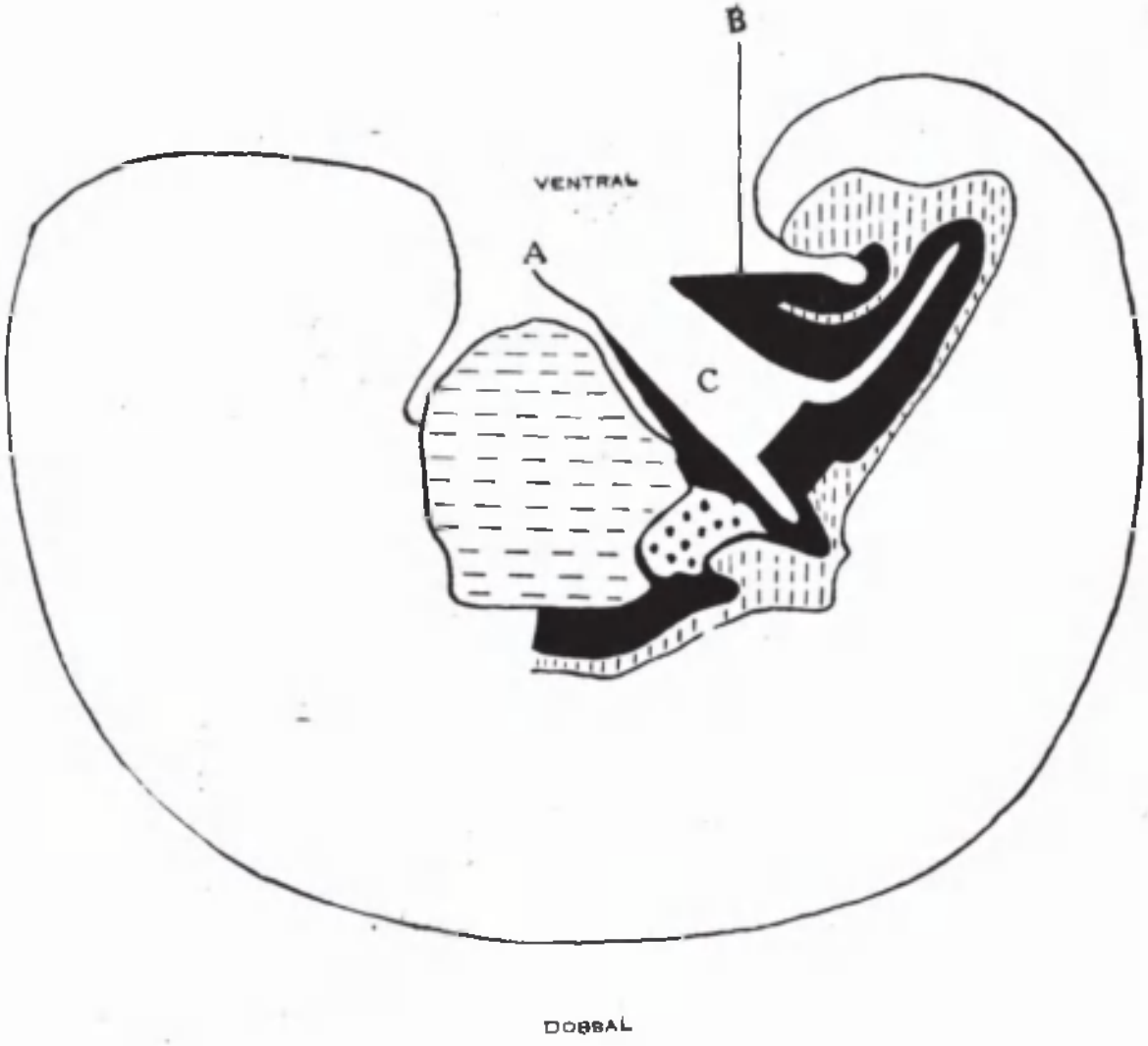
Embryo McIntyre I differs from the four-somite embryo of Sternberg in the absence of any extensive connection of amnion and chorion, i.e. a "primary amnio-chorionic field". There is no amnio-embryonic stalk as described by Florian in presomite embryos. In this respect it can be compared to Embryo Bi.XI (Florian) of ten somites to which it has also some external resemblance.

Embryo 2.6 mm. (Text-Fig. 2).

Following the pronounced involution of the embryonic body the ectodermal surface of the pericardium forms the cranial part of the ventral aspect. There is still a broad yolk sac connection which however in comparison to the 1.4 mm embryo has a marked "waisting" at the junction with the mid gut.

Between the attachment of the amnion and the cranial aspect of the yolk sac connection is a broad band of mesoderm, the anterior mesodermal field, which is continuous dorsally with the splanchnopleure on the floor of the gut. A prolongation of the coelom - the posterior coelomic portal - separates the body stalk from the mesoderm on the caudal side of the yolk sac connection. As the tail fold develops this coelomic portal is taken still further into the embryonic body to form the pelvic cavity. The most caudal structure in the somatic stalk is the allantoic or body stalk. This has an oblique attachment, being directed to the left while the yolk sac is to the right (Pl. XII, Fig. 45). In consequence of this deviation of the body stalk the amnion clothes the greater portion of its left lateral aspect (Pl. XII, Fig. 44), and much of the right side is extra-amniotic.

As has already been noted the cranial aspect of the yolk sac connection is lying against the anterior mesodermal field. There is now a body cavity which has a relatively extensive communication with the extra-embryonic coelom on each side of the yolk sac connection, i.e. where the ventral wall remains "open". Each intercoelomic communication is bounded medially by the yolk sac connection and laterally by the body wall with the amnial reflection. At the rim or point of amnial reflection are the umbilical veins, the left larger than the right. Here



Text-Fig. 11. Embryo 4.5 mm. Reconstruction of a median sagittal section. x 50. Description in text. Yolk sac is not shown.

Interrupted horizontal lines = Pericardium.
Interrupted vertical lines = Gut.
Black = Mesoderm. Large dots = Liver.
C = Coelom.
A = Amnion.
B = Body Stalk.

the somatopleure of the lateral body wall becomes continuous with the mesoderm of the amnion. There is a marked increase of mesoderm at the site of amnial reflection (Pl. XII, Fig.46).

Embryo 4.5 mm. (Text-Fig. 11).

The further folding of the head and tail ends is responsible for the relative decrease in the extent of the "open" ventral aspect and the increased dorsi-ventral convexity for the greater depth of intra-embryonic coelom. Moreover a part of the extra-embryonic coelom has been taken into the body anteriorly as well as posteriorly, and now a coelomic prolongation separates the proximal end of the yolk duct from the anterior mesodermal field and septum transversum (Pl. XIII, Fig. 50). The connection of the intestine to the yolk sac has become narrowed to a tube-like communication which at this stage could be called the vitelline duct.

The open ventral aspect is limited cranially by the amnion reflected on to the caudal wall of the completely rotated pericardium, and caudally by the allantoic stalk* which in this embryo has a more or less median position.

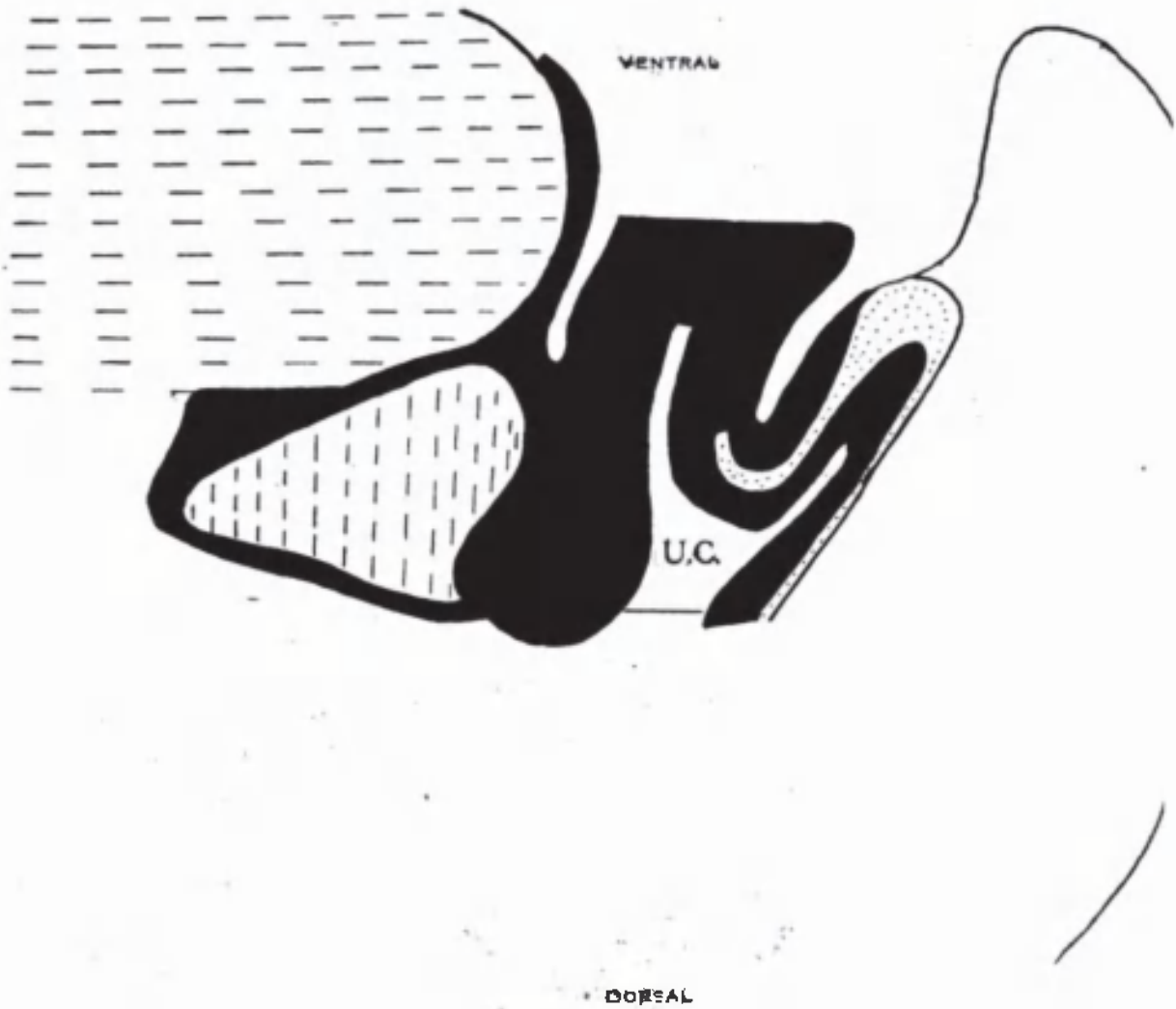
The lateral boundaries are the somatopleure of the body wall and more ventrally the thickened mesoderm on the inner aspect of the amnion. This thickening of the amnial mesoderm is much more apparent than in the

* From now on the allantoic stalk will be referred to as "stalk".

2.6 mm embryo. In its forward growth it carries with it the reflection of the amnion on each side and forms lateral tissue plates* which extend from the "stalk" to the septum transversum (Pl. XIII, Fig. 4B). There is therefore in this embryo a part of the extra-embryonic coelom enclosed between the stalk, the cranial reflection of the amnion and the lateral tissue plates, i.e. there is a short umbilical cord.

The earlier site of lateral amnial reflection is indicated by the position of the umbilical veins, each of which runs in a ridge of tissue projecting from the internal aspect of the somatopleure. This is also the junction of the lateral body wall with the lateral tissue plates and of the exocoelom with the body cavity. The lateral tissue plates consist externally of amnial ectoderm, internally of endothelium from the amnial mesoderm and a thick middle coat of proliferated embryonic connective tissue. This young connective tissue may result from migration of somatopleure cells but more probably is a derivative of the amnial mesoderm. The lateral tissue plates are deeper caudally and "taper" towards the septum transversum so that in the wax reconstruction they have the appearance of cranial extensions or pillars of the stalk.

* The term "lateral tissue plate" shall be used to denote the amnion with its thickened mesoderm ventral to the umbilical veins.



Text-Fig. 12. Embryo 7 mm. Reconstruction of a median sagittal section. x 50. Description in text.
Interrupted horizontal lines = Pericardium.
Interrupted vertical lines = Liver.
Small dots = Gut and allantoic diverticulum.
U.C.= Umbilical cord coelom.
Black line indicates the plane of the umbilical veins.

The smooth mesothelium of the cranial aspect of the stalk forms the caudal lining of the enclosed exocoelom. An umbilical loop of intestine is not yet formed.

The amnion covers the posterior aspect and sides of the proximal portion of the "stalk" (Pl. XIII, Fig. 48) - the posterior aspect of the middle portion, while the distal part is entirely extra-amniotic (Pl. XII, Fig. 47).

Embryo 7 mm. (Text-Fig. 12).

This is the youngest embryo of the series to possess a formed umbilical cord. Coincident with this is the first appearance of a short supra-umbilical abdominal wall, and thus the cranial attachment of the cord is a little distance caudal to the pericardium.

Comparison of Text-Figs. 11 and 12 gives some indication of the changes by which the "open" ventral wall of the embryo is now the site of attachment of the umbilical cord.

The lateral tissue plates whose formation had commenced in the 4.5 mm embryo undergo further growth by proliferation of their connective tissue and in their ventral extension carry with them the amnial reflection. There is also proliferation of the mesoderm at the cranial reflection of the amnion. Therefore the amnion at its embryonic attachment will at this stage enclose a circular band of embryonic connective tissue made up of the "stalk" caudally, the lateral tissue plates on each side, and

cranially the proliferated amnial mesoderm, which together form the umbilical cord.

The anterior mesodermal field, which in the 4.5 mm embryo is caudal and dorsal to the pericardium, is here divided by the developing liver into the cranial portion forming the pericardio-peritoneal membrane and the ventro-caudal portion which in part forms the mesodermal basis of the supra-umbilical wall (vide part II). This ventro-caudal mesoderm is continuous with the cranial mesoderm of the umbilical cord, the two together forming an intercoelomic septum which separates the umbilical cord coelom from the liver ventrally and from the body cavity more dorsally (Pl. XIV, Fig. 52).

The umbilical veins run in the dorsal part of the intercoelomic septum to reach the liver (Pl. XIII, Fig. 51).

The completed cord includes a part of the exocoelom - the umbilical cord coelom. In this embryo it consists of a wide proximal portion and a narrow slit-like prolongation (Text-Fig. 12; Pl. XIV, Figs. 52 and 53). The proximal portion has a caudal extension between the gut and the allantois and dorsally a wide communication with the intra-embryonic coelom. It is bounded caudally by the "stalk", cranially by the inter-coelomic septum, and laterally by the lateral tissue plates.

In a transverse section of the cord some distance

distal to its attachment, there are a number of large spaces in the loose embryonic connective tissue more especially to the cranial side. One of these spaces contains blood clot and has a distinct but not an endothelial lining (Pl. XIV, Fig. 54). These large spaces result from confluence of a number of smaller ones. The umbilical cord coelom increases considerably in size in older embryos, very probably by the "taking in" of these spaces and a proliferation and extension of the endothelial lining. Politzer and Sternberg remark on the normal occurrence of spaces in cord tissue and state "uber ihre Bedeutung konnen nur vermutungen ausgesprochen werden, doch schient es uns moglich, dass ihre Auftreten, zumindest im proximalen Abschnitte des Nabelstranges, mit der Vergrosserung der Nabelstrangcoelomhohle in Zusammenhang steht."

The mid gut is differentiated and there is a definite loop of intestine in the umbilical cord coelom.

In Text-Fig. 12 the black line represents the level of the division between the intra and extra-embryonic coeloms as indicated by the position of the umbilical veins. It will be observed that the gut is lying in the ventral part of the body cavity, so that in its growth it almost inevitably protrudes into the umbilical cord coelom.

The cranio-caudal width of the cord at its point of attachment to the embryo is 0.5 mm.* The length of the attachment cranial to the umbilical cord coelom is .24 mm,

* Will be referred to from now on as "cord attachment."

Text-Fig. 13. Embryo 8.5 mm. Reconstruction of a median sagittal section. x 50. Description in text.
Interrupted horizontal lines = Pericardium.
Interrupted vertical lines = Liver.
Oblique lines = Blood vessel. Black = Mesoderm.
Small dots = Gut.
U.C. = Umbilical cord coelom.
Black line indicates the plane of the umbilical veins.

which is in fact the cranio-caudal measurement of the inter-coelomic septum*, while the wide umbilical cord coelom measures .4 mm.

Embryo 8.5 mm. Text-Fig. 13.

This embryo has been recently acquired and therefore was not described in parts I and II.

The umbilical cord has an inclination towards the right, and there is a small yolk sac also on the right side. The embryo is cut transversely, and the umbilical cord longitudinally. The cord extends almost to the chorion, but there is a small extra-amniotic stretch of "stalk" distally and to the left.

The ventral aspect has straightened out somewhat compared to that of the 7 mm embryo. This is due to the forward and caudal extension of the liver and the formation of a longer supra-abdominal wall. The cranial portion of the cord consists of a loose embryonic connective tissue which, dorsal to the cord attachment, fuses with the denser tissue on the ventral aspect of the liver to form the inter-coelomic septum (Text-Fig. 13). It should be noted that with the stretching of the ventral wall the inter-coelomic septum is no longer in the dorsi-ventral plane but makes an angle of about 45 degrees with it and thus the cord is tending to become "prised out" of the

* Will be referred to from now on as "cranial attachment" of cord.

embryonic body. The length of the cord attachment is 1.2 mm, and of its cranial attachment .6 mm. This increase (c.f. 7 mm) is in fact the result of the more horizontal position of the intercoelomic septum. The widest part of the umbilical cord coelom is at its communication with the body cavity, the coelomic portal,* and measures ,6 mm.

In a longitudinal section of the cranial half of the cord (Pl. XIV, Fig. 55) can be observed the distal prolongation of the umbilical cord coelom containing the vitelline stalk. This part of the coelom is much larger than the corresponding extension in the 7 mm embryo. On the left the amnion is reflected from the cord while still a short distance from the chorion, and at the point of reflection the endothelium of the coelom becomes continuous with the mesothelium of the amnion. Proximal to this point the endothelium and amnial ectoderm are separated by a thickness of mesenchyme - the proliferated connective tissue of the lateral tissue plates.

Pl. XV, Fig. 56, shows the left umbilical vein in the projecting ridge of tissue situated at the base of the intercoelomic septum and separating the intra-embryonic coelom from the broad proximal umbilical cord coelom. The coelomic portal has its greatest diameter in the caudo-cranial axis and is narrow from side to side, but broadens out posteriorly where the vein turns up into the cord

* The communication of extra and intra-embryonic coeloms.

Text-Fig. 14. Embryo 12.5 mm. Reconstruction of a median sagittal section. x 25. Description in text.
Interrupted horizontal lines = Pericardium.
Interrupted vertical lines = Liver.
Small dots = Gut. Oblique line = blood vessel.
Black = Mesoderm.
U.C. = Umbilical cord coelom.

(Pl. XV, Fig. 57). A small right umbilical vein is still present.

A noticeable feature in this embryo as in the 7 mm one is the fact that the umbilical cord actually penetrates the embryonic body for some distance, and accordingly there is a relatively shallow intra-embryonic coelom at this level. It is therefore not surprising that the growing intestine should find its way into the extra-embryonic coelom.

The liver still occupies but a small part of the abdominal cavity, and can have little or no influence on the position of the gut at this time.

Embryo 12.5 mm. Text-Fig. 14.

The cord attachment extends over 1.9 mm and the cranial attachment is over 1 mm. The increased length of the cranial attachment is simply due to the more horizontal position of the inter-coelomic septum which in turn has been brought about by the caudal and ventral extensions of the now rapidly growing liver.. As a consequence of both these factors the cord is still further "prised" out of the embryonic body, and the body cavity has a much increased dorsi-ventral depth. Above the cord is the supra-umbilical area, and caudal to its lower attachment is a small infra-umbilical area of abdominal wall.

The coelomic portal has a cranio-caudal width of .5 mm, but a short distance distal to this the umbilical

Text-Fig. 15. Embryo 14 mm. Reconstruction of a median sagittal section. x 25. Description in text.
Vertical lines = Liver. Horizontal lines = Blood vessel.
Black = Mesoderm.
U.C. Umbilical cord coelom.

cord coelom widens out to 1.1 mm. There is thus in this embryo a bottle-neck communication between the intra and extra-embryonic coeloms; a characteristic feature in all the older specimens.

The expansion of the umbilical cord coelom itself is mainly at the expense of the cranial mesoderm.

A section at the level of the cranial attachment of the cord (Pl. XV, Fig. 58) shows the myotomic downgrowths fusing in the mid line ventrally to form a denser connective tissue on the superficial aspect of the umbilical vein. At the level of the coelomic portal the downgrowths are not so definite and do not reach the sides of the cord (Pl. XV, Fig. 59). The stalk tissue with the vessels is on the right side of the cord (Pl. XVI, Fig. 60).

The significance of the zone of mesodermal condensation on the caudal aspect of the cord has already been dealt with in part I.

Embryo 14 mm. Text-Fig. 15.

In this embryo the umbilical cord in the first part of its course turns towards the head and the umbilical vessels occupy the left aspect. The extent of cord attachment measures 1.6 mm - an absolute and relative decrease from the corresponding figure in the preceding embryo. The cranial attachment is .8 mm, while the inter-coelomic septum is now lying at an angle of about 45 degrees to the horizontal.

Text-Fig. 16. Embryo 16.1 mm. Reconstruction of a median sagittal section. x 25. Description in text.
Vertical lines = Liver. Horizontal lines = Blood vessel.
Black = Mesoderm.
U.C.= Umbilical Cord Coelom.

A narrow coelomic portal (cranio-caudal width .6 mm) is the entrance into a large umbilical cord coelom which but a short distance from the cord attachment has expanded to a cranio-caudal breadth of 2 mm, and is responsible for the increased circumference of this part of the umbilical cord. A narrow prolongation of the cord coelom still with its endothelial lining can be followed into the more distal sections (Pl. XVI, Fig. 61).

Although not so well marked as in the 12.5 mm embryo, the myotomic downgrowths can be discerned in the upper half of the abdominal wall and traced into a mesodermal condensation on the anterior aspect of the umbilical vein (Pl. XVI, Fig. 63). In the mid abdominal region, however, i.e. at the level of the coelomic portal, the downgrowths fade away before reaching the ventral aspect (Pl. XVI, Fig. 62).

Embryo 16.1 mm. Text-Fig. 16.

The area of cord attachment is 1.3 mm, the cranial attachment .5 mm and the coelomic portal .7 mm.

Above the cord the midventral wall is a narrow band of loose embryonic connective tissue (Pl. XVII, Fig. 64). At the level of the cranial attachment of the cord the mesoderm ventral to the liver and the immediate cord tissue (Pl. XVII, Fig. 65) is of a more compact texture, and this denser connective tissue can also be observed extending some little way into the pillars of

Text-Fig. 17. Embryo 23 mm. Reconstruction of a median sagittal section. x 25. Description in text.
Vertical lines = Liver. Horizontal lines = Blood vessel.
Black = Mesoderm.
U.C.= Umbilical cord coelom.

the cord flanking the coelomic portal (Pl. XVII, Fig. 66), more markedly to the left side with the umbilical vessels.

The myotomic downgrowths in this embryo only extend a little over half way round the ventral wall and are not continued into the denser tissue reaching the proximal end of the cord.

At this stage the liver occupies a large proportion of the abdominal cavity, and in the mid line extends caudally below the coelomic opening.

Embryo 23 mm. Text-Fig. 17.

The extent of umbilical cord attachment is 2 mm, the cranial attachment is .7 mm, and the cranio-caudal width of the coelomic portal is 1 mm. In this embryo the inter-coelomic septum is in the horizontal plane, and the liver in the midventral line reaches the upper half of the coelomic portal. A little distal to the embryo the cord coelom has a cranio-caudal measurement of 1.6 mm.

In the upper part of the abdominal wall the myotomic downgrowth terminates some distance lateral to the midventral line whose mesoderm is of a loose texture similar to the connective tissue of the cord (Pl. XVII, Fig. 67). Caudally this is replaced by a more compact tissue which is continuous on the one hand with the myotomic downgrowth (Pl. XVIII, Fig. 68), and on the other extends into the proximal part of the inter-coelomic septum. It also extends into the pillars of the cord on each side of

Text-Fig. 18. Embryo 40 mm. Reconstruction of a median sagittal section. x 20. Description in text.
Vertical lines = Liver. Horizontal lines = Blood vessel.
Black = Mesoderm.
U.C.= Umbilical cord coelom.

the coelomic portal more particularly to the left around the umbilical vessels (Pl. XVIII, Fig. 69). With the condensation of mesoderm on the caudal aspect of the cord (vide part I), there is thus a ring of compact tissue at the cord attachment which forms the circumference of the coelomic portal.

Embryo 30 mm.

The length of the cord attachment is 1.8 mm, of which .6 mm represents the extent of the cranial attachment of the horizontal inter-coelomic septum. The cranio-caudal width of the coelomic portal is 1 mm, while the greatest cranio-caudal diameter of the umbilical cord coelom is 3 mm.

This embryo is cut longitudinally, and shows the relative proportions of the structures mentioned above, including the narrow neck of the cord coelom and the large size of the liver. In Pl. XXI, Fig. 82 can be observed the denser mesoderm round the umbilical vein at the cranial attachment of the cord.

Embryo 40 mm. Text-Fig. 18.

The extent of cord attachment extends over 2 mm of the ventral body wall. There is a very small cranial attachment of 0.4 mm and a coelomic portal of 1.3 mm opening into a wide umbilical cord coelom which, however, on account of the obliquity of the section through the cord, could not be measured. From the embryo the umbilical cord

takes a cranial direction, and its coelom, with the endothelial lining, can be followed as a narrow prolongation into the more distal sections (Pl. XIX, Fig. 73).

The liver occupies an even greater proportion of the abdominal cavity than in the 23 mm embryo, and in the mid line encroaches not only ventrally but also dorsally on the upper half of the coelomic pprtal. At this level the intra-abdominal part of the intestine is lodged in a groove between the above ventral and dorsal portions of the liver. The umbilical vessels and allantois occupy the left aspect (Pl. XIX, Fig. 72) of the proximal part of the cord, the arteries and allantois turning to the caudal aspect at the attachment, while the umbilical vein is directed cranially. There is a broad linea alba in the supra-umbilical abdominal wall formed by a fusion of the sheaths of the recti muscles which provides a fibrous condensation on the superficial aspect of the intra-abdominal part of the umbilical vein (Pl. XVIII, Fig. 70). At the attachment of the cord the muscle sheaths fuse with the umbilical ring of compact tissue surrounding the coelomic portal (Pl. XVIII, Fig. 71).

Embryo 42 mm. A. Text-Fig. 19.

Unfortunately in this embryo the cord has been cut close to the body and only a small part is included in the sections. Moreover a few of the sections in the critical umbilical region have been rather badly damaged,

but a sufficient number remain to make it clear that the umbilical loop of intestine is in the abdominal cavity.

This return is probably recent and possibly just completed as the intra-embryonic coelom is still open to the cord coelom. The position of the loop of intestine indicated in Pl. XIX, Fig. 75, is in fact suggestive that the process of re-entry is still in progress. The liver has decreased in size and does not encroach on the coelomic portal in the mid line (cf. 40 mm embryo).

The extent of cord attachment is 2.1 mm, and the coelomic portal is markedly narrowed in its transverse diameter (Pl. XIX, Fig. 75).

The supra-umbilical portion of the linea alba is formed by the fusion of the sheaths of the recti muscles, and more caudally the sheaths are continued into the zone of compact embryonic connective tissue encircling the attachment of the cord (Pl. XIX, Fig. 74).

Embryo 42 mm B.

This embryo is included in the series as it demonstrates the presence of an empty umbilical cord coelom after the withdrawal of the gut. The cord coelom is much reduced in size from that in the 40 mm embryo, and is occupied by a quantity of blood clot (Pl. XX, Fig.76). In the more distal part there is an absence of the endothelial lining and the wall is irregular and formed simply of the connective tissue of the cord (Pl. XX, Fig. 77).

In the proximal cord coelom the endothelial cells are being separated off (Pl. XX, Fig. 78) preparatory to the ultimate degeneration and disappearance of the endothelium.

The anterior sheath of the recti muscles is continuous on all sides with the compact tissue encircling the now much narrowed coelomic portal (Pl. XX, Fig. 79).

Embryo 60 mm.

A description of the relevant sections will be given as these include only the anterior abdominal wall in the region of the cord attachment, and accurate graphic reconstruction was not possible. The length of the cord attachment is 3.2 mm.

In the supra-umbilical region (Pl. XXI, Fig. 80) the now well formed broad linea alba lies superficial to the umbilical vein whose coats are differentiated. Posteriorly between the vein and the peritoneum is a layer of fibrous tissue - the umbilical fascia - the variations and significance of which have been worked out by Gorelow.

The character of the tissue of the umbilical cord shows considerable change from that in the 40 mm and 42 mm embryos (Pl. XXI, Fig. 81). There has been much proliferation of embryonic connective tissue which resembles more closely adult fibrous tissue. This proliferation is more apparent at the attachment of the cord in the vicinity of the blood vessels. The coats of the vessels themselves have

increased in thickness, and the allantoic arteries have a layer of visceral muscle. In the distal sections of the cord there is a less dense and more open appearance. On each side the sheaths of the recti muscles are continued into the broad band of compact fibrous tissue which forms the cranial attachment of the cord, lies on the superficial aspect of the umbilical vein, and can in turn be followed into the supra-umbilical linea alba (Pl. XXI, Fig. 81).

At the proximal end of the cord the umbilical vein takes the left and cranial side, while the allantoic structures are on the caudal and right aspects.

Pl. XXI, Fig. 83, is a photograph of a section about midway through the cord attachment. The muscle sheaths run into the cord tissue on each side. In this embryo there is no umbilical cord coelom and the body cavity is shut off from the cord by the peritoneum.

At the caudal end of the cord attachment (Pl. XXI, Fig. 84) there is a band of compact tissue superficial to the allantoic arteries and allantois. This merges on each side with the sheath of the rectus muscle and caudally is continued into the infra-umbilical division of the linea alba.

In this embryo the encircling band of compact tissue at the cord attachment is a particularly noticeable feature, and by its proliferation is responsible not only for the closure of the umbilical ring, but also a

reinforcement of the immediate abdominal parietes.

DISCUSSION AND CONCLUSIONS.

Formation of the Umbilical Cord.

The umbilical cord is formed essentially by the closing in of the somatic stalk. In young embryos the somatic stalk is bounded by the attachment of the amnion round the broad ventral aspect. The approximation of the amnial reflections is brought about by the ever increasing involution of the embryonic body. Following rotation of the pericardium the cranial reflection of the amnion moves from the ventral to the caudal pericardial wall, and finally at the 7 mm stage the amnion is reflected on to the newly formed supra-umbilical wall. The allantoic stalk covered posteriorly and laterally with amnion is rotated ventrally and while part of the stalk is thereby taken into the body of the embryo the relative distance between the caudal and cranial amnial reflections, i.e. the breadth of somatic stalk, is decreased. In addition there is a relative narrowing in the transverse axis as a result of the formation of the vitelline duct coupled with the great dorsi-ventral convexity of the embryonic body.

The lateral tissue plates make their first appearance in the 4.5 mm embryo. They arise from a proliferation of the embryonic connective tissue between the ectoderm of the amnion and its mesothelial or endothelial

lining, and in their forward growth they carry with them the lateral amnial reflections which will now lie some distance ventral to the umbilical veins and thus ventral to the embryonic rim. They connect the allantoic stalk to the septum transversum and represent the beginning formation of the umbilical cord.

By a proliferation of the mesoderm the tissue plates continue to grow in length and thickness. There is also an increase of the corresponding mesoderm at the cranial reflection of the amnion which might be said to form a third or anterior tissue plate. At a later stage - the 7 mm embryo - a portion of the exocoelom has been enclosed by these thick endothelial lined tissue plates which encircle it laterally and in front. The caudal boundary is the cranial surface of the body stalk.

This is the umbilical cord and it finally stretches from the embryo to the chorion.

Umbilical Cord Coelom.

In any given embryo the level at which the umbilical vein enters the body wall indicates the boundary between intra and extra-embryonic coelom.

In the 2.6 mm embryo there is, on the ventral aspect, a wide communication between the intra and extra-embryonic coeloms. Posteriorly the coelom extends as a caudal recess some distance into the body of the embryo. This caudal recess is extra-embryonic coelom which has

"rotated" into the embryonic body as the tail fold forms. Anteriorly the coelomic portal has the opening of the coelomic tubes on each side of the mid line. There is as yet no median prolongation of the coelom and the cranial wall of the yolk sac connection lies against the septum transversum (Text-Fig. 2).

With the further involution of the embryo (e.g. Embryo 4.5 mm) the cranial wall of the now constricted yolk sac connection becomes separated from the septum transversum by an extension of the coelom, and a short length of gut intervenes between them.

The intra-embryonic coelom is therefore to some extent increased by the inclusion of part of the exocoelom.

The umbilical cord coelom in the first instance consists of a narrow slit-like distal part and a wide proximal part which receives the opening of the caudal recess and communicates with the body cavity. It enlarges, pari passu, with the growth of the umbilical loop of intestine until it attains a maximum size in embryos between 30 mm and 40 mm. In these older specimens the umbilical cord coelom occupies a proportionately greater extent of the cranio-caudal diameter of the cord, and therefore some of this increase in size is at the expense of cord tissue. The opinion has already been expressed that there is a confluence of spaces normally found in the cord mesenchyme, that these open into the cord coelom, and the endothelium extends into and forms a lining for them.

The coelomic portal is in the earlier stages the widest part of the cord coelom. It, however, soon becomes relatively narrow and constitutes a "bottle-neck" inter-coelomic passage.

Eventration of the Gut.

In the 4.5 mm embryo there is a short length of gut between the cranial margin of the yolk sac connection and the septum transversum, This is the first indication of a mid-gut loop and it is intra-embryonic. The proximal umbilical cord coelom, in the 7 mm embryo, contains the umbilical loop of intestine and there it remains and develops till about the 42 mm stage.

Why should a portion of intestine grow for a period outside the body of the embryo? To state that it does so because of lack of space within the abdominal cavity leaves still unexplained this apparent temporary architectural miscalculation. There seems no adequate reason why the intestine should not grow as well if not better inside an abdominal cavity of the requisite size. "Es sieht daher tatsaechlich hier so aus, als ob die Natur unnötigerweise eine konstante embryonale Missbildung hervorriefe, die sie nachher die Mühe haben musse, wieder zu reparieren."(Broman).

There are two aspects of the problem of what has been described as the physiological hernia.

Firstly, the method of production - in other words, how does the hernia occur? The various theories and

suggestions appertaining thereto are the result of the study of the relevant factors in the developing human embryo. Secondly, why does the hernia occur? Observation of human ontogeny alone would leave this question still unsolved, and the final answer is only found in terms of comparative embryology.

The Method of Production.

The most apparent factor in the production of the hernia is the connection of the intestine with the yolk sac. In the early stages the broad yolk sac connection maintains the gut in the ventral portion of the relatively shallow body cavity, so that when the mid-gut develops by constriction of the yolk sac it very quickly comes to lie in the proximal part of the umbilical cord coelom which at that time has a wide communication with the body cavity (Text-Fig. 12). As the embryo becomes folded off and the body cavity enlarges there would be a tendency for the umbilical loop to re-enter the intra-embryonic coelom, but it is maintained in or actually drawn further into the exocoelom by the yolk stalk. The vitelline duct itself becomes obliterated, according to Politzer and Sternberg, between the 7 mm and 9 mm stage, and soon after severs its connection with the intestine. There, however, still remains attached to the ileal mesentery the mesodermal yolk stalk containing the vitelline artery which does not disappear till about the 15 mm stage (Broman), and this is

an important factor in the maintenance of the extra-embryonic position of the gut. In the present series of embryos there is no trace of a yolk stalk in the 7 mm embryo, but it is present very definitely in the older 8.5 mm specimen. In a rabbit embryo in which the gut has returned to the abdominal cavity, there is still present a mesodermal stalk connecting the mesentery to the umbilical cord. Broman states that in the cat and the seal the yolk stalk persists for a much longer period than in the human.

It has been suggested (Mall) that the rapidly developing liver "squeezes" the gut into the exocoelom, but the umbilical loop of intestine can be observed in its extra-embryonic position at a stage, e.g. 7 mm, when the liver occupies only a small proportion of the abdominal cavity. The later great extension of liver tissue combined with the narrow intercoelomic communication will certainly help to maintain the extra-embryonic position of the gut, but hepatic growth is not responsible for its initial production.

Why should the Hernia occur?

The primitive gut or enteron is formed by an extension of the endoderm round the yolk mass. In amphibians, such as the frog, the enteron with enclosed yolk is within the body of the quickly formed larva.

Where the yolk furnishes nourishment over a more prolonged period, as in Elasmobranchs, reptiles and birds,

it would obviously be impracticable to harbour this inert mass within a growing embryo, and so the original plan is modified - the yolk sac remains for a time extra-embryonic and lies within an extra-embryonic extension of the coelom. The large and heavy yolk sac acts as a drag on the intra-embryonic intestine to which it is attached, and this portion will be brought without the embryo to form the umbilical loop in the exocoelom.

In reptiles and birds the yolk sac is taken into the body of the embryo at a late stage - the umbilical cord coelom is incorporated in the body cavity and its somatopleure with the body wall.

In placental mammals the rôle of the yolk sac is of comparatively minor significance and confined to the early stages, but it still plays a part, however transient, in the physiology of the embryo, and its extra-embryonic modification serves as a basis for still more elaborate nutritional preparations. As a concomitant of the extra-embryonic position of the yolk sac there is a portion of the definitive intestine in the umbilical cord coelom. The part played by the yolk sac is soon over; its further development or inclusion within the embryo would serve no useful purpose. It therefore atrophies and severs its connection with the intestine which it leaves within the exocoelom.

The physiological hernia does not therefore occur

a priori but rather is incidental to the extra-embryonic position of the yolk sac. It is a by-product of a plan which utilises part of the primary enteron as a storehouse for nutriment. In mammals much of this scheme is still further modified, but as the presence of the hernia indicates it is not altogether discarded.

Later changes in the form of the Umbilical Cord.

In the stages immediately succeeding the formation of the umbilical cord there is an increase absolute and relative in the cranio-caudal length of its embryonic attachment, for whereas at 7 mm this area is one-fourteenth of the total embryonic length it accounts for one-seventh of the total length at 8.5 mm and 12.5 mm. After this the rate of growth lags behind that of the embryo as a whole, and at 42 mm and 60 mm the proportion is only one to twenty. The umbilicus can therefore be regarded as a relatively fixed area.

At the level of its proximal attachment the umbilical cord consists of the embryonic connective tissue of the inter-coelomic septum cranially and the stalk mesoderm caudally, which, together with the lateral amnial plates, form the respective boundaries of the umbilical cord coelom.

The relative proportion of cord structure formed by intercoelomic septum and coelomic portal undergoes a change as development proceeds. The former which at an

early stage forms more than half, is, in the older embryos, reduced to less than half of the sagittal diameter of the cord at its proximal attachment, while the latter is increased accordingly. This increase, however, is by no means commensurate with the enlargement of the more distal cord coelom, and the result is a narrow bottle-necked inter-coelomic communication.

The inter-coelomic septum is situated in the first instance with its long axis dorsi-ventrally, and the cord is "sunk" for quite a considerable distance into the embryonic body. With the ventral and caudal extension of the liver the inter-coelomic septum is rotated through 90 degrees so that its long axis is now in the cranio-caudal plane and the cord is "eased out" of the body of the embryo.

Dense embryonic connective tissue encircles the attachment of the cord. It forms an umbilical ring of mesodermal condensation surrounding the coelomic portal, and is present in the 16.1 mm embryo, but more emphatically so in the 23 mm embryo. The compact tissue first appears in the stalk mesoderm, situated superficial to the allantoic vessels (vide part I). Cranially it lies ventral to the umbilical vein and on each side extends into the tissue of the lateral pillars of the cord bounding the coelom. When the myotomic downgrowths reach the ventral aspect their anterior portions, i.e.

the sheaths of the recti muscles, become continuous with the tissue of the umbilical ring.

Umbilical Veins.

The umbilical veins are first encountered running from the body stalk to the septum transversum in a projecting ridge of somatopleure which indicates the ventral limit of the body cavity. When the umbilical cord is formed they are still situated in the mesoderm on each side of the coelomic portal. From there they run in the dorsal part of the inter-coelomic septum to reach the liver. After the change in position and size of the inter-coelomic septum the surviving left vein winds round the left side and comes to lie on the cranial aspect of the cord. The interparietal course of the vein is in the dorsal portion of the inter-coelomic septum until the diminution in size of the liver at the time of the re-entry of the gut into the abdominal cavity.

Ventralisation of the Gut.

It is generally agreed that there is a comparatively rapid passage of the umbilical loop of intestine into the abdominal cavity in embryos of from 40 mm to 42 mm. I have been unable to find described any intermediate stage with a partial reduction of the gut, but nevertheless it is obvious, as stated by Frazer, "that there is no question of the entrance of the contents of the sac en masse into the abdomen", but that the coils of gut "slip

back in a continuous movement."

In the chick the large yolk sac together with the sac containing the intestine is taken into the body of the embryo about the 19th day. The distal wall of the yolk sac, according to Lille, is fused with the allantois. This part of the allantois has a muscular wall, and by its contraction initiates the propulsion of the yolk sac towards the embryo. The movement is completed by the pressure of the inner wall of the amnion which possesses an interlacing system of muscle fibres.. The umbilicus is closed by the act of inclusion (except for a small central aperture) as the inner wall of the amnion is attached on the one hand to the body wall and on the other to the distal pole of the yolk sac.

There are no muscular fibres in the mammalian amnion nor any other means of exerting pressure on the umbilical sac from without. Therefore it must be assumed that there is an intra-embryonic influence sufficiently effective to overcome the resistance of the narrow inlet. This could be (A) of the nature of a direct pull, or (B) a suction force by the establishment of a negative abdominal pressure (i.e. negative relative to that in the exocoelom).

Under A have been cited (1) a rotation, and increase in size, of the intra-abdominal loop of intestine (Mall; (2) shortening of the vitelline vessels (Rathke);

(3) a dorsal pull exerted on the gut by a strong caudal growth of the liver (Broman).

A negative intra-abdominal pressure would be caused by the expansion of the abdominal cavity and diminished growth rate of liver (Frazer). Certainly coincident with the entrance of the gut there is a decrease in the size of the liver, but this might be the effect rather than the cause, as the presence of additional gut would cancel the negative pressure and allow the liver to "contract".

The study of this series of embryos has failed to reveal any additional factor which would further aid in a solution of the problem.

As far as the question lends itself to elucidation in terms of physical forces the evidence favours the creation of a negative abdominal pressure and a "suction" influence rather than a direct pull.

To be reckoned along with any mechanical explanation, however plausible, of embryological phenomena, is the biological urge towards the completion of a specific form which finds its modern expression in the terms "organiser", "growth centre", etc., and which so far has defied all effort to place it within any known hierarchy of physical laws.

Obliteration of the Umbilical Cord Coelom and Closure of the Umbilical Ring.

The passage of the umbilical loop of gut

into the abdominal cavity leaves a still open coelom in the umbilical cord, as has been observed in the 42 mm B Embryo. Apart from this direct evidence of the presence of the empty exocoelom, any question of its incorporation in the embryonic body would be negatived by the following observations:- (a) the extent of the cord coelom in the older embryos (23 mm and 40 mm); (b) its prolongation into the distal cord, and (c) the bottle-necked coelomic portal.

The first step towards obliteration is probably a certain amount of collapse of the wide proximal cord coelom, then a degeneration of the endothelial lining (Pl. XX, Fig. 78) would permit of the filling up of the space by the proliferation of contiguous fibrous tissue. Such an increase of connective tissue is strikingly apparent in the 60 mm embryo where there is not only a greater density of tissue, but it is of a more mature type. It is particularly concentrated in the region of the proximal attachment of the cord, and could be regarded as the result of increased activity of the ring of fibrous tissue already described. This proliferating zone is responsible for the closure of the umbilical ring and forms a collar encircling the base of the cord and extending into the abdominal wall. Above and below it plays a part in the formation of the supra and infra-umbilical portions of the linea alba, and is continued into and reinforces the

rectus sheath on each side.

It is perhaps of some significance that in the human and probably other placental mammals the umbilical cord as in some lower vertebrates makes its contribution to the body wall, and that this contribution traced to its ultimate source is a derivative of the primary mesoderm.

Congenital Hernia due to Maldevelopment of the Umbilical Region.

Recorded in the literature are many and varied forms of congenital deficiencies of the anterior abdominal wall with a correspondingly formidable array of names and a somewhat confusing choice of classification.

Ectopia vesicae and absence of an anterior abdominal wall (eventration) have already been discussed in parts I and II respectively, and here remarks will be confined to herniation which results from maldevelopment of the umbilical cord and neighbouring parietes.

A. Arrested Formation of the Umbilical Cord.

In the Hunterian Pathological Collection of Glasgow University is a specimen (No. 50-113) of a six months foetus labelled "Hernia into the Umbilical Cord". The greater portion of the abdominal wall is occupied by a large thin-walled sac about the size of a hen's egg which contains most of the abdominal viscera. A stalk or cord arises from the apex of the sac. There is no neck to the sac, but a wide circular aperture opens into the body cavity proper: this is the Exomphalos of Fraser's

classification. In the specimen there is a supra and infra-umbilical portion of the abdominal wall and some attempt at closure of the somatic stalk to form an umbilical cord (cf. cases of eventration), but the band of mesodermal condensation normally present at the embryonic attachment of the cord is absent, and in consequence there is no proper umbilical ring and the coelomic portal has expanded pari passu with the exocoelom.

B. Persistence of the Physiological Hernia.

Specimen No. 50-112 of the Hunterian Collection is also labelled "Hernia into the Umbilical Cord", but is an entirely different condition from the preceding example. The large sac, which has been opened, contains the major portion of the gut including the caecum and appendix, and communicates with the intra-embryonic coelom by a narrow constricted neck. The intestinal wall is firmly adherent to the upper rim of this umbilical ring. Thunig thinks that adhesion of the intestine to a patent umbilical ring is a primary aetiological factor in persistent physiological hernia. It is equally possible that a premature narrowing of the coelomic portal by a precocious proliferation of the fibrous tissue of the umbilical ring might defeat attempts at reduction. With the growth of the contained gut and a further relative constriction of the neck a condition akin to incarceration would exist, and secondary inflammatory adhesions develop.

It should be noted that as the caecum and appendix are normally the last parts of the gut to enter the abdominal cavity they will perforce be included in the hernial sac in all cases of the above condition.

C. Non-Closure of the Umbilical Ring.

If the umbilical ring remains patent there may be a persistent umbilical cord coelom, or a new peritoneal sac may be formed. In either case the entrance into the sac of a loop of bowel will result in a hernia into the umbilical cord which, of course, occurs after the reduction of the physiological hernia. Such a hernia may be symmetrical or asymmetrical depending on the position of the allantoic stalk in the cord. Clinically this is the commonest type of umbilical hernia and is the "simple umbilical hernia" of Schwalbe, the "small umbilical hernia" of Politzer and Sternberg, the postnatal umbilical hernia of Fraser, and includes "congenital hernia" into the cord and infantile umbilical hernia (R. Maingot).

It has been shown that the closure of the umbilical ring is effected by a proliferation of the encircling band of compact mesoderm. Partial failure or absence of this proliferation would leave a patent umbilical ring - a potential hernial site.

Defects of the Parietes in the Umbilical Region.

From observations on the older embryos of the series, one concluded that there is a contribution of

mesoderm from the tissue of the umbilical cord to the abdominal parietes.

The linea alba immediately above and below the cord attachment and the sheath of the rectus muscle on each side are formed by a fusion of the anterior portion of the myotomic downgrowths with connective tissue from the compact condensation round the base of the umbilical cord. It is suggested by Schwalbe that partial deficiencies of the abdominal wall are due to a mesodermal failure of one or two particular somites related to a scoliotic deformity of the vertebral column. Difficult to reconcile with this view is the fact, also stated by Schwalbe, that the abdominal muscles are normal and the recti form the lateral boundaries of the parietal deficiency.

A defective proliferation or insufficiency at one or other point of the umbilical ring of compact mesoderm would result in a weakness of the corresponding part of the umbilical region of the abdominal wall. This might affect the linea alba above or below the umbilicus, or the immediate lateral parietes - all of them sites of potential hernia. Such a condition has been variously designated as amniotic umbilicus (Tennant), amniotic linea alba (Thunig), or, where a hernia has developed, amniotic hernia (reshman).

An aggravation of the deficiency in the sub-umbilical region is exemplified in ectopia vesicae, while

its counterpart above would cause a condition approaching partial eventration. Perhaps the most common result of such a parietal defect is a small asymmetrical hernia above or to one or other side of an apparently normal umbilical cord.

In each and all of the above malformations leading to herniae in this region of the abdominal wall, one is of the opinion that the initial error or fault can be traced to that mesoderm which by its proliferation forms the amnial tissue plates of the umbilical cord, closes the umbilical ring, and contributes to the umbilical part of the abdominal parietes. The earlier the flaw the more serious the consequences, as in severe forms of exomphalos, while its later occurrence is the aetiological factor in the minor defects of "small umbilical" or "amniotic" herniae. Is it of more than passing interest that in deficiencies of the anterior abdominal wall the offending tissue is the mesenchyme of the early embryonic rim - the site of fusion of primary and secondary mesoderm?

S U M M A R Y .

1. The umbilical cord is formed by the growth of lateral tissue plates which extend on each side from the allantoic stalk to the septum transversum.
2. The umbilical cord coelom enlarges by the extension of the endothelial lining into the large spaces in the cord tissue formed by the confluence of smaller

spaces.

3. The temporary physiological herniation of a part of the gut is a concomitant of the extra-embryonic position of the yolk sac which itself is an expression of a modification to meet nutritional requirements.
4. The observations support the suggestion already offered by Frazer that the return of the gut into the abdominal cavity is dependant on a "negative" intra-abdominal pressure.
5. The obliteration of the umbilical cord coelom is effected by a proliferation of the denser fibrous tissue which forms an encircling collar at the embryonic attachment of the cord.
6. This circular zone of mesodermal condensation contributes to the linea alba above and below, and to the rectus sheaths on each side of the umbilicus.
7. Some fault of the junctional mesoderm, i.e. the tissue at the embryonic rim where there is union of primary and secondary mesoderm, is responsible for congenital herniation which results either from maldevelopment of the cord itself or from deficiency of the neighbouring parietes.

As in parts I and II I have again to record indebtedness to my Chief, Professor Blair, for his continued guidance and supervision of the work. Dr P. Bacsich was

consulted on several questions of histological interpretation.

The 42 mm B Embryo was kindly given on loan by Professor T. Nicol and Dr Gladstone, of King's College, London.

REFERENCES.

BROMAN, I. (1932). Das Rätsel des Physiologischen Nabelbruches. Verhandl. Anat. Gesellsch. Heft LXXV.

FLORIAN, J. (1930). The Formation of the Connecting Stalk and the extension of the Amniotic Cavity towards the Tissue of the Connecting Stalk in Young Human Embryos. Jour. Anat., vol. LXIV.

FRASER, J. (1926). The Surgery of Childhood. Arnold, London.

FRAZER, J. E. (1931). Manual of Embryology. Baillière, Tindall & Cox, London.

FRESHMAN, E. (1933). Congenital Umbilical Hernia. Lancet; September 23rd.

GORELOW, M. A. (1934). Zur Anatomie des Nabelkanals. Arch. f. Klin. Chir., No.CLXXXI.

KERR, J.G. (1919). Text Book of Embryology. vol. II. McMillan & Co., London.

LILLE, (1908). Development of the Chick. George Bell & Sons, London.

MAINGOT, R. (1936). Post-Graduate Surgery. Medical Publications Ltd.

MALL, F.P. (1897). Handbuch d. Entwgesch. des Menschen. Bd.II.

POLITZER, C. and STERNBERG, H. (1930). Uber die Entwicklung der ventralen Korperwand und des Nabelstranges beim Menschen. Z. f. Anat. u. Entw. Bd. XCII, Heft 4.

Do. Do. (1931). Beiträge zur Pathologischen Anatomie und zur Allgemeinen Pathologie. Beitr. Path. Anat., Bd. LXXXVIII.

SCHWALBE, E. (1909). Die Morphologie der Missbildungen. vol. III, pt. i.

STERNBERG, H. (1927). Beschreibung eines menschlichen Embryos.mit vier Ursegmentpaaren. Z. ges. Anat. 1. Z. Anat. Entwgesch. Bd. LXXXII.

TENNANT, R. (1921). Hernia into the Umbilical Cord. British Medical Journal, Februaby 19th.

THUNIG, A. (1936). Hernia into the Umbilical Cord and related Anomalies. Arch. of Surgery, vol. XXXIII.

PLATE I.

Fig. 1. Photograph of a wax plate reconstruction of Embryo McIntyre I. The arrows indicate the plane of the graphic reconstruction. (Text-Fig. 1A).

Figs. 2–4. Photomicrogpaphs of sections of Embryo McIntyre I. x circa 160. Description in text.

Fig. 2. Section 146.

" 3. Section 136.

" 4. Section 76.

Y = Cavity of the yolk sac.
H = Head process.
A = Archenteric canal.

PLATE I

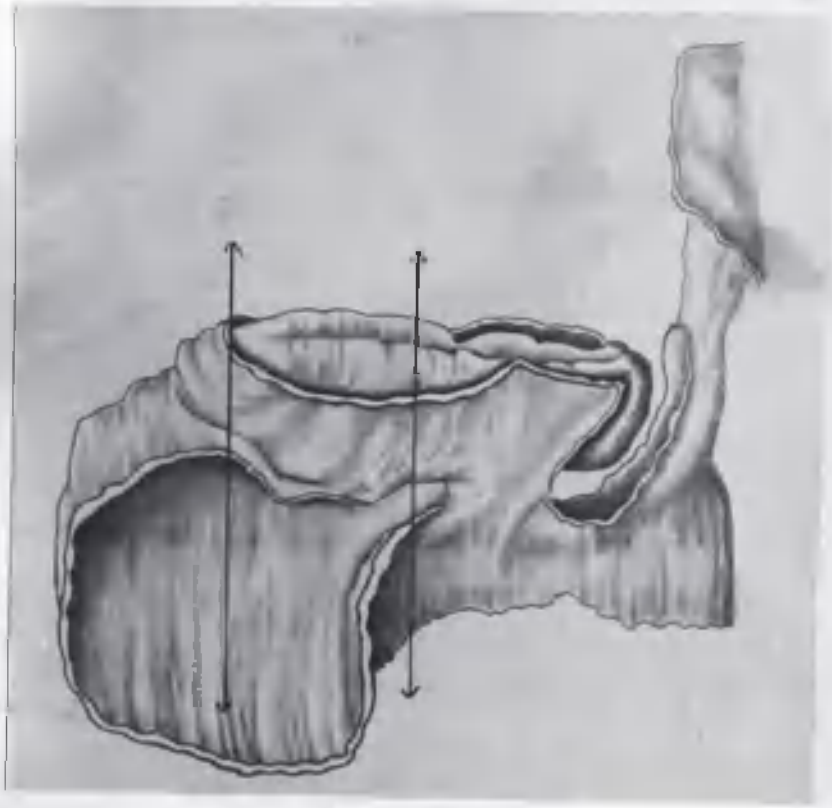


Fig. 1.

Fig. 2.

Fig. 3.

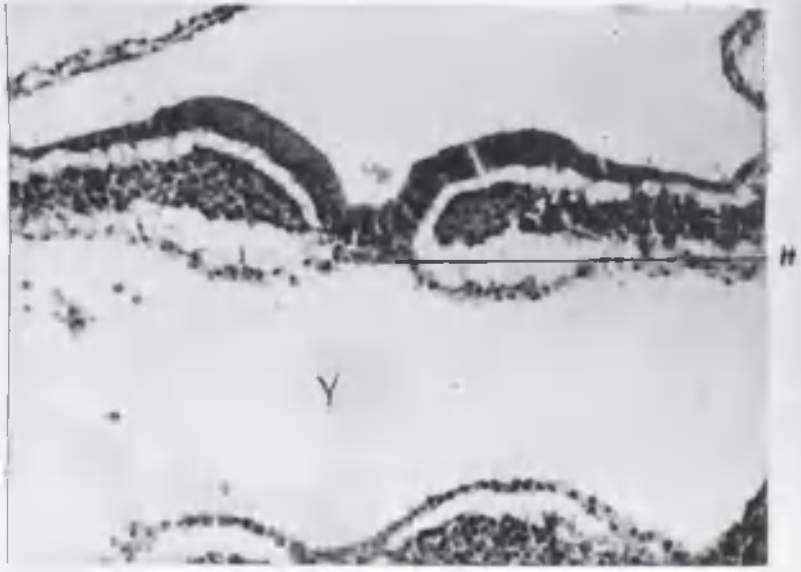


Fig. 4.

P L A T E I I .

Figs. 5-8. Photomicrographs of sections of Embryo McIntyre I. x circa 160. Description in text.

Fig. 5. Section 55.

" 6. Section 53.

" 7. Section 52.

" 8. Section 48.

Y = Cavity of yolk sac.
B.P.= Bucco-pharyngeal membrane.
M = Mesoderm.

PLATE II

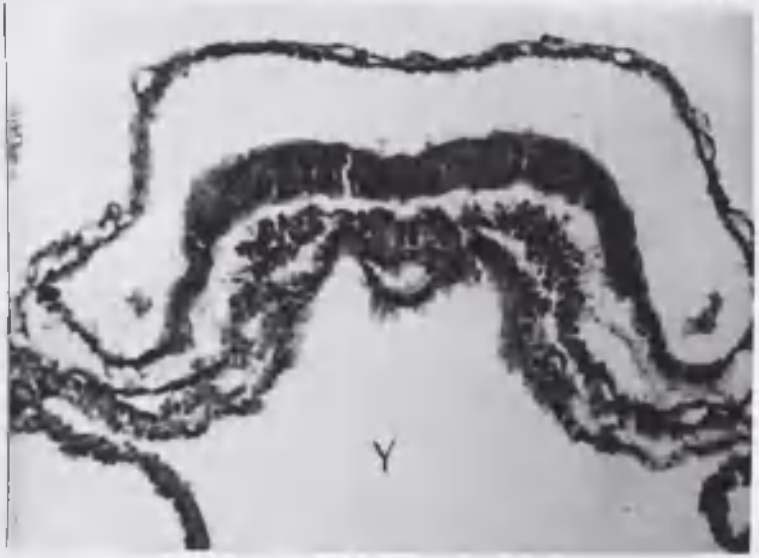


Fig. 5.

Fig. 6.

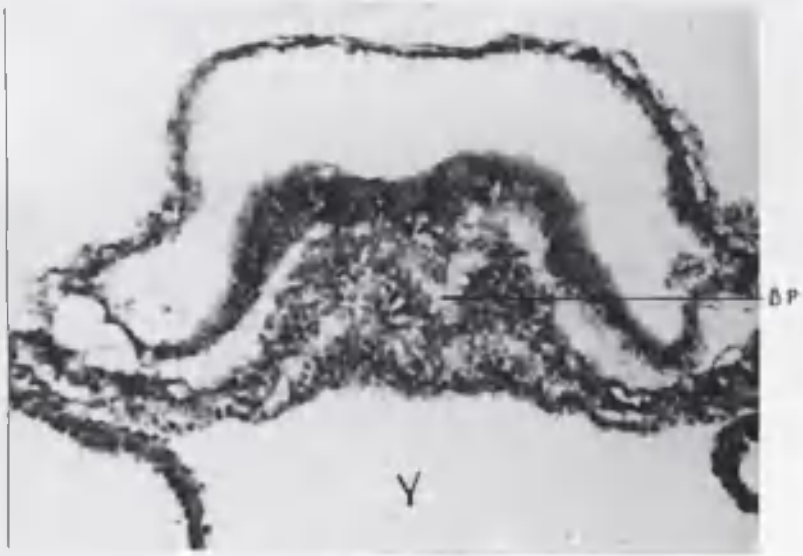


Fig. 7.

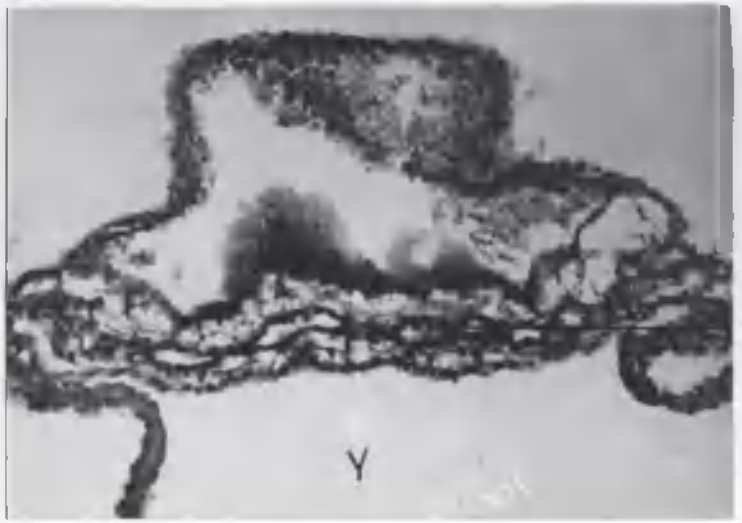


Fig. 8.

PLATE III.

Figs. 9-12. Photomicrographs of sections of Embryo 2.6 mm. x circa 75. Description in text.

Fig. 9. Section 297.

" 10. Section 304.

" 11. Section 309.

" 12. Section 302.

M = Mesoderm.
C = Coelomic passages.
L = Liver diverticulum.

PLATE III

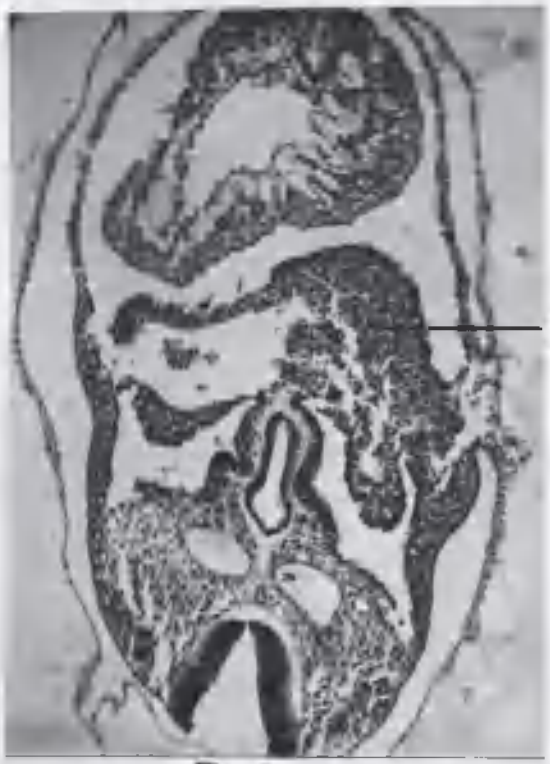


Fig. 9.

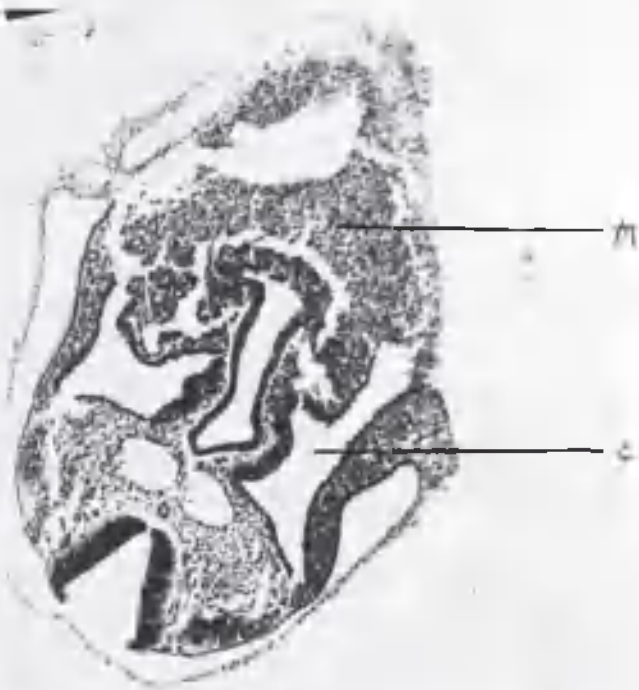


Fig. 10.

Fig. 11.

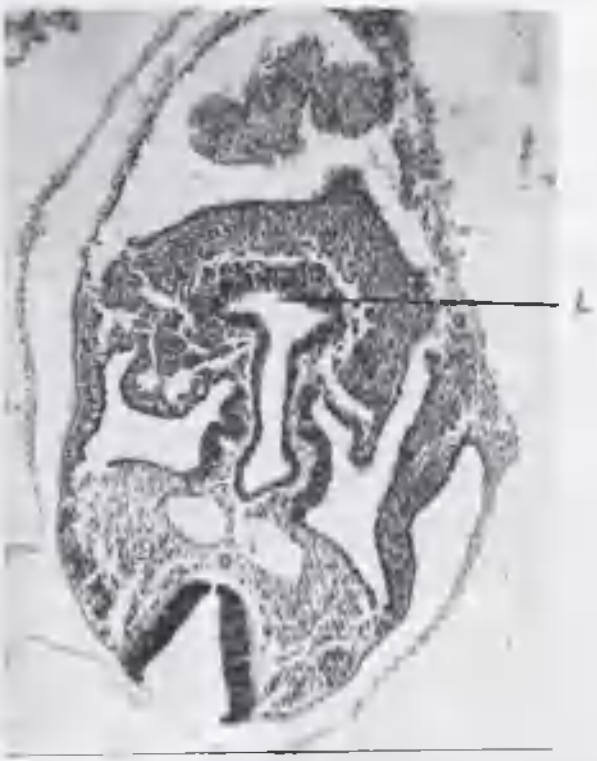


Fig. 12.

P L A T E I V .

Fig. 13 Photograph of a wax plate reconstruction of Embryo 4.5 mm. The arrows indicate the plane of the graphic reconstruction (Text-Fig. 3).

Figs.14-16. Photomicrographs of sections of Embryo 4.5 mm. Description in text.

Fig. 14. Section 156. x circa 40.

" 15. Section 200. x circa 40.

" 16. Section 203. x circa 75.

A = Reflection of amnion.

M.L.= Mesoderm with liver cells.

PLATE IV

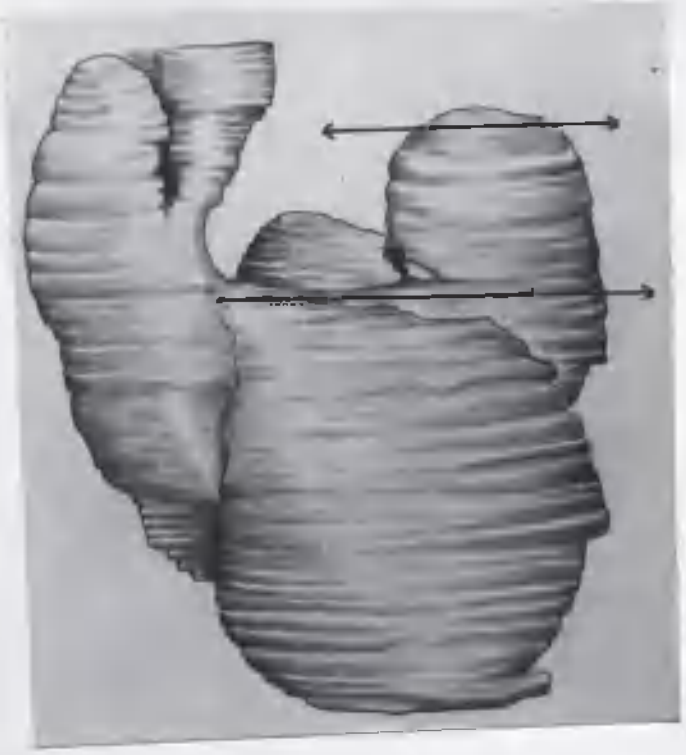


Fig. 13

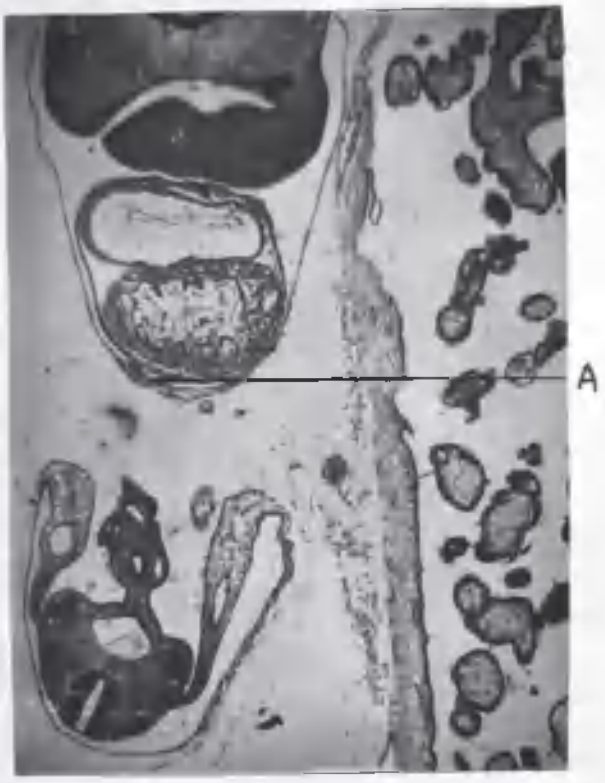


Fig. 14.

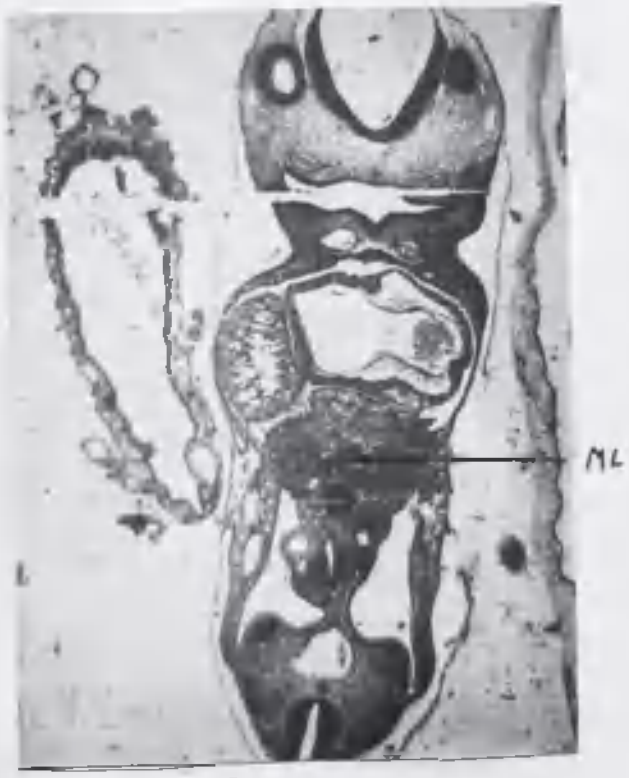


Fig. 15.

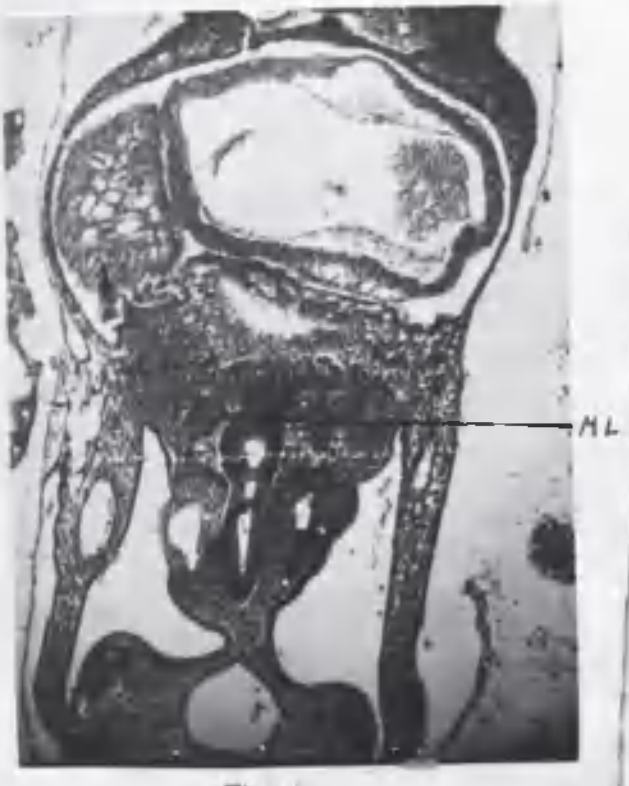


Fig. 16.

P L A T E V.

Fig. 17. Section 210 of Embryo 4.5 mm. Photomicrograph. x circa 75.

Fig. 18. Photograph of wax plate reconstruction of Embryo 7 mm. The arrows indicate the plane of the graphic reconstruction. (Text-Fig. 4A).

Figs. 19-20. Photomicrographs of sections of Embryo 7 mm. x circa 27. Description in text.

Fig. 19. Section 349.

" 20. Section 393.

C = Coelomic passage.
M = Mesoderm.
P = Pleuro-peritoneal opening.
U = Umbilical vein.

PLATE V

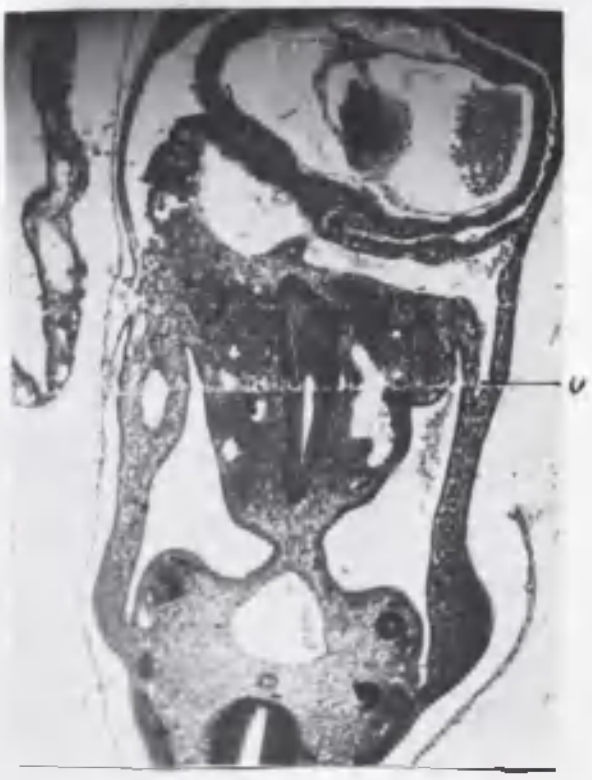


Fig. 17.

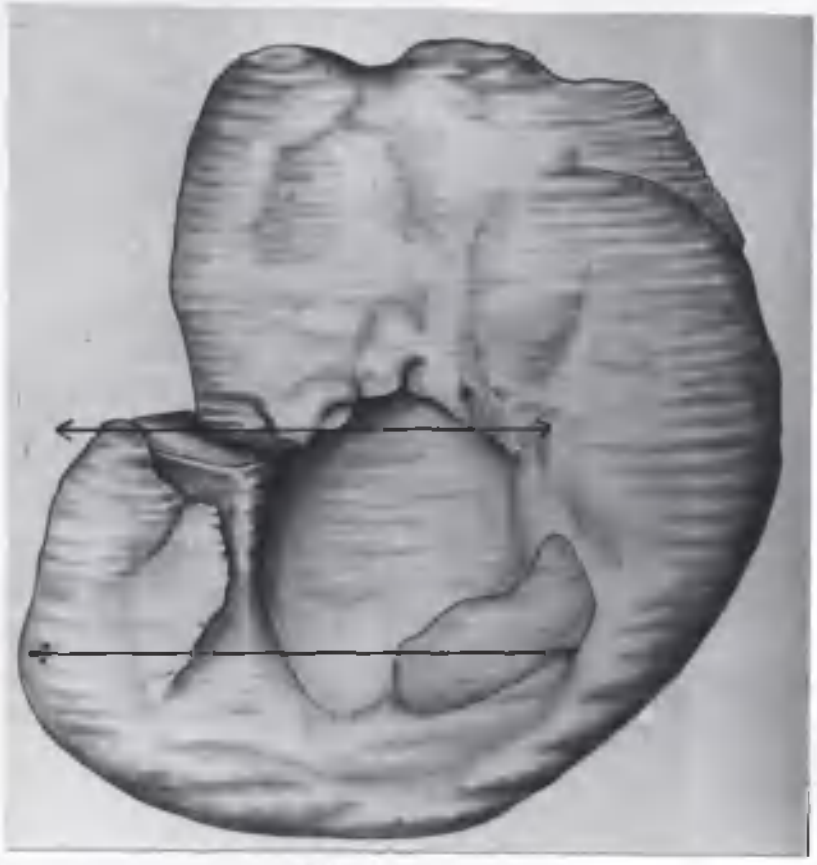


Fig. 18.

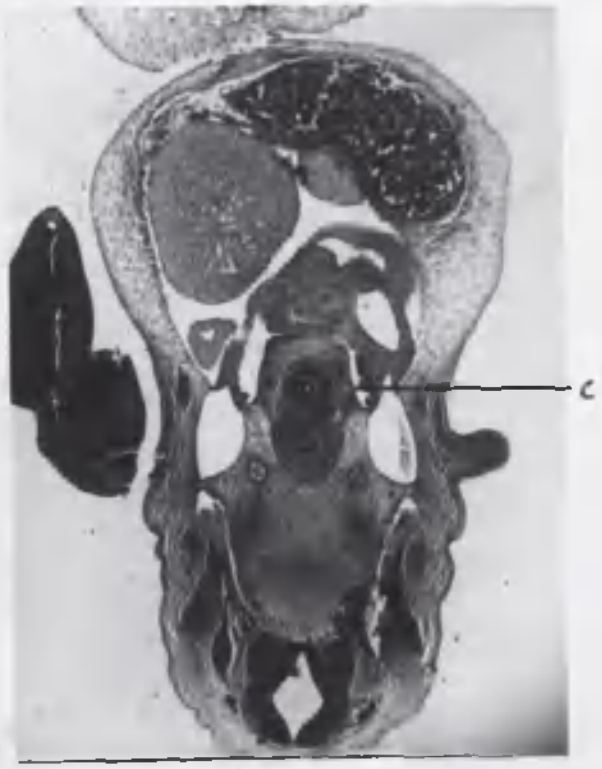


Fig. 19.

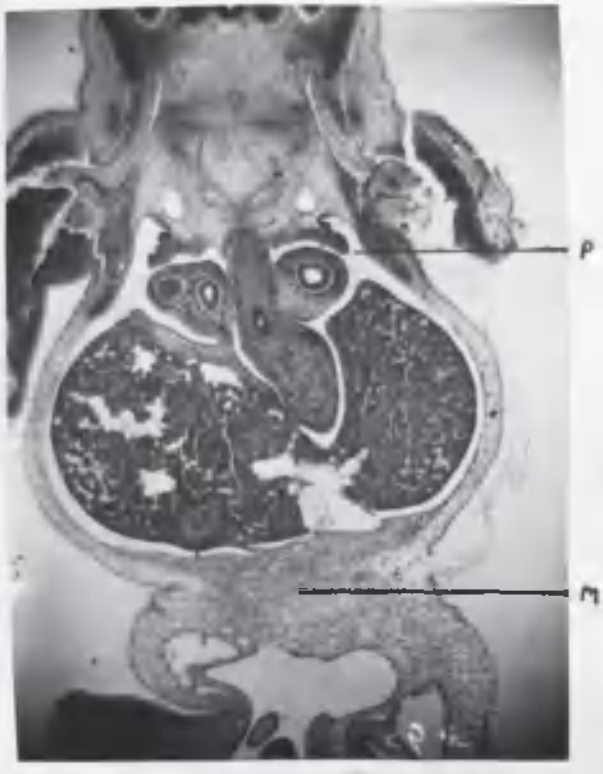


Fig. 20.

PLATE VI.

Figs. 21-23. Photomicrographs of sections of Embryo 7 mm. x circa 27. Description in text.

Fig. 21. Section 369.

" 22. Section 390.

" 23. Section 378.

Fig. 24. Section 649 of Embryo 12.5 mm. Photomicrograph. x circa 30. Description in text.

C = Coelomic passage.
P = Pleuro-peritoneal opening.

PLATE VI

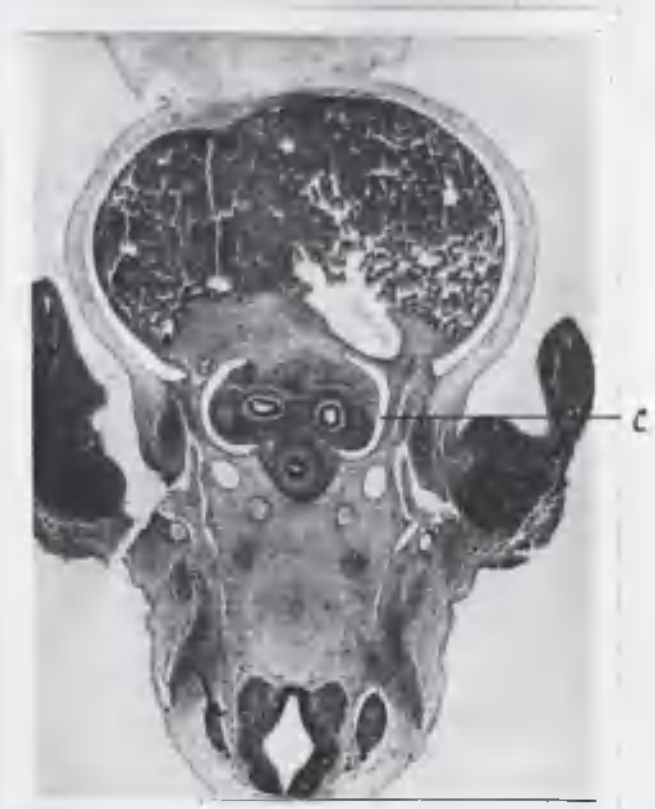


Fig. 21.

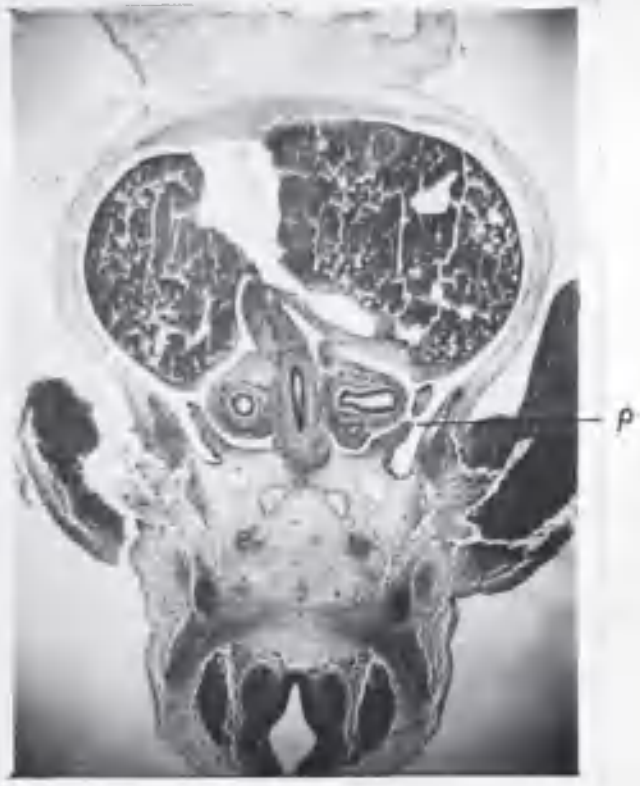


Fig. 22.

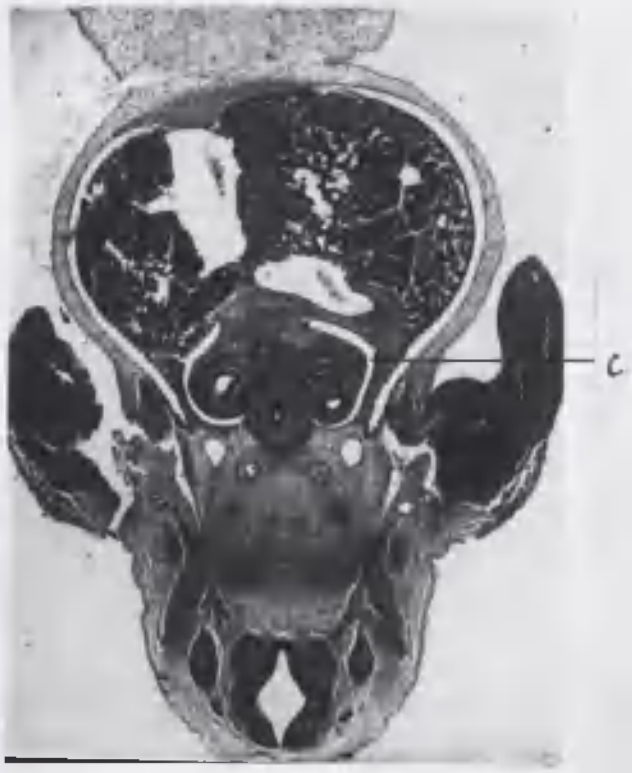


Fig. 23.

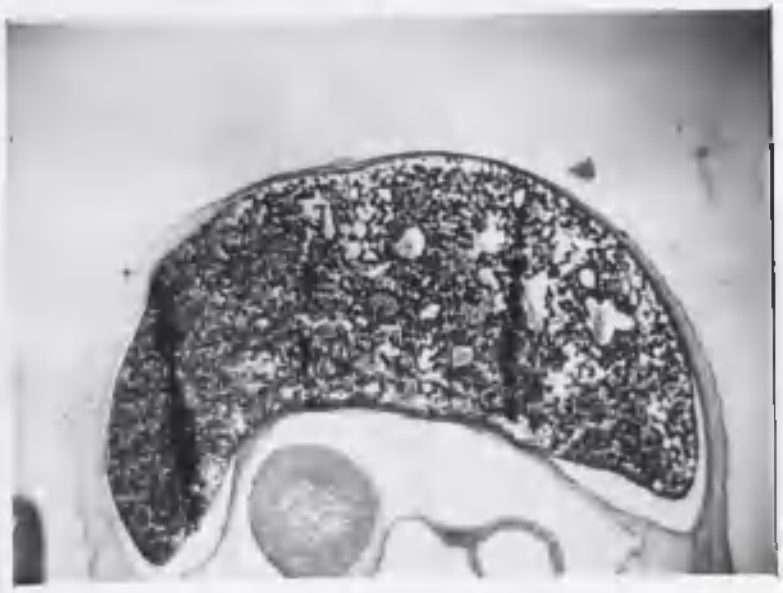


Fig. 24.

P L A T E V I I.

Figs. 25-28. Photomicrographs of sections of Embryo 12.5 mm. x circa 27. Description in text.

Fig. 25. Section 635.

" 26. Section 681.

" 27. Section 728.

" 28. Section 690.

P.P. = Pericardio-peritoneal membrane.
P.D. = Pleuro-pericardial membrane.
U. = Umbilical vein.
D.V. = Ductus venosus, opening into the sinus venosus.

PLATE VII

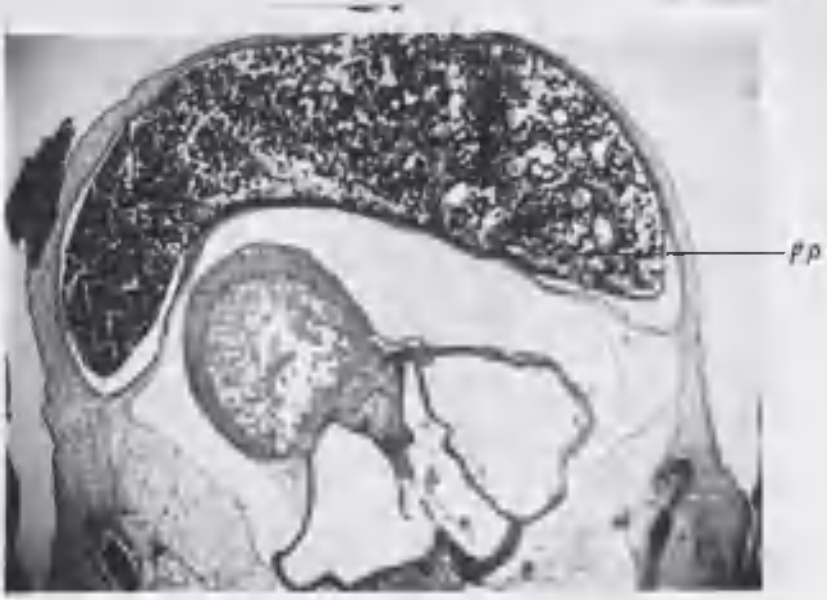


Fig. 25.

Fig. 26.

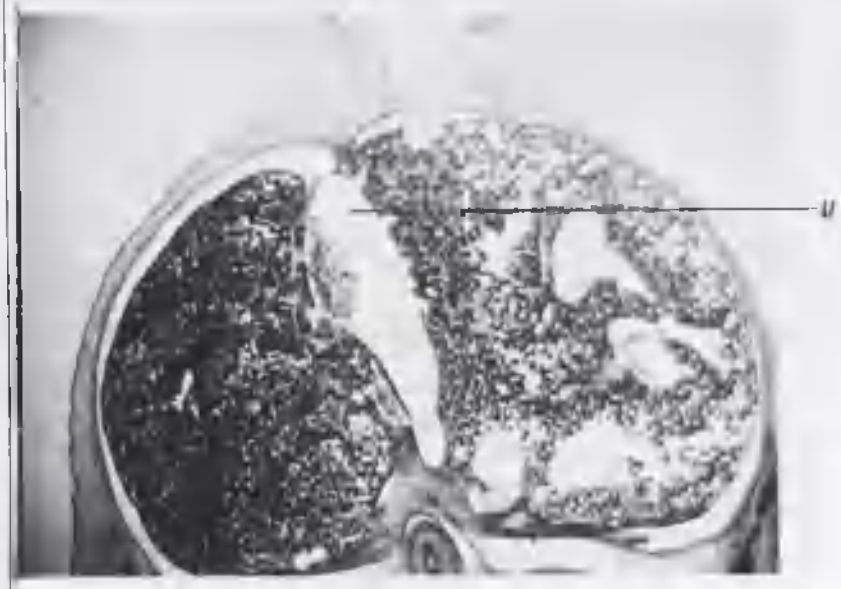


Fig. 27.

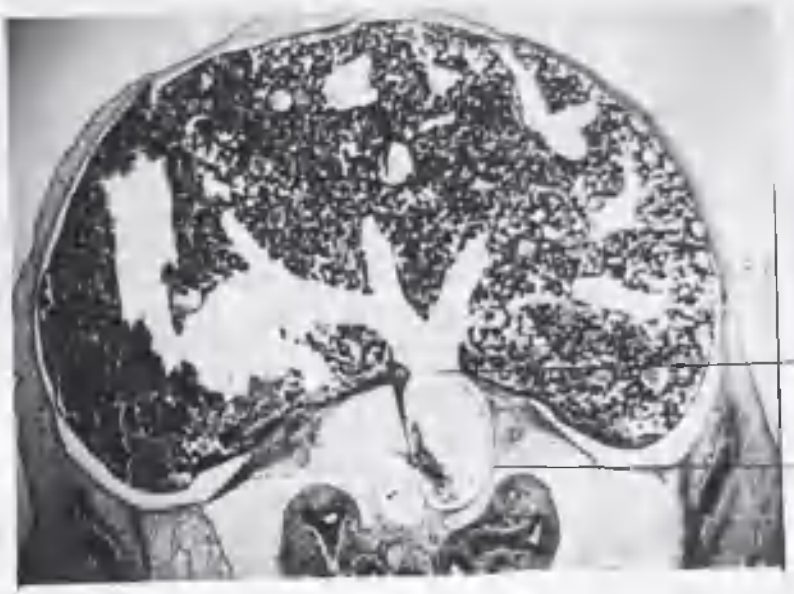


Fig. 28.

P L A T E V I I I.

Fig. 29. Section 736 of Embryo 12.5 mm.
Photomicrograph. x circa 27.
Description in text.

Figs.30-32. Photomicrographs of sections of
Embryo 14 mm. x circa 23.
Description in text.

Fig. 30. Section 731.

" 31. Section 800.

" 32. Section 820.

P.P.= Pericardio-peritoneal membrane.
P.D.= Pleuro-pericardial membrane.
Pl.P.= Pleuro-peritoneal membrane.
P = Pleuro-peritoneal opening

PLATE VIII

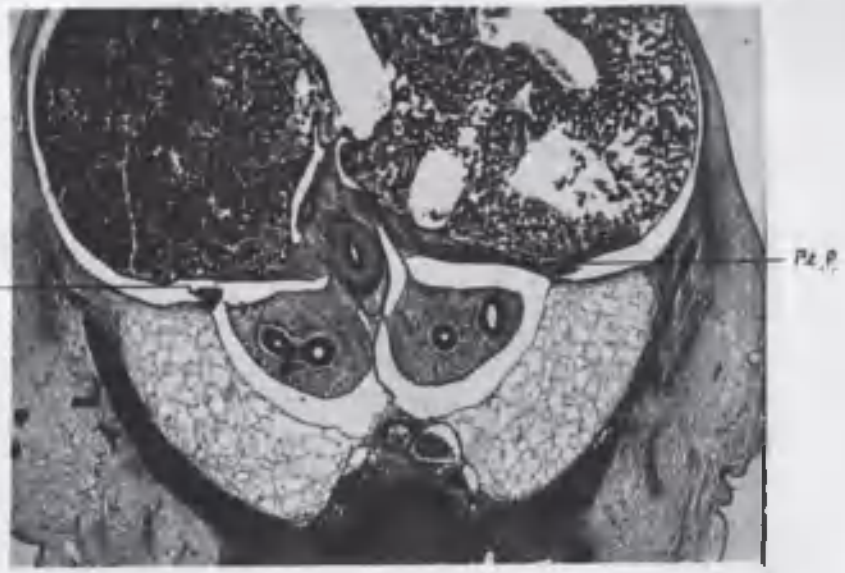


Fig. 29.

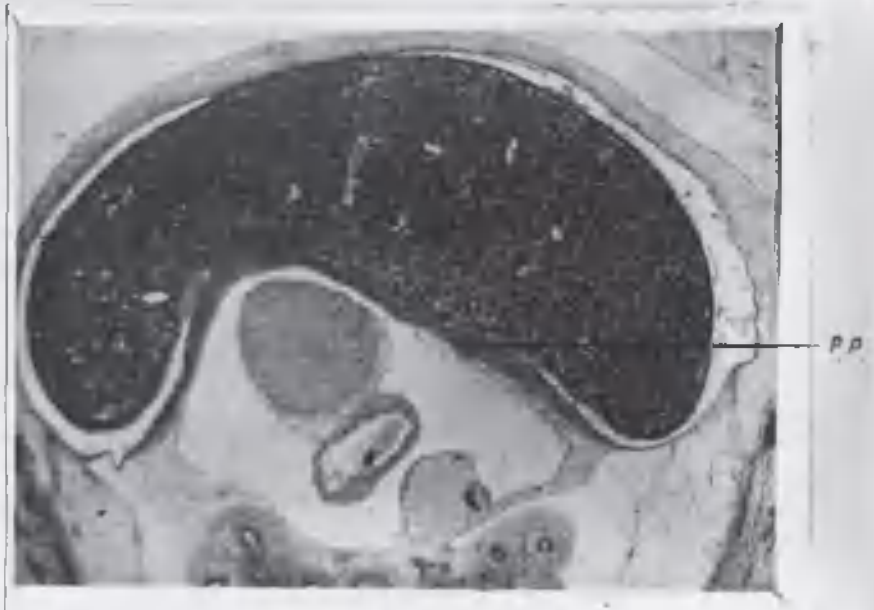


Fig. 30.

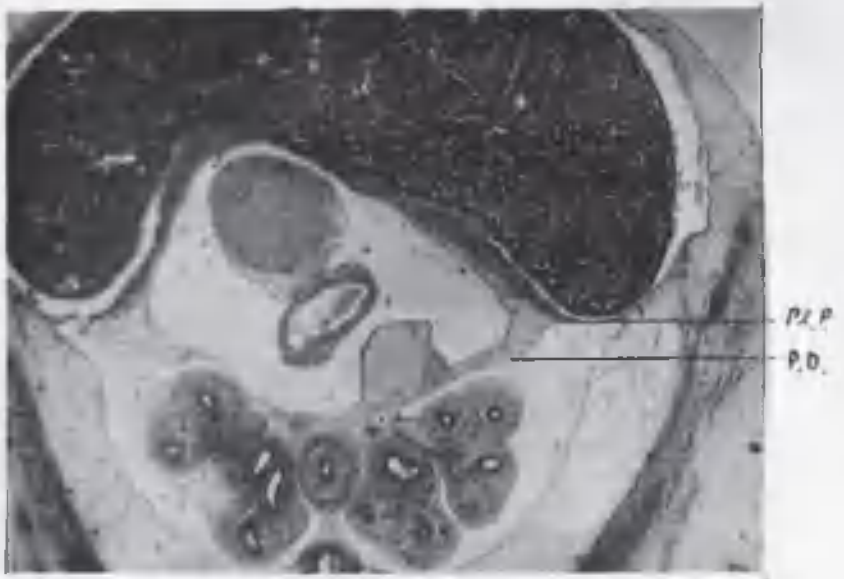


Fig. 31.

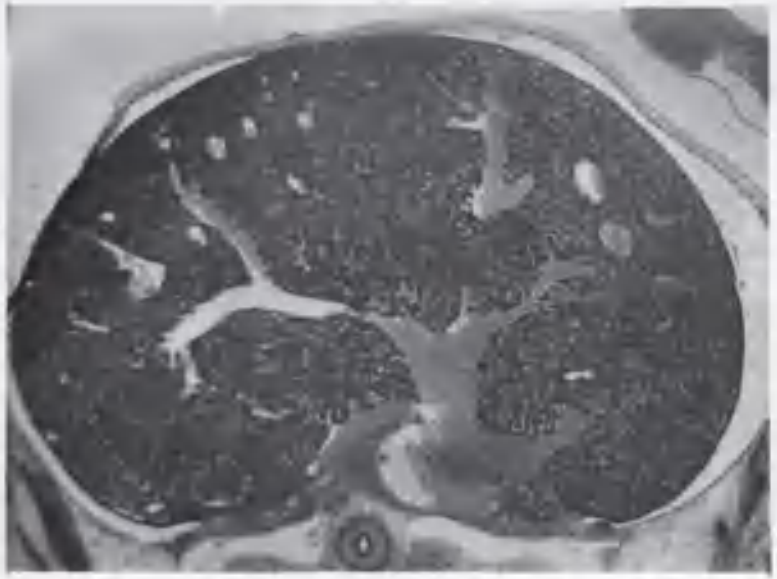


Fig. 32.

P L A T E I X.

Fig. 33. Section 851 of Embryo 14 mm. Photomicrograph. x circa 23. Description in text.

Figs.34-35. Photomicrographs of sections of Embryo 16.1 mm. x circa 19. Description in text.

Fig. 34. Section 1097.

" 35. Section 1162.

Fig. 36. Section 785 of Embryo 23 mm. Photomicrograph. x circa 16. Description in text.

P = Pleuro-peritoneal opening.
X = Paraxial downgrowth.

PLATE IX

Fig. 33.

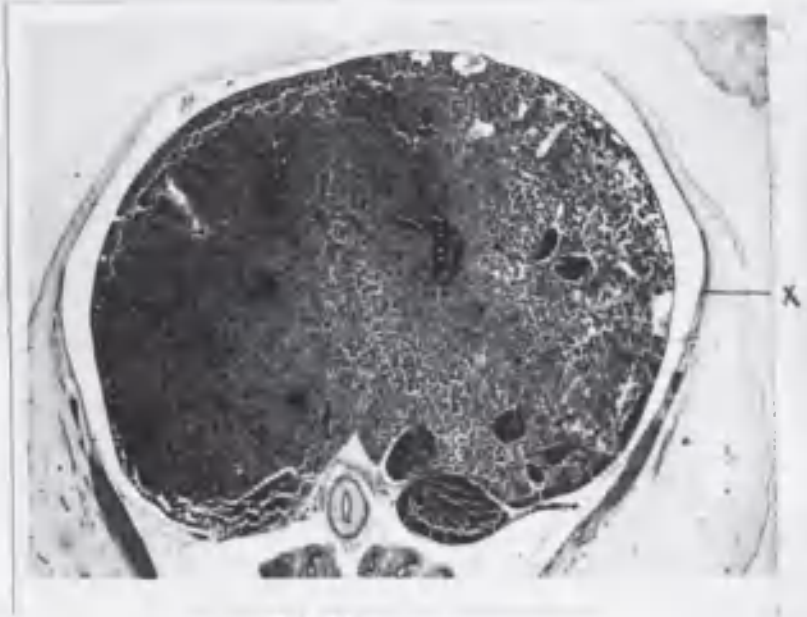


Fig. 34.

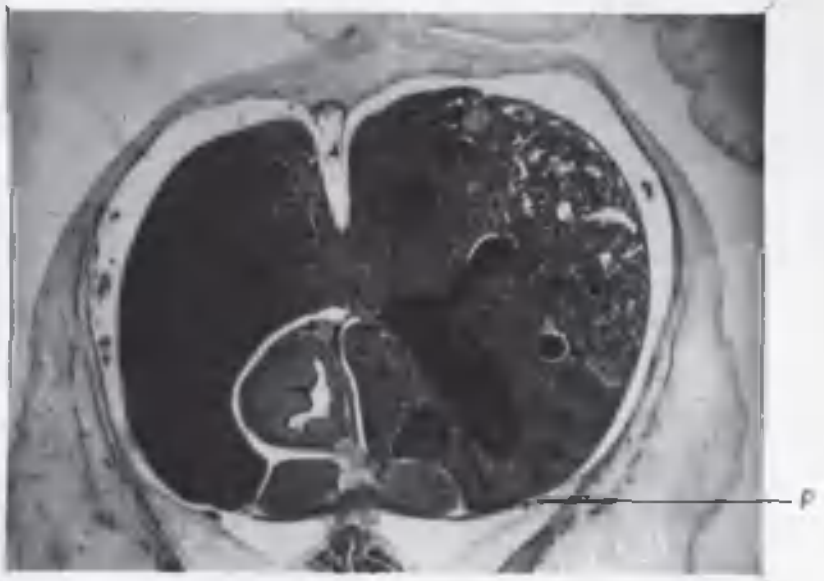


Fig. 35.

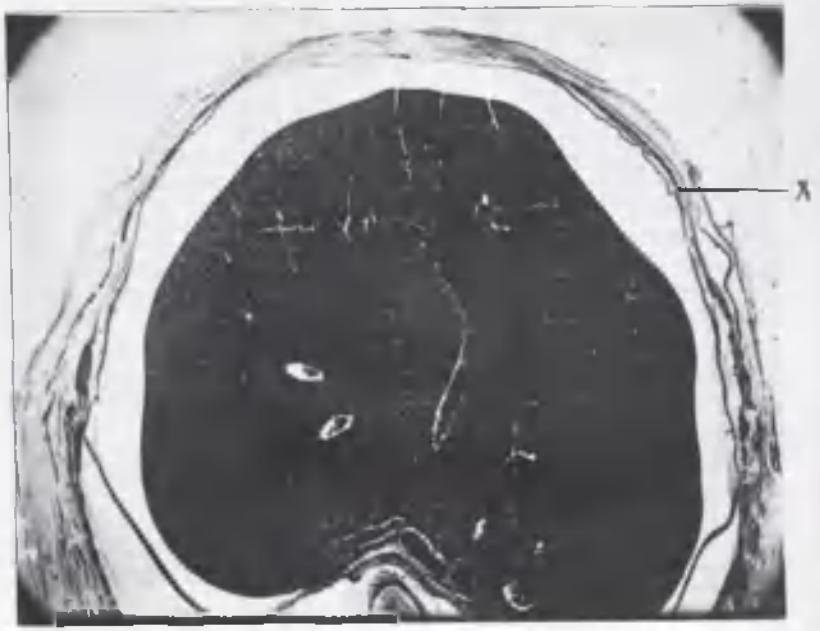


Fig. 36.

P L A T E X.

Figs.37-38. Photomicrographs of sections of Embryo 23 mm. x circa 16. Description in text.

Fig. 37. Section 743.

" 38. Section 873.

Fig. 39. Photomicrograph of Section 310 of Embry 30 mm. x circa 5. Description in text.

Pl.P.= Pleuro-peritoneal membrane.
P.D.= Pleuro-pericardial membrane.
P.P.= Pericardio-peritoneal membrane.

PLATE X

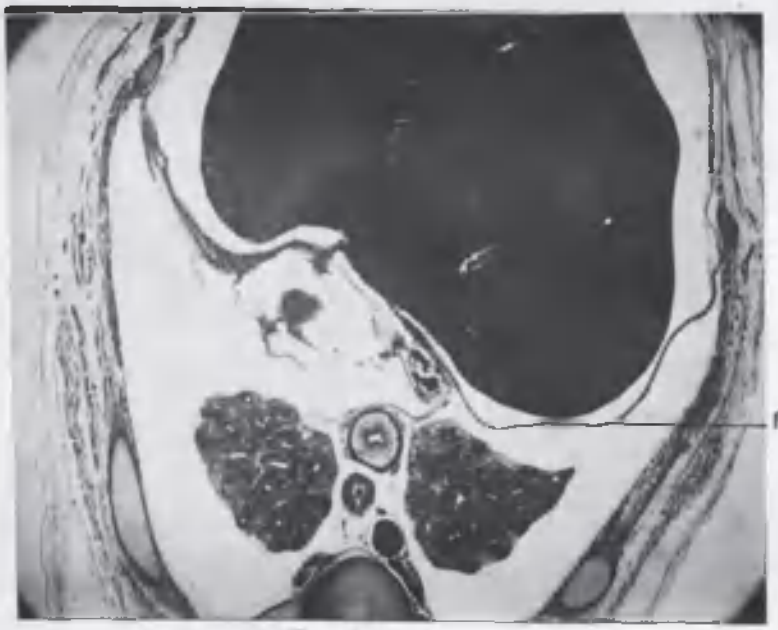


Fig. 37.

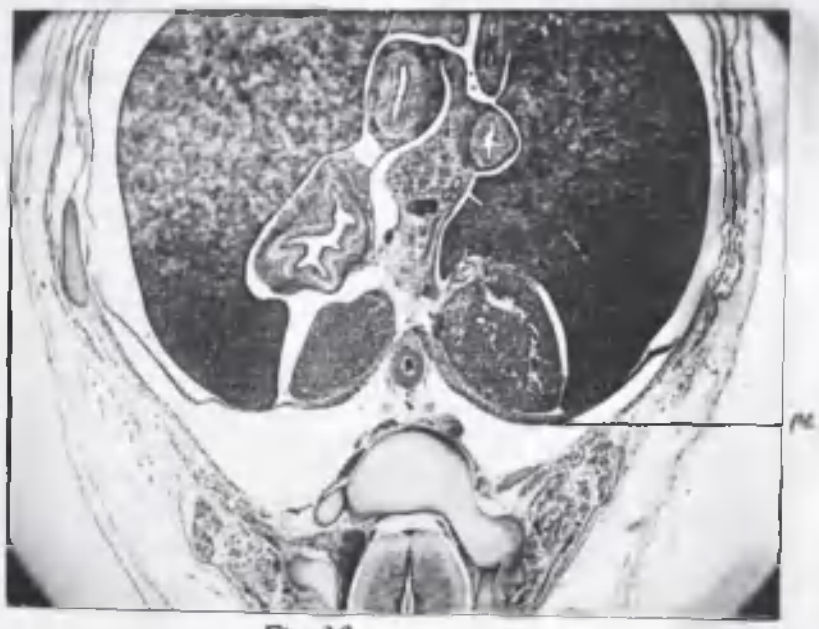


Fig. 38.

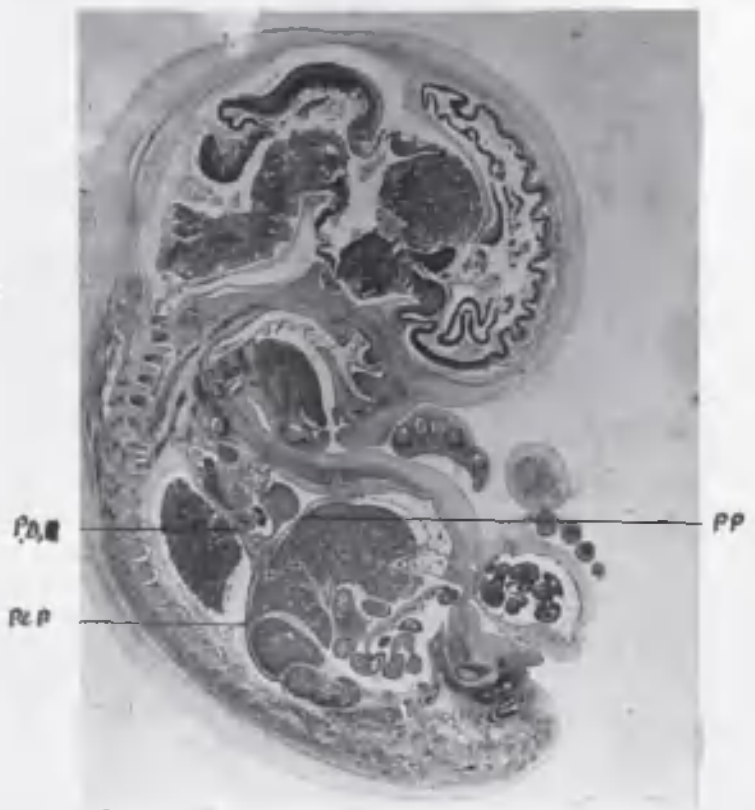


Fig. 39

P L A T E X I .

Figs.40-41. Photomicrographs of sections of Embryo 40 mm. x circa 9. Description in text.

Fig. 40. Section 1036.

" 41. Section 1109.

Fig. 42. Photograph of Specimen No. 50.115 showing eventration.

Fig. 43. Photograph of Specimen No. 50.115 showing retroflexion.

R = Recti muscles.
C = Costal fibres of diaphragm.
V = Vertebral fibres of diaphragm.

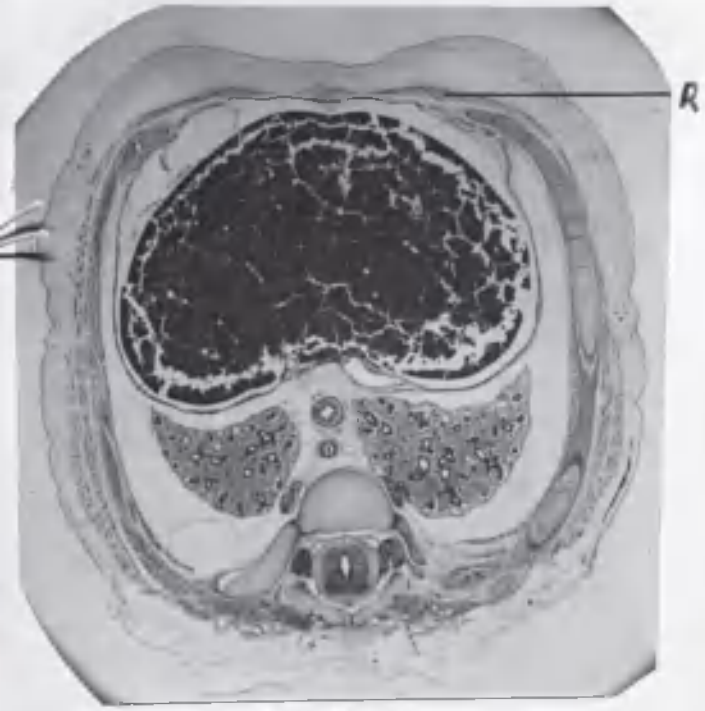


Fig. 40.

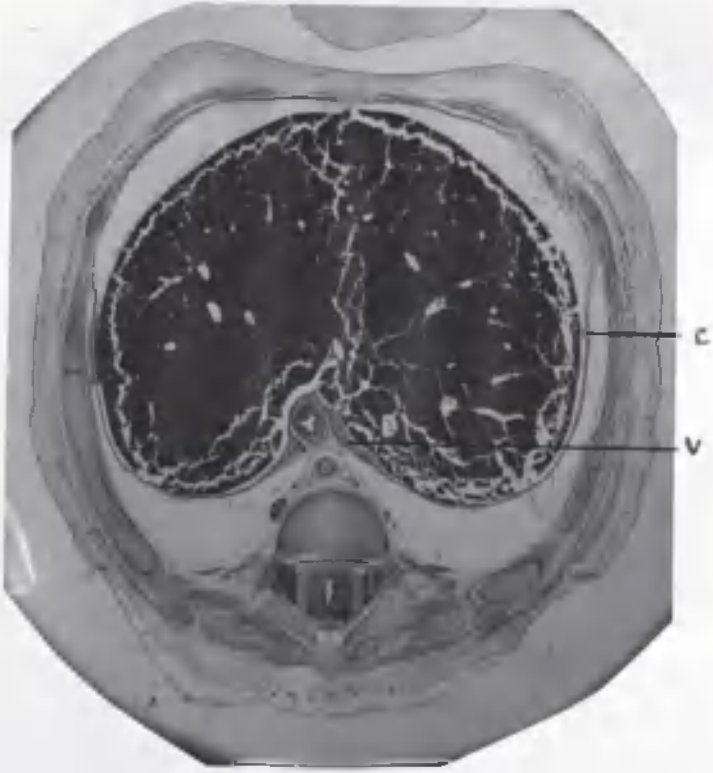


Fig. 41.

Fig. 42.

Fig. 43.

P L A T E X I I .

Figs. 44-46. Photomicrograph of sections of Embryo 2.6 mm. x circa 75. Description in text.

Fig. 47. Photomicrograph of section of Embryo 4.5 mm. x circa 75. Description in text.

A = Amnion.
L.T. Lateral Tissue Plate.

PLATE XII

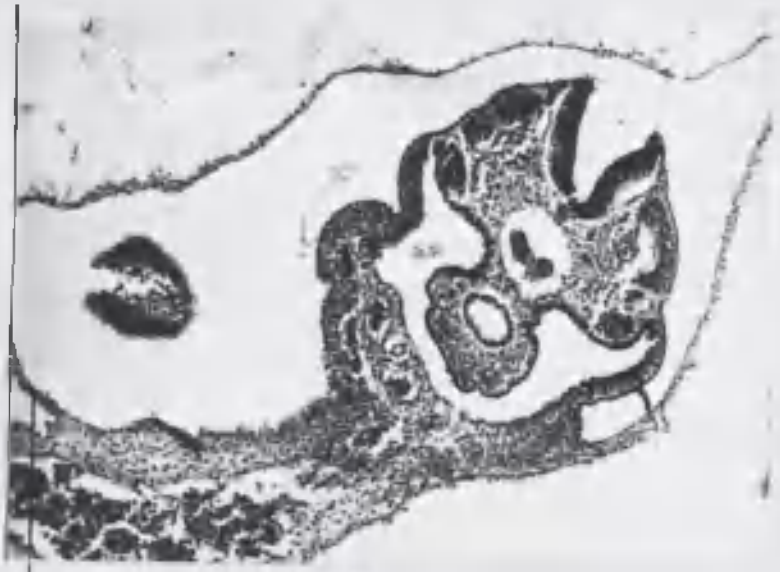


Fig. 44.

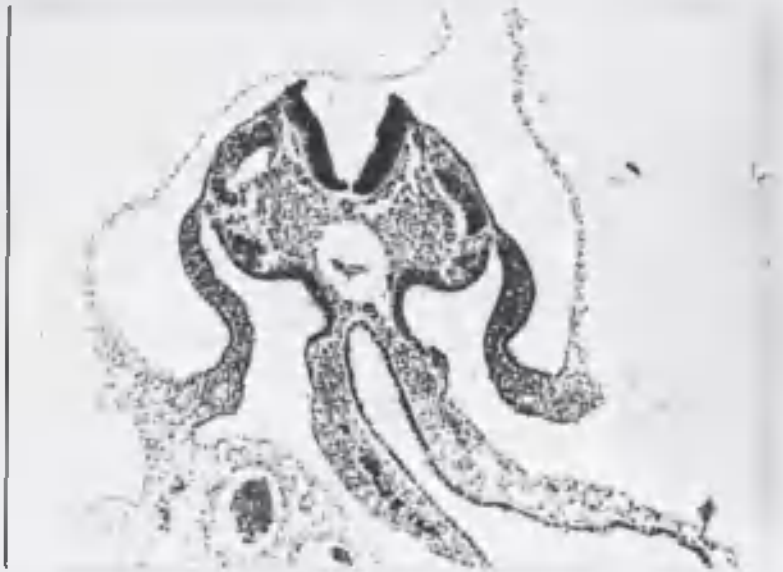


Fig. 45.

Fig. 46.

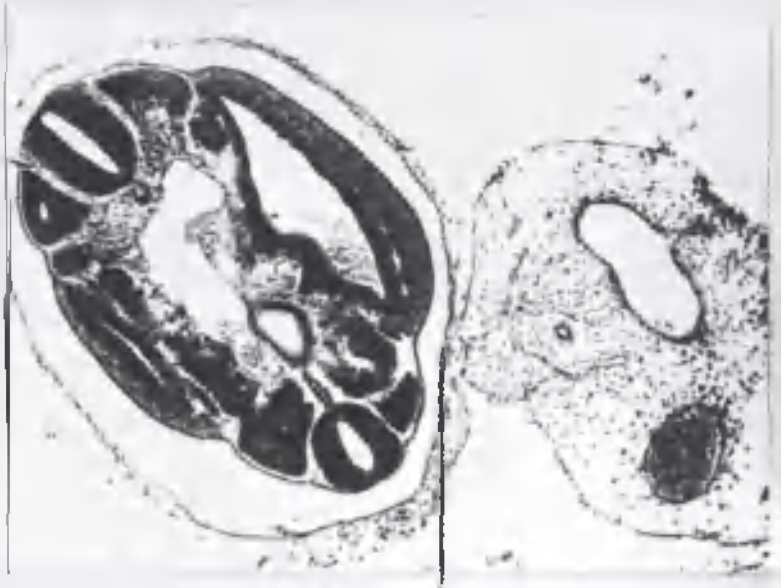


Fig. 47.

PLATE XIII.

Figs. 48-50. Photomicrographs of sections of Embryo 4.5 mm. x circa 75. Description in text.

Fig. 51. Photomicrograph of section of Embryo 7 mm. x circa 20. Description in text.

A = Amnion.
L.T.= Lateral Tissue Plate.
U = Umbilical Vein.
C = Coelom.
U.C.= Umbilical Cord Coelom.

PLATE XIII

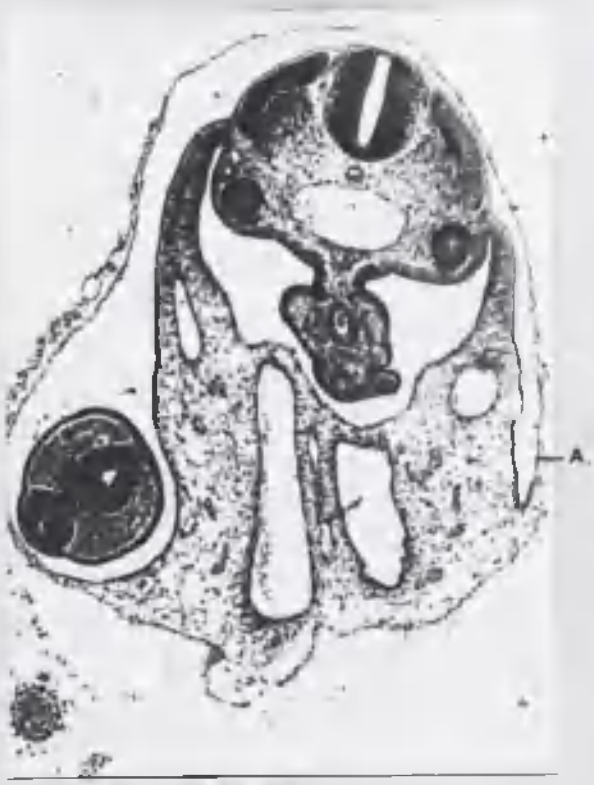


Fig. 48.

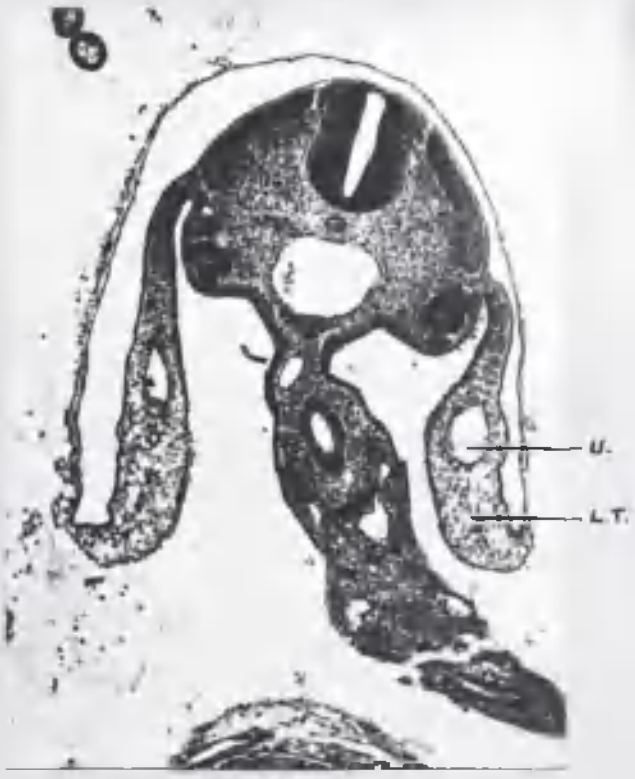


Fig. 49.

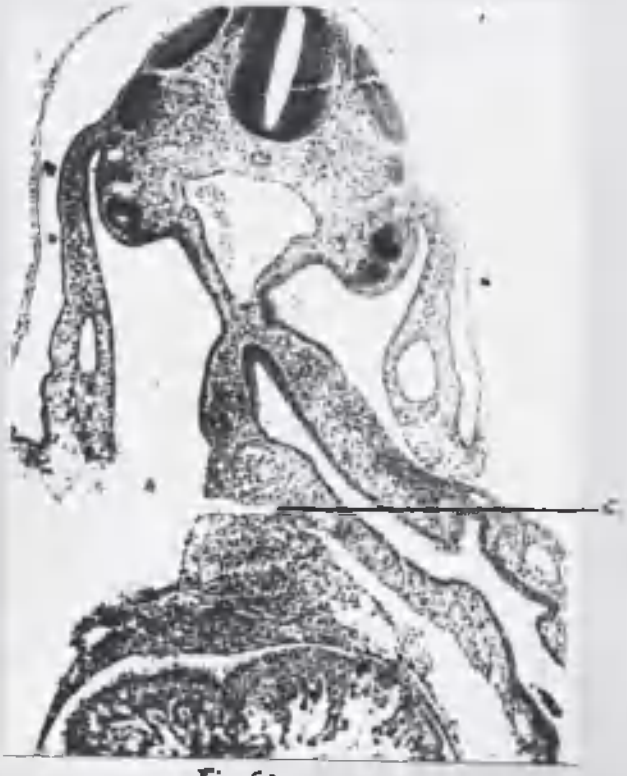


Fig. 50.

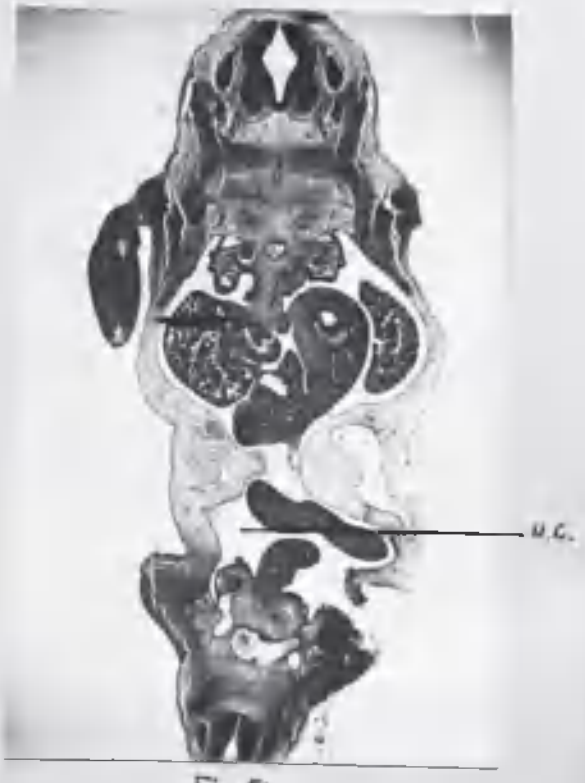


Fig. 51.

PLATE XIV.

Figs. 52-53. Photomicrographs of section of Embryo 7 mm. x circa 20.

Fig. 54. Photomicrograph of section of distal part of umbilical cord of Embryo 7 mm. x circa 100.

Fig. 55. Photomicrograph of section of Embryo 8.5 mm. x circa 20.

U.C.= Umbilical cord coelom.
I = Intercoelomic septum.
D = Distal slit-like part of umbilical cord coelom.
S = Space in umbilical cord.

Description in text.

PLATE XIV.

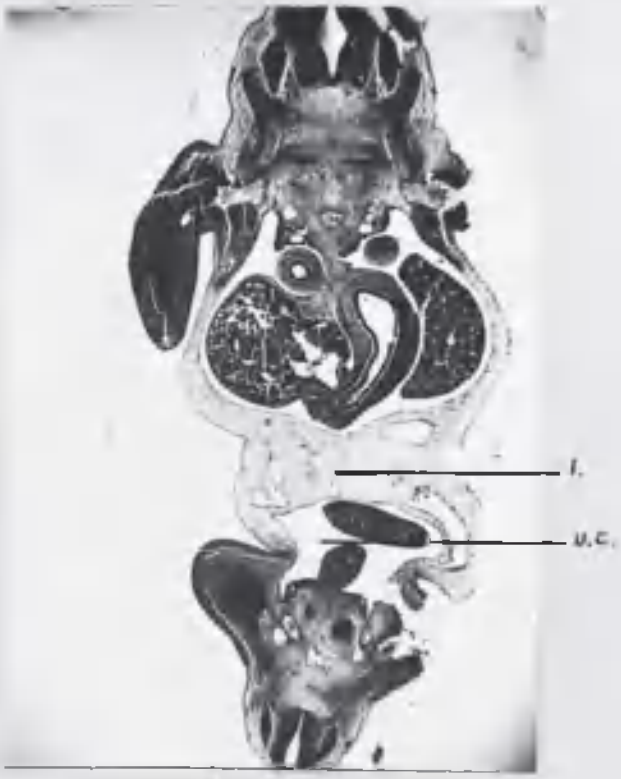


Fig. 52.

Fig. 53.

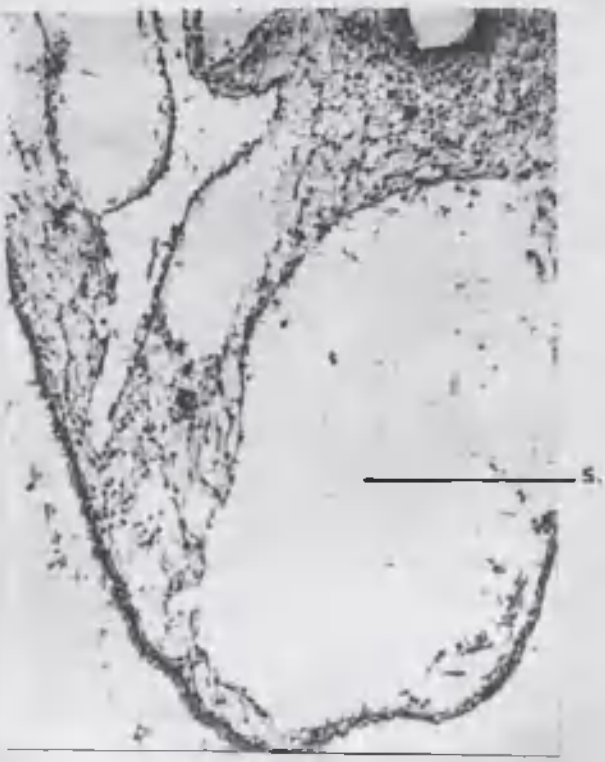


Fig. 54.

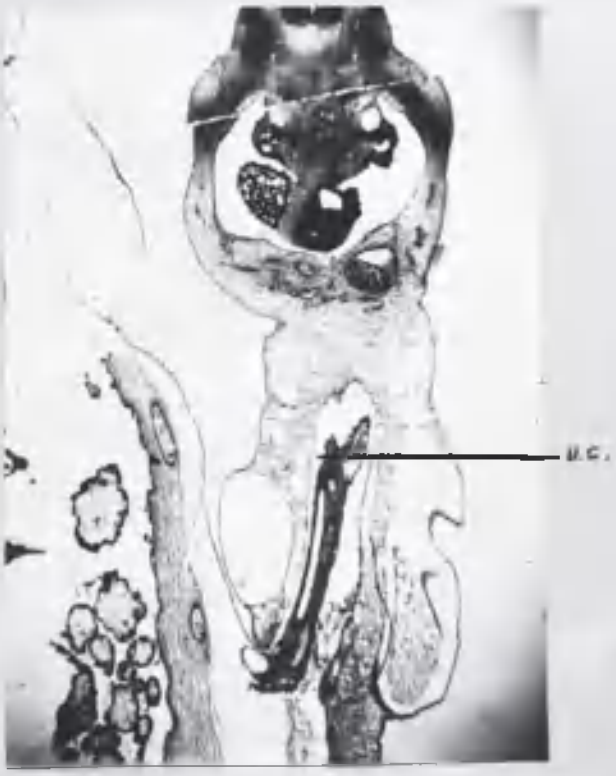


Fig. 55.

PLATE XV.

Figs. 56-57. Photomicrographs of sections of Embryo 8.5 mm. x circa 20.

Figs. 58-59. Photomicrographs of sections of Embryo 12.5 mm. x circa 14.

U = Umbilical vein.
U.C.= Umbilical cord coelom.
I = Intercoelomic septum - with denser mesoderm.
M = Myotomic downgrowth.

Description in text.

PLATE XV

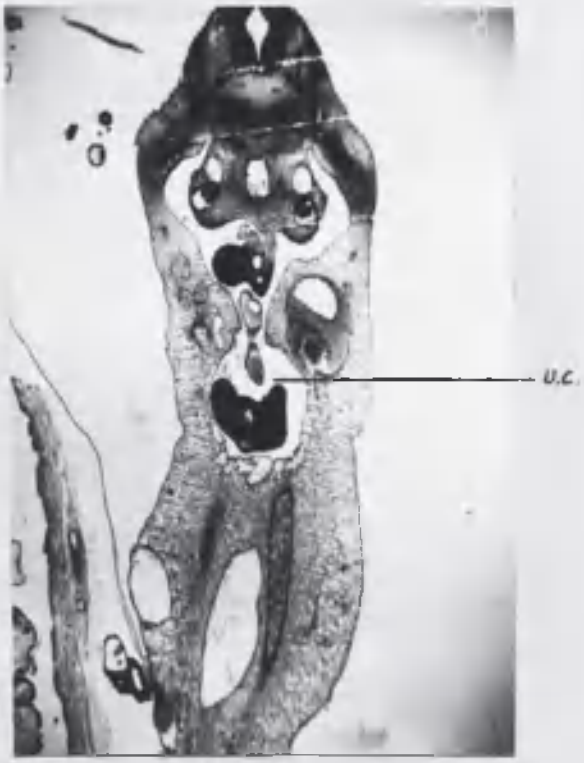


Fig. 56.

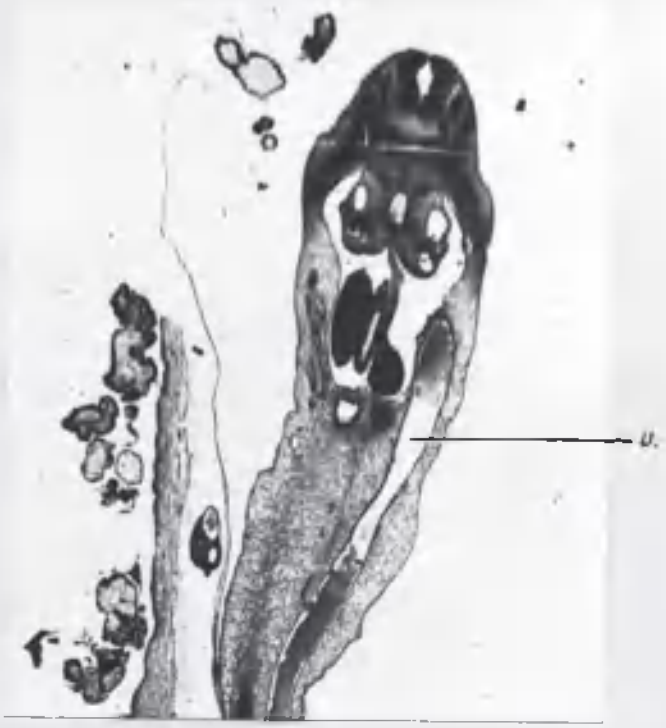


Fig. 57.

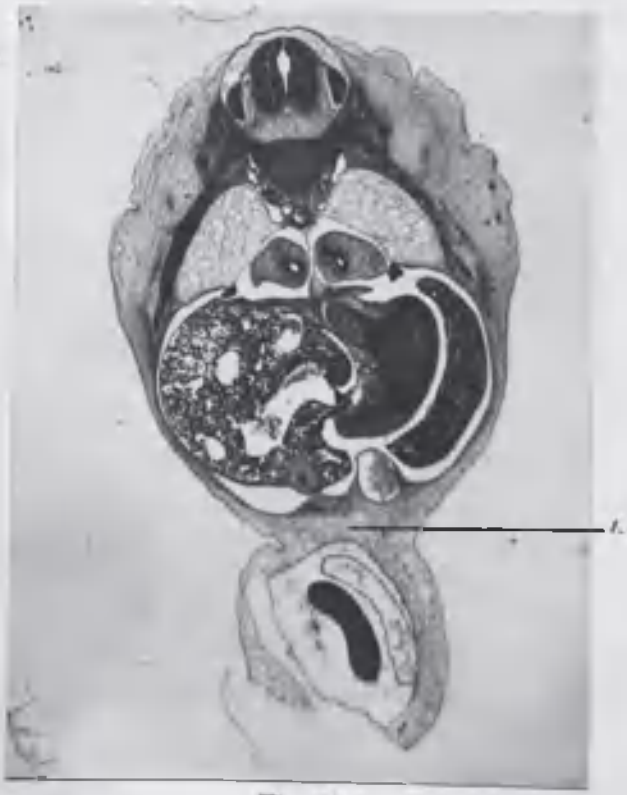


Fig. 58.

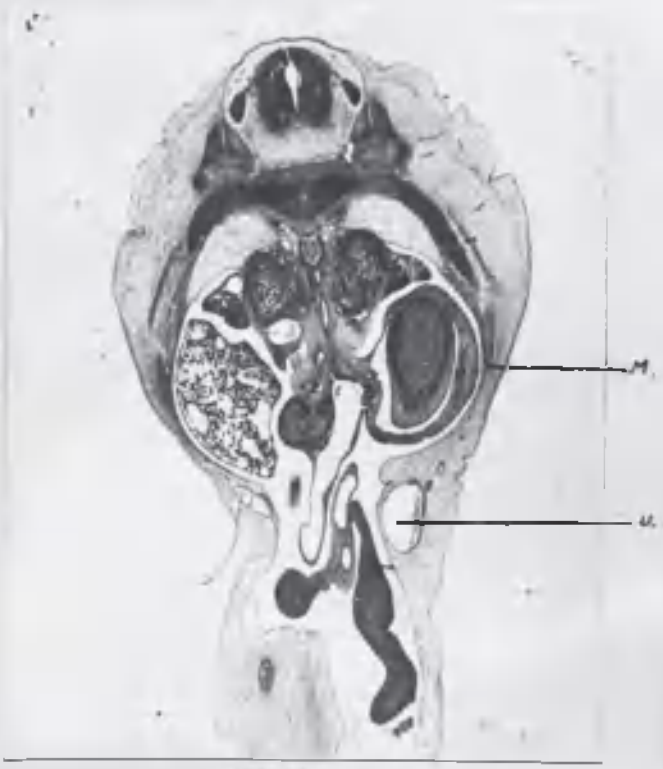


Fig. 69.

PLATE XVI.

Fig. 60. Photomicrograph of section of Embryo 12.5 mm. x circa 14.

Fig. 61. Photomicrograph of section of distal part of umbilical cord of Embryo 14 mm. x circa 25.

Figs. 62-63. Photomicrographs of sections of Embryo 14 mm. x circa 14.

D = Extension of umbilical cord coelom into distal part of the cord.
M = Myotomic downgrowths.
I = Intercoelomic septum with denser mesoderm around umbilical vein.

Description in text.

PLATE XVI

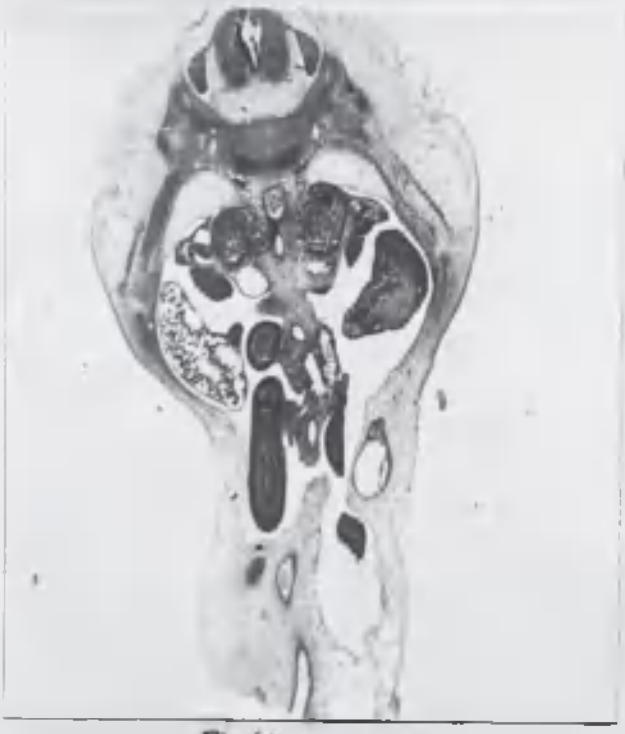


Fig. 60.

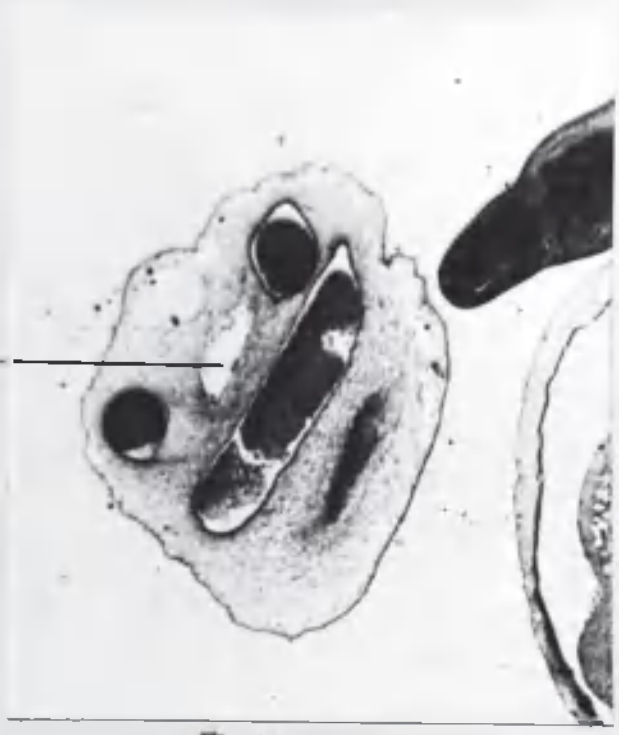


Fig. 61.

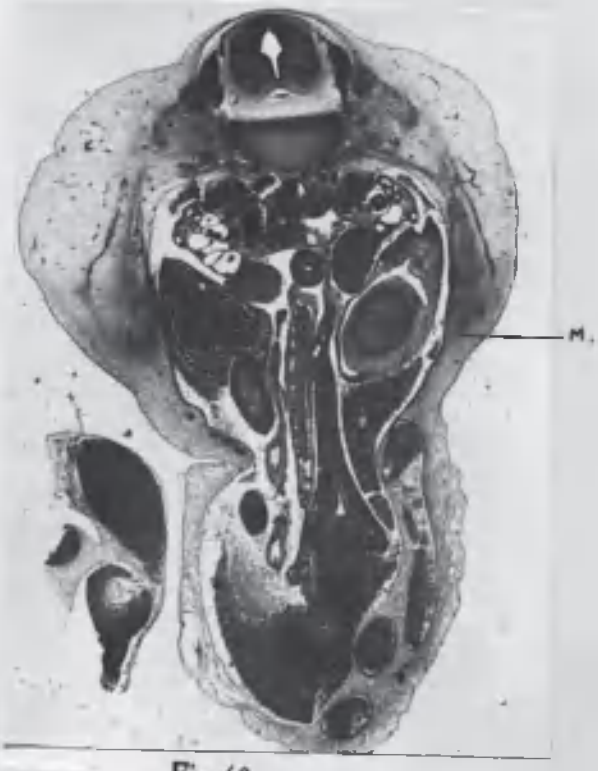


Fig. 62.

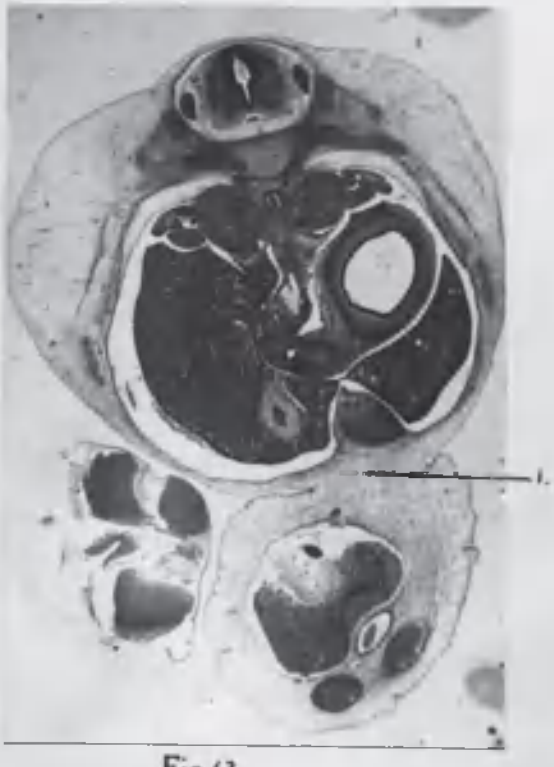


Fig. 63.

P L A T E X V I I .

Fig. 64. Photomicrograph of section of Embryo 16.1 mm. x circa 19.

Figs. 65-66. Photomicrographs of sections of Embryo 16.1 mm. x circa 12.

Fig. 67. Photomicrograph of section of Embryo 23 mm. x circa 12.

E = Denser connective tissue in the midventral line extending into the cord.
S = "Stalk" tissue.

Description in text.

PLATE XVII

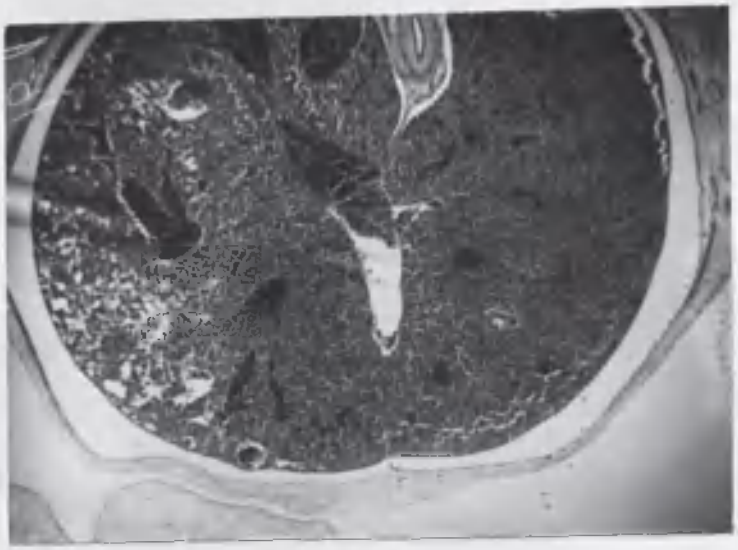


Fig. 64.

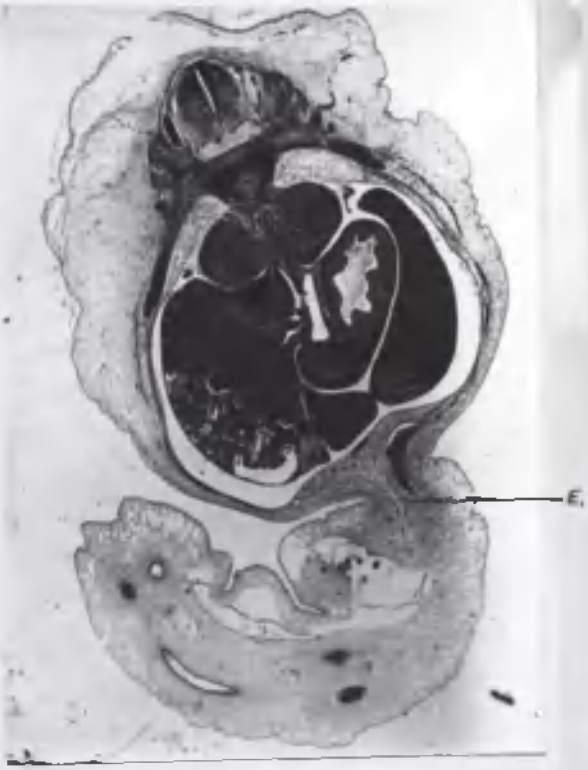


Fig. 65.

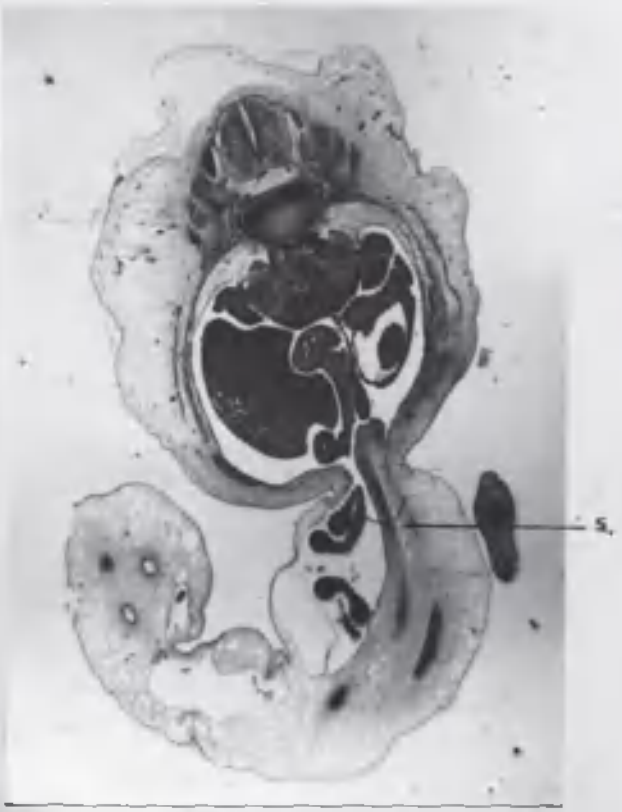


Fig. 66.

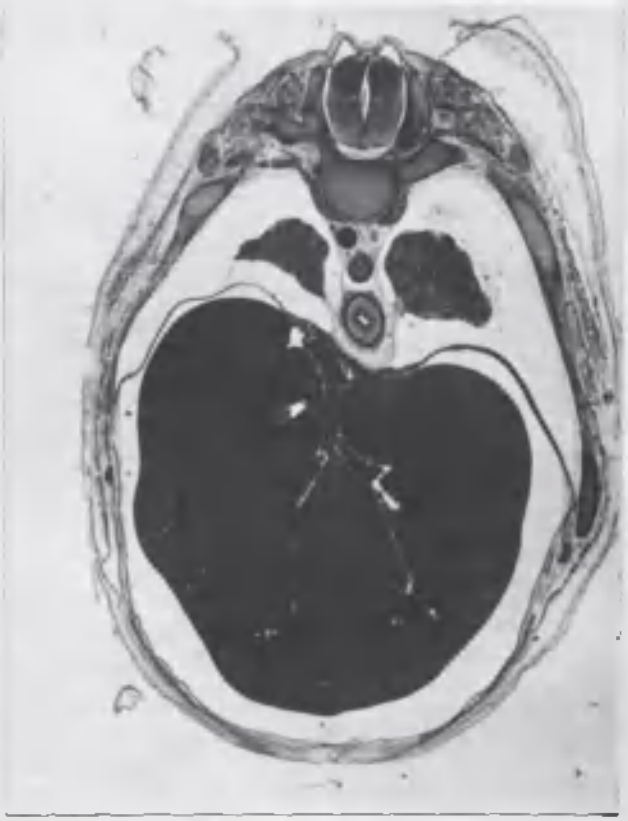


Fig. 67.

PLATE XVIII.

Fig. 68. Photomicrograph of section of Embryo 23 mm. x circa 12.

Fig. 69. Photomicrograph of section of Embryo 23 mm. x circa 8.

Figs. 70-71. Photomicrographs of sections of Embryo 40 mm. x circa 7.

E = Denser tissue in mid ventral line extending into the cord.

Description in text.

PLATE XVIII

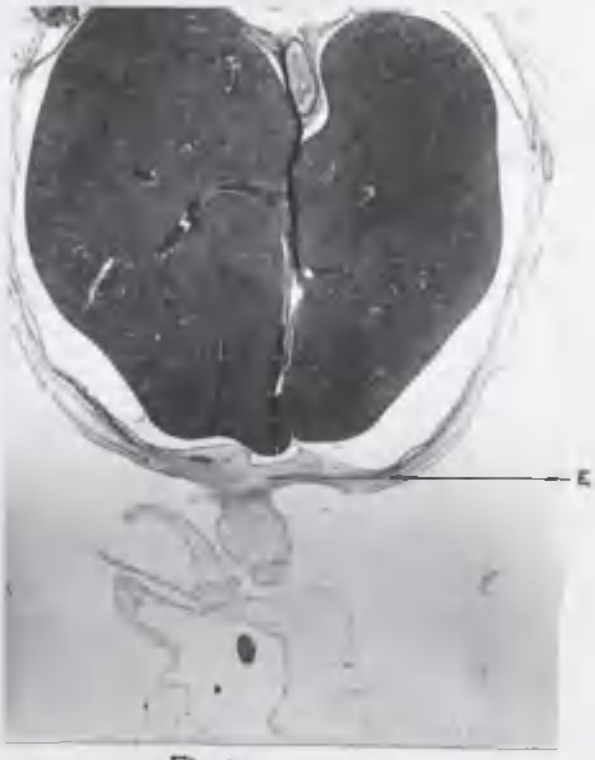


Fig. 68.

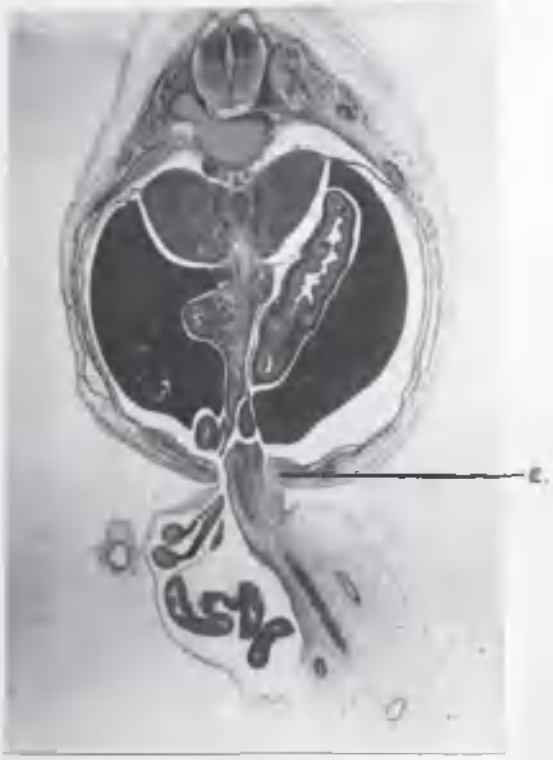


Fig. 69.

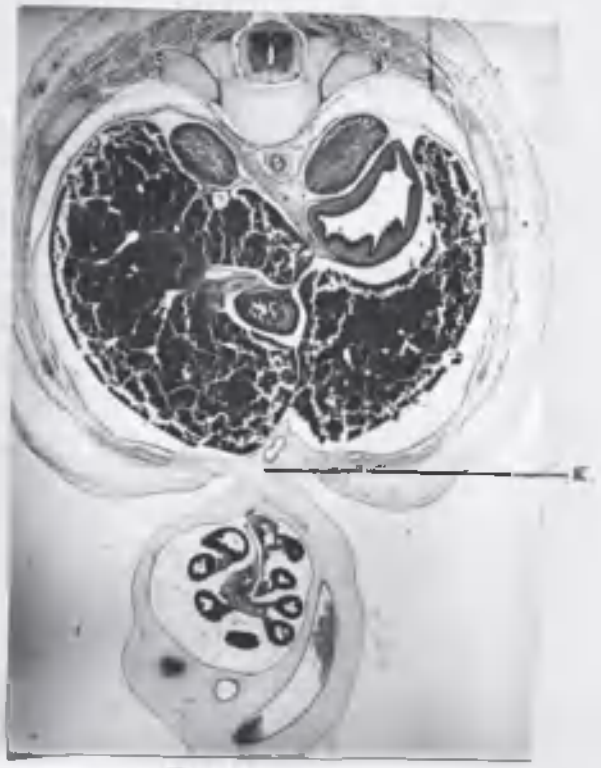


Fig. 70.

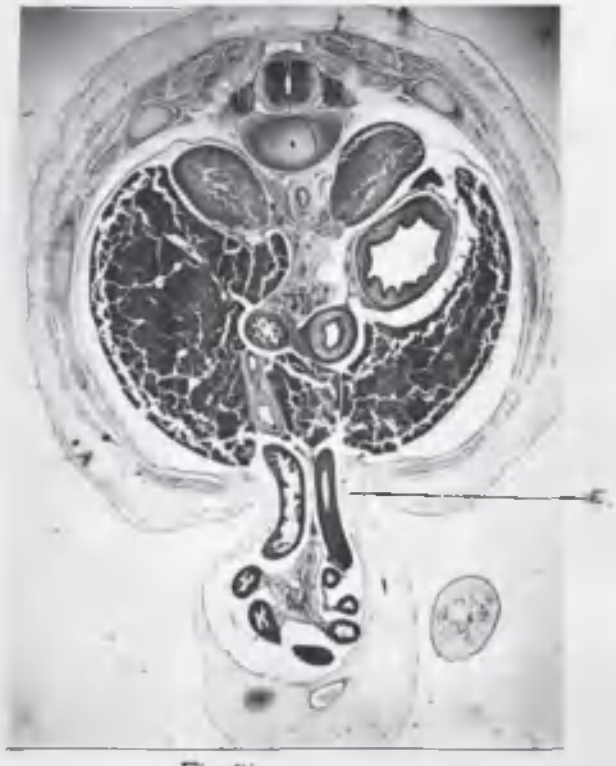


Fig. 71.

P L A T E X I X .

Fig. 72. Photomicrograph of section of Embryo 40 mm. x circa 7.

Fig. 73. Photomicrograph of distal section of umbilical cord of Embryo 40 mm. x circa 25.

Figs. 74-75. Photomicrographs of sections of Embryo 42 mm A. x circa 10.

D = Extension of umbilical cord coelom into distal part of cord.
E = Denser tissue in mid ventral line extending into the cord.

Description in text.

PLATE XIX

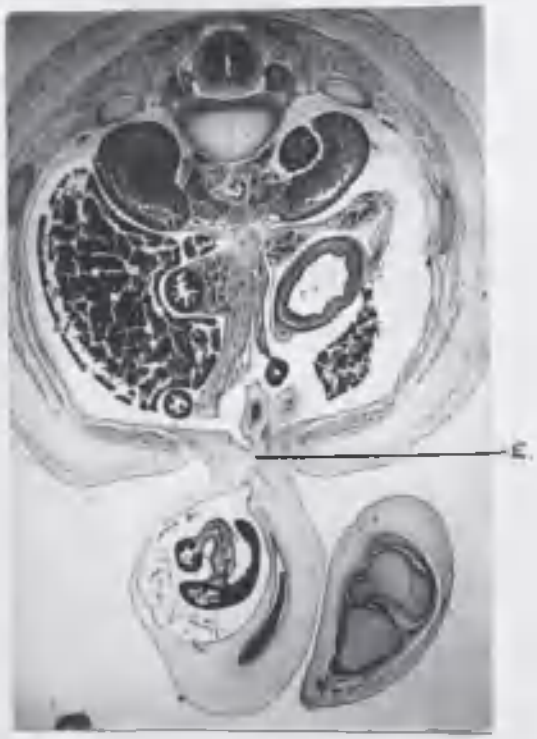


Fig. 72.

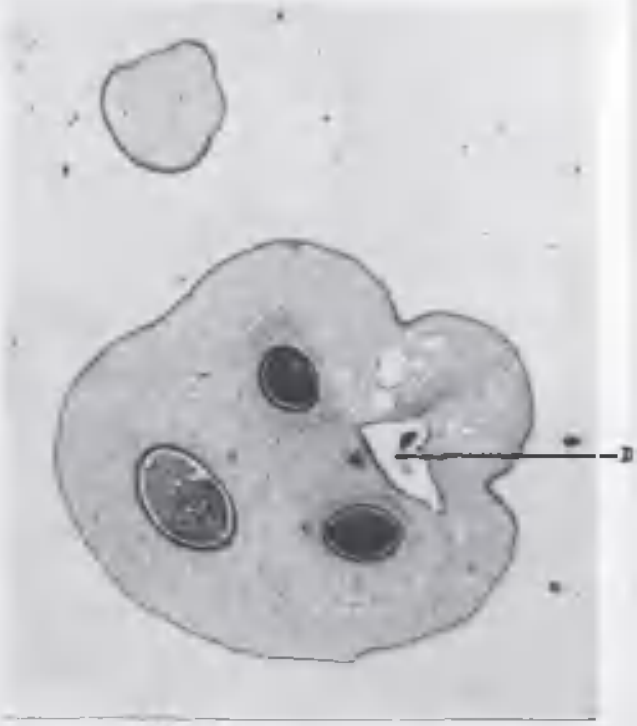


Fig. 73.

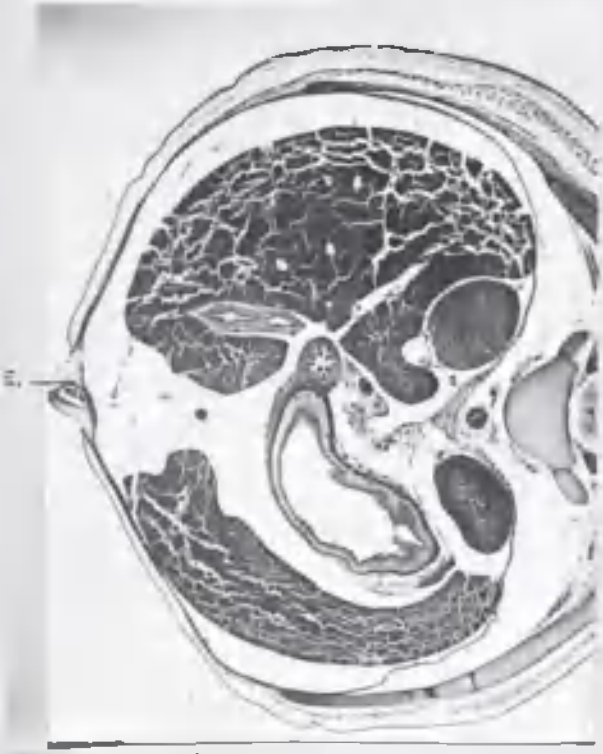


Fig. 74.

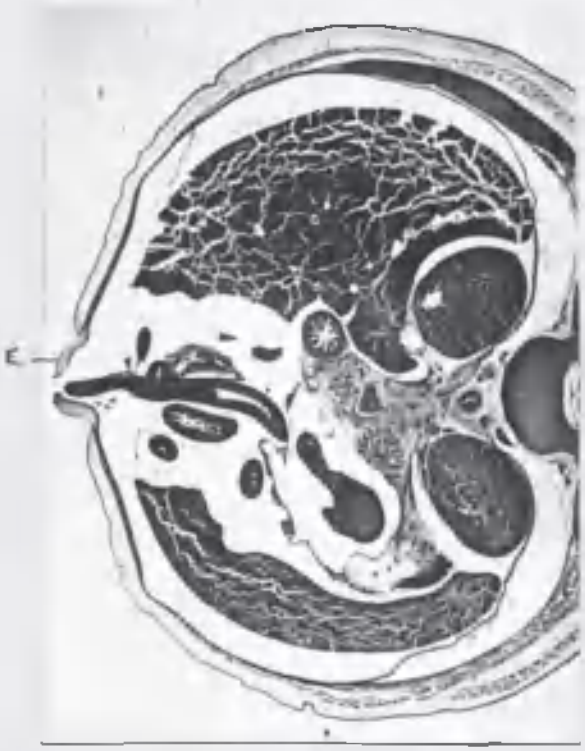


Fig. 75

PLATE XX.

Fig. 76. Photomicrograph of section of Embryo 42 mm B. x circa 9.

Fig. 77. Photomicrograph of section of umbilical cord of embryo 42 mm B: site indicated by arrow in Fig. 76. x circa 100.

Fig. 78. Photomicrograph of endothelial lining of umbilical cord coelom of Embryo 42 mm B. x 300.

Fig. 79. Photomicrograph of section of Embryo 42 mm B. x circa 9.

U.C.= Umbilical cord coelom.
E = Denser mesoderm extending into cord and continuous with rectus sheath.
L = Degenerating endothelial cells.
B = Linea alba (supra-umbilical part).

PLATE XX

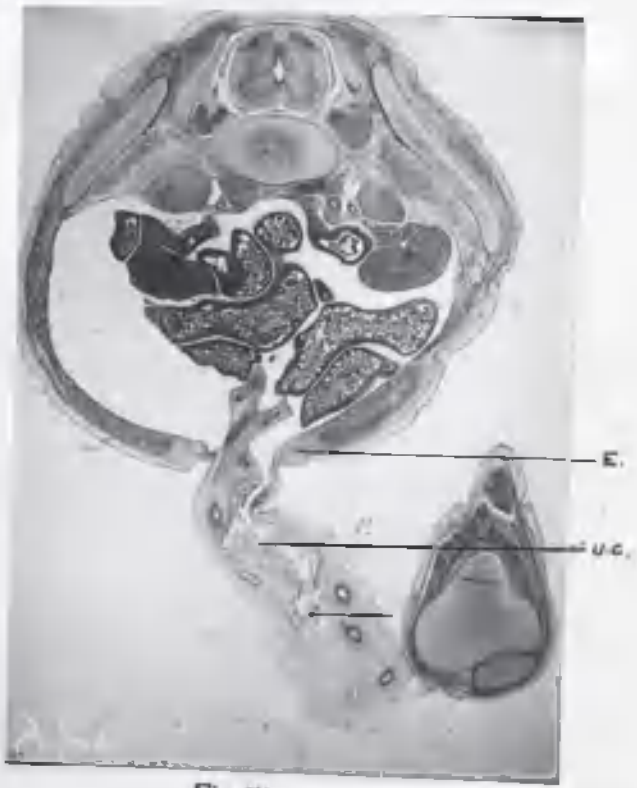


Fig. 76.

Fig. 77.

Fig. 78.

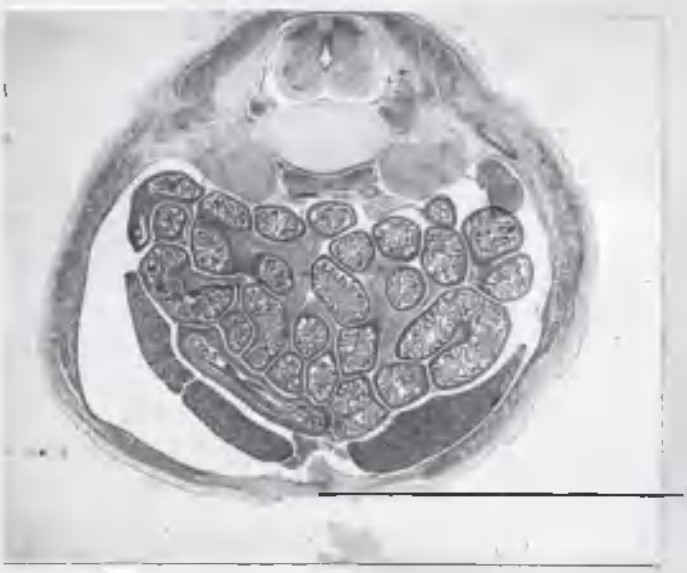


Fig. 79.

P L A T E X X I .

Figs. 80-81, 83,84. Photomicrographs of sections of Embryo 60 mm. x circa 7.

Fig. 82. Photomicrograph of section of Embryo 30 mm. x circa 5.

B = Linea alba formed from rectus sheath.
E = Denser tissue of the mid ventral line extending into the cord.
F = Denser tissue on superficial aspect of allantoic vessels.

Description in text.

PLATE XXI

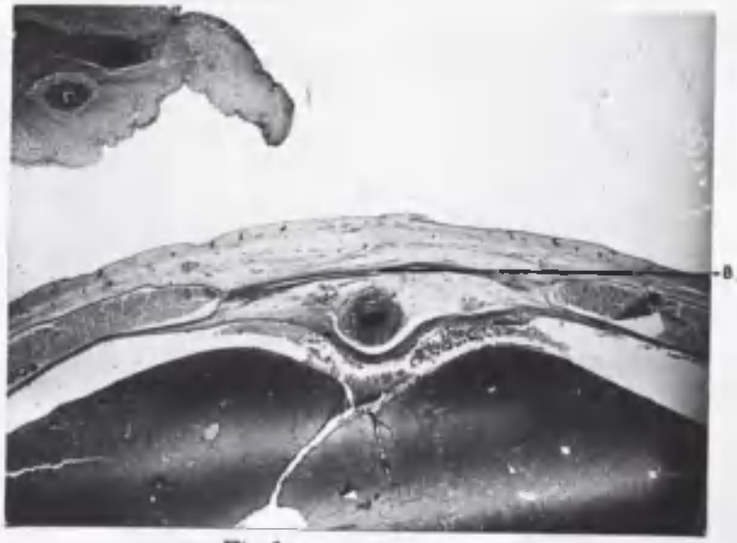


Fig. 80.

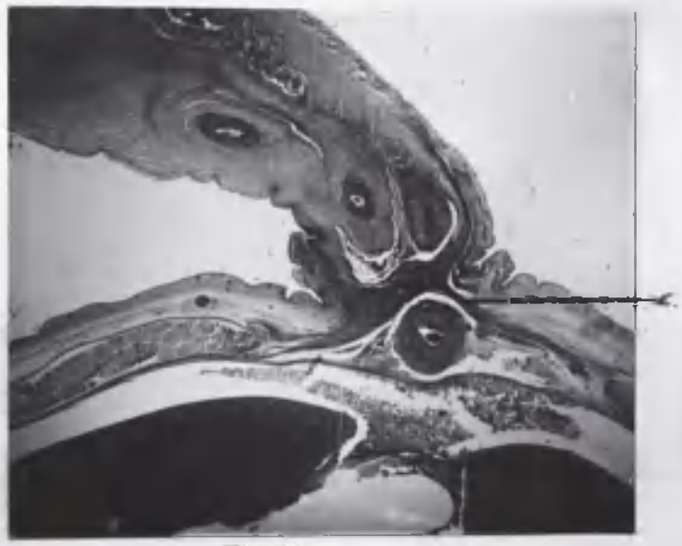


Fig. 81.

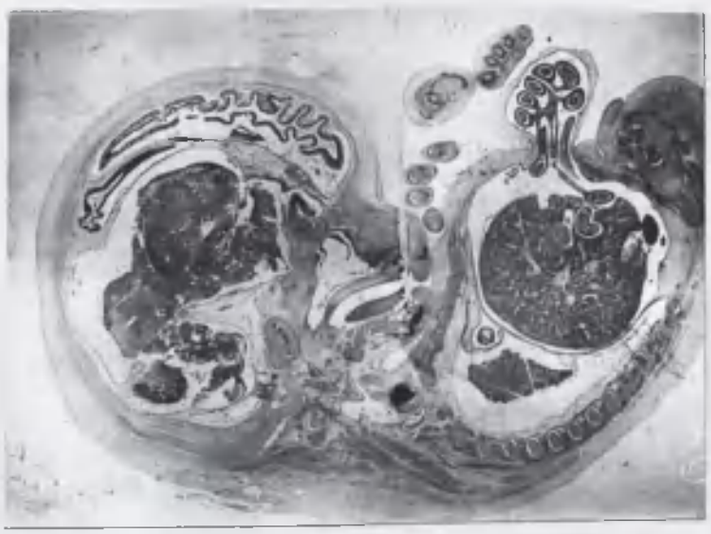


Fig. 82.

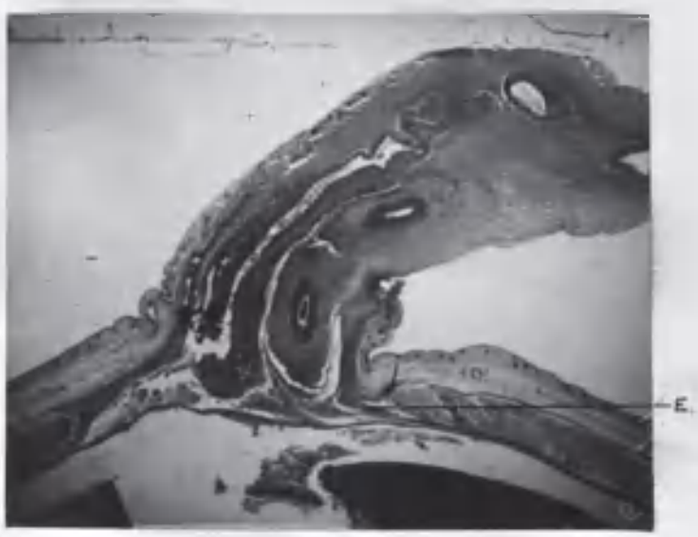


Fig. 83.

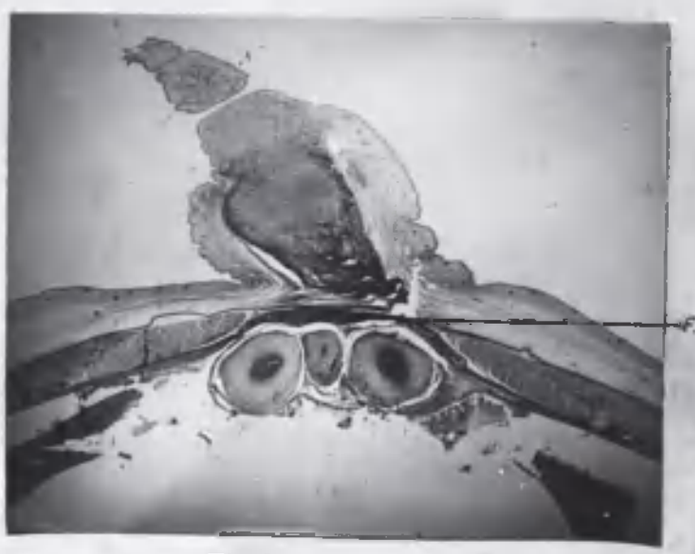


Fig. 84.