A HUMAN OVUM AT THE PREVILLOUS STAGE

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The specimen which is described in this communication consists of what is believed to be a normal ovum that has been not long imbedded in the uterus, and it represents the youngest stage of human development that has so far been recorded in this country. It was discovered by one of us (J. H. D.) during the course of a post-mortem examination of a woman, aged 28, who had died from internal hydrocephalus due to fibrous adhesions at the base of the brain which were probably the result of trauma. The post-mortem examination was made not more than ten hours after death, and there is no reason to suppose that the specimen is not normal.

A large corpus luteum was seen in one ovary and this directed particular attention to the uterus; on opening this along the anterior wall the mucous membrane was found to be thick and velvety, and on the posterior wall, towards the fundus, there was seen a small vesicle (Fig. 1[1]) projecting above the surface which was thought to be an early ovum. A small wisp of fibrinous material was adherent to the summit of the vesicle. No menstrual history was available.

The opened uterus was fixed in formalin and, after being photographed, a block of tissue containing the vesicle was removed, cut at 4μ, and stained with iron-haematoxylin and eosin; blocks of tissue from other parts of the uterus were also removed for study of the structure of the endometrium at a distance from the vesicle; this endometrium presents the characters typical of the premenstrual phase, with large, tortuous and active glands, and a rich blood supply; the sections show, too, that the fixation and preservation are good. In the sections of the block of tissue containing the vesicle the mucous membrane is 5 mm. thick and is divisible into a stratum compactum, 0·3 mm. thick, and a stratum spongiosum (Fig. 2).

The implantation site can be recognized in the sections with the unaided eye by the pink stain which has been taken up by some dilated glands lying at the base of the area. Contrary to what has been found in several young specimens, and to what might have been expected from the appearance of the intact vesicle, the implantation site is not much raised above the surface in the sections. Implantation has occurred between the mouths of two glands which are bent round the ovum, and the site of implantation occupies the stratum compactum only. The ovum is not covered with a decidua capsularis,

[1] Figs. 1–11 are shown on Plates 1–6.

and the point of entry of the ovum into the endometrium is seen (Figs. 5, 7) as a crater-shaped area, from which the uterine epithelium is deficient, overlying the summit of the ovum. The aperture of entry is 0·23 mm. wide; it is filled, as with a bung, by the 'operculum' (Teacher, 1924) and is capped by the 'closing coagulum' or 'Gewebspilz' (Peters, 1899). The latter appears as a loose mass of fibrinoid material containing some leucocytes and it was seen as the small wisp, referred to above, when the uterus was opened.

The ovum (Fig. 3) consists of a slightly flattened chorionic vesicle, the blastocyst, which has an internal measurement of 0·47 mm. in the equatorial plane, i.e. from side to side, and of 0·28 mm. in the polar plane, i.e. from the surface inward. The inner surface of the blastocyst is smooth and has the embryonic rudiment attached at its base; the outer surface is irregular owing to cellular and syncytial processes growing out from it into the implantation cavity. These processes are stained deeply with haematoxylin and they stand out in sharp contrast with the clear cavity in which they lie (Fig. 4). The smooth inner surface of the blastocyst is lined with primary mesoderm, and inside this there is the exocoelomic vesicle (Heuser, 1938) enclosed by the exocoelomic membrane (Heuser's membrane). The embryonic rudiment is composed of a thick ectodermal plate which forms the ventral wall of the amniotic cavity, and of a rather thinner entodermal plate which is continuous at its margins with the exocoelomic membrane. There is no yolk sac.

There are no chorionic villi and thus the specimen belongs to the group of ova at the previllous stage, which includes the Miller (1913, and Streeter, 1926), the Kleinhans (Grosser, 1922), the Müller (1930), and the two new Hertig ova of which a preliminary account only has so far appeared (Hertig & Rock, 1939). Further, it corresponds with Streeter & Wislocki's (1938) stage II for the macaque, which they term the 'stage of trophoblastic lacunae' and which they estimate to belong to the period from the 11th to the 14th day. The implantation cavity appears (Figs. 4–6) as an almost empty, clear and circumscribed area and thus stands out in sharp contrast with the adjacent endometrium on the one hand and the darkly stained trophoblast on the other; it is this character of the implantation cavity which gave to the specimen a cystic appearance when first seen in the uterus with the unaided eye.

The trophoblast. Growing from the outer surface of the blastocyst are the trophoblastic processes. In the account which follows, the terminology employed by Ramsey (1938) in her description of the Yale embryo will be used. Thus we are able to recognize central cytotrophoblast, peripheral cytotrophoblast, and plasmoditrophoblast or syncytium.

The central cytotrophoblast (Figs. 7, 8) forms the true wall of the blastocyst; it is composed of a single layer of lining cells which, for the most part, appear rather condensed and flattened and have darkly stained, round or oval nuclei, but poorly defined cell walls; in some sections the nuclei are packed closely together giving a dark border to the blastocyst, while in others, particularly in the region of the operculum, they are few and far between.

The peripheral cytotrophoblast (Figs. 4–8) appears as sheets, or columns, of cells growing from the blastocyst wall into the implantation cavity; in other words, it is an extension outward of the central cytotrophoblast. The cells are larger and have more clearly defined walls than have those of the central cytotrophoblast, their nuclei generally are not so darkly stained, nor do they fill the cell to the same extent, so that there is often a clear space left between the nucleus and the cell wall. Beyond the peripheral cytotrophoblast, and also extending in amongst its cell columns, are grey, filmy masses and strands which may be nucleated or non-nucleated; this tissue is the plasmoditrophoblast, or syncytium (Figs. 5–8). It is devoid of any cell boundaries, and in some places nuclei occur in clumps, like the 'heaped-up epithelial nuclei' described by Streeter & Wislocki (1938).

In the plasmoditrophoblast brown granules are seen in many places; similar granules have been described by Johnstone (1914) and Greenhill (1927). Johnstone suggested (p. 270) that they are composed of molecules of blood pigment adherent to a minute droplet of fat, the fat itself having disappeared in the course of the process of fixation and staining. We are of opinion that this pigment is a formalin-haemoglobin precipitate, and the fact that it is found mostly at the implantation site and in the cells of distended glands which form lacunae of blood rather supports this view, since these are sites of haemorrhage, and it is well known that in slightly autolysed tissues such precipitates are common in histological material. The ovum, and the autolytic ferments present in the trophoblast, may well be responsible for some degree of local autolysis. Greenhill implies (p. 340) a similar origin of the granules in his specimen. It has not been possible to make any microchemical analysis of these granules as it would have involved an interruption in the series of slides, but it may be mentioned that they are anisotropic, as are the formalin precipitates. The frequent occurrence of these granules in association with leucocytes provides further support for their origin from blood.

Several authors have referred to the foam-like condition of the syncytium of early stages due to the presence of innumerable vacuoles of various sizes, and the general opinion seems to be that this vacuolated syncytium has been derived from a more solid plasmodium which has grown out from the blastocyst wall. Thus Bryce (1908) suggests (p. 43) that the spun-out condition of the plasmodium or syncytium is due to the formation in the vacuoles of a digestive fluid which, after rupture of the vacuoles, is replaced by maternal blood; the large amount of blood in the implantation cavity is a striking feature of the ovum T.B. 1. Streeter (1926), in his account of the Miller ovum, describes the lacunae as being small near the wall of the ovum and larger as the periphery is approached, and he refers to them (p. 37) as representing the 'histological picture of a process by which a solid mass of trophoblast becomes converted into a sponge-like syncytium'. The Miller ovum shows a less definite implantation cavity than the present specimen.

In our ovum the vacuolated network (Figs. 7, 8) seems to be made up

largely of coagulated protein with branching cells scattered through it; these cells appear to be partly trophoblastic and partly stromal, and some are degenerate. This appearance is no doubt produced, so far as the protein is concerned, by fixation, and it seems probable that in life the contents were mainly fluid or gelatinous with strands of fibrin, amongst which the cells of the trophoblast were growing out from the blastocyst as in a tissue culture. We believe that our ovum, the Miller ovum, and the ovum T.B. 1, show progressive stages in the dissolution of the originally more solid plasmodium, the present specimen being at a stage intermediate between the Miller ovum, and the ovum T.B. 1, where the vacuoles have become filled with blood. The Müller ovum we believe to be at a stage similar to ours. The embryo Kleinhans, judged by the condition of the implantation cavity, seems to be at a stage intermediate between the present specimen and the ovum T.B. 1, for it shows a cavity which is fairly clear cut but which contains rather more blood than is present in our specimen. By the same criteria, the two new Hertig ova are both at stages earlier than either the present specimen or the Miller ovum; Hertig's no. 7700 in particular shows an almost solid plasmodium surrounding the trophoblast wall.

Teacher (1924) refers to the two generations of syncytium, the destructive and temporary syncytium—the 'Implantations-syncytium' of Grosser—and the permanent syncytium of the chorionic villi—the 'Zotten-syncytium' of Grosser. It is this first generation of syncytium that we have before us, and we get the impression that it shows evidence of destructive action and also of being in a process of degeneration, for it is a degenerate tissue and yet it seems able to open into capillaries and, contrary to what Streeter found in the Miller ovum, into glands also. Streeter further stated that he was unable to find any evidence of destruction or ingestion of the stroma cells by the syncytial loops; in the present specimen, as serial sections are examined from the non-implantation area towards the blastocyst, the first change seen is that the stroma becomes oedematous, the spaces between the cells are increased, and their nuclei become enlarged and paler. By the appearance of their nuclei these maternal stroma cells can be distinguished from the cells of the trophoblast, and in sections through the periphery of the implantation cavity they can be recognized without any doubt, though they are not numerous and their period of survival would appear to be short; here and there they can be seen lying in a mass of the filmy grey tissue that has been recognized as syncytium.

It may be suggested here that much of the lacy, network-like, appearance of the trophoblast seems to be due to destruction of its cells, by autolysis or by extracellular digestion, or by a combination of both processes; the general picture suggests the presence of some rather active ferment, or of conditions causing autolysis. We believe that many of the spaces between the trophoblastic branches may contain autolysed blood, the more so because the red cells in many of the capillaries in the vicinity are autolysed, though not in those farther away. This interpretation is in conformity with the suggestion we made above concerning the origin of the pigmented granules. Thus, there does seem

to be evidence of the digestion of the stroma cells by the syncytium in this specimen, and we believe that such destruction must have been extensive, for there is little evidence of the stroma having been simply pressed outward, as Streeter found to be the case in the Miller ovum, though in some places it is arranged more or less in concentric lamellae as if it had been pushed aside to some extent. It does seem that the main method of enlargement of the cavity, with the necessary removal of the stroma cells, is by a process of oedema of the stroma, degeneration of its cells and their autolysis or digestion. It is noteworthy that there is a strip—the 'border-zone'—of degenerated and necrotic stroma all round the implantation cavity, except where it is in contact with a gland (Figs. 4, 5).

The implantation cavity. The implantation cavity measures 1·0 mm. in its equatorial diameter and 0·575 mm. in its polar. As has been mentioned above, it appears as an almost empty, clear and circumscribed area, and though this character of emptiness is an appearance only, yet in this character and in the sharp outline of the cavity the specimen shows a condition different from what is found in other early ova, with the exception of that described by Müller, in that these have an implantation cavity more or less filled with blood, and with an irregular and indefinite outline. The cavity rests on two glands which have been so greatly distended with blood that their epithelium has been quite flattened and resembles the endothelial lining of a blood vessel, for which it was at first mistaken (Figs. 3, 5 and 8). The distension affects mainly the deeper parts of the glands. Brewer (1937) states that in all human pregnancies reported there is an accumulation of blood in the uterine glands, and, in the Edwards-Jones-Brewer ovum which he describes, the glands are certainly very distended with blood, but the only specimen besides the present one that shows a comparable distension is that described by Herzog (1909). As to the cause of the distension in the present specimen, it is clear that in the case of one gland at least it is due to the fact that it does not open on the surface, its lumen being occluded with syncytium and its mouth incorporated in the implantation cavity. It is therefore distended in part with blood, and in part with its own secretion which has no exit. In another case, the gland has burst on to the surface (Fig. 6) and its contents have been expelled into the uterine cavity where they form a wisp of fibrinous material impregnated with leucocytes.

The closing coagulum and the operculum. A wisp of fibrinous material has been alluded to already as the closing coagulum which caps the aperture of entry of the ovum into the uterine mucous membrane (Figs. 1, 3, 5, 7 and 8). The structure of this coagulum and of the contents of the implantation cavity is essentially similar, and it may be regarded as a part of the contents of the cavity which has become free on the surface owing to the absence of any decidua capsularis, and to the disappearance of the uterine epithelium over the point of entry of the ovum. The closing coagulum is also continuous in part with the contents of the gland which has burst on one side of the ovum. The

very thin covering of the ovum was recognizable in the intact specimen, for the ovum had the appearance of a tiny cyst, like a blister in the thick mucous membrane, with its pole glistening through the thin covering. It is interesting to note, in connexion with the origin of the closing coagulum, that Brewer (1937) showed a much larger and more organized 'blood clot' overlying the surface epithelium at the implantation site, and he suggested that its character indicated previous bleeding into the uterine lumen; the implantation cavity in Brewer's ovum contains a good deal of blood, and this may explain the difference in the appearance of the closing coagulum in his specimen and in ours.

The implantation cavity does not surround the ovum completely, for in its superficial part it is interrupted by the presence of the operculum (Figs. 2, 5). As so well described by Schlagenhaufer & Verocay (1916), quoted by Teacher (1924, p. 179), the operculum, 'as the stopper of a bottle, as the keystone of a vault...closes the entrance to the implantation cavity with its precious contents'. It is clearly an outgrowth of the central cytotrophoblast at the superficial pole of the ovum, and it fills the space between this part of the ovum and the uterine cavity. In structure it is like the peripheral cytotrophoblast of the rest of the ovum, except that it is rather less cellular and more vacuolated; in it are some small masses of syncytium and a few degenerated maternal stroma cells. The whole mass has a degenerated appearance and gives the impression of being a tissue, derived from proliferation and outgrowth of the cytotrophoblast, which has nearly outlived its usefulness. In some sections (Fig. 8) the operculum and the closing coagulum are continuous. Over the aperture of entry the uterine epithelium is deficient (Figs. 5, 7). Farther laterally it forms the sides of the crater-like area occupied by the operculum, but both here and in the adjacent glands it is flattened and has the appearance of having been stretched. This is quite unlike the appearance of the epithelium lining the uterus and the glands generally, which is columnar.

The blood vessels. Fig. 9 is a photograph of a section through the middle of the ovum, and on it have been marked with ink all the blood vessels. It shows that the endometrium is well supplied with blood. Small, thick-walled, spiral arteries and larger and thinner veins are seen in the stratum spongiosum, but capillaries only are present in the stratum compactum. There is no definitive blood sinus at the base of the ovum, such as is described by von Möllendorff (1921*a*) in the embryo 'Sch.', and by Ramsey (1937, 1938) in the Yale and Lockyer embryos; instead, there are numerous small vessels round the implantation site which ultimately join into two main veins, one rather larger than the other. The capillaries of the stratum compactum are opened by the syncytium and become incorporated in the implantation cavity, giving rise, at least in part, to the clear spaces of the cavity.

The embryonic rudiment. The embryo is found on the inner surface of the basal wall of the blastocyst. It consists of a thick ectodermal embryonic plate which forms the ventral wall of an otherwise thin-walled amniotic cavity, and

of a rather thinner entodermal plate which has not yet differentiated into any part of a definitive yolk sac. Spreading out from the sides of the amniotic cavity are the cells of the primary mesoderm which, when traced in a lateral direction, form a continuous lining for the inside of the blastocyst (Figs. 7, 8, 10 and 11). Within this primary mesoderm there is an even thinner layer (Figs. 5, 7 and 8), the exocoelomic membrane (Heuser, 1938); this encloses a large, more or less spherical, cavity which we thought at first was the yolk sac, admittedly a good deal larger than we had expected to find in an ovum at this stage. This membrane will be referred to in more detail after the other parts of the embryo have been described. It is unfortunate that a number of sections containing the embryo have been lost and it is thus not possible to make a complete reconstruction, but the following are the measurements of the embryo taken in the middle of the ten sections in which it occurs:

Embryonic disc	0·1 × 0·02 mm.
Endodermal plate	0·14 × 0·016 mm.
Amniotic cavity	0·04 × 0·09 mm.

The cells of the ectodermal and entodermal plates do not differ much; in each (Figs. 10, 11) the cells are closely packed, here and there piled up two deep, but standing in a columnar arrangement in the ectoderm and lying end to end in the entoderm. The cell boundaries are not well defined, but the nuclei are large and granular, exceeding those of the central cytotrophoblast but equalled by some of those of the peripheral cytotrophoblast.

In a discussion of the formation of the human yolk sac Stieve (1931) shows a section through the embryo Werner which resembles our embryo in having what he thought to be a large yolk sac. This was our interpretation also at first, but we have since had the opportunity and advantage of seeing Dr Streeter's beautiful photographs of the two new Hertig ova, of having his personal opinion about them, and of having read Heuser's (1938) paper on the 'Early development of the primitive mesoblast in embryos of the rhesus monkey'. The stages illustrated in Heuser's publication are of particular interest, for Streeter (1933) has shown that the difference in detail of form and in rate of differentiation and growth between man and monkey does not become appreciable till the end of the second month, and that known ages of macaques may be transferred to human embryos at least for the first month or six weeks. It is therefore profitable to compare our ovum with the stages of the macaque described by Heuser, since, as we have suggested above, our specimen falls into the stage of development which Streeter & Wislocki attribute in the macaque to the period from the 11th to the 14th day, and Heuser gives photographs of embryos of the 11th, 12th and 13th day.

The most striking difference between each of these specimens and our ovum is seen in the condition of the entoderm. We have described the entoderm plate as being nearly equal in thickness to the ectoderm plate and have stated that there is no definitive yolk sac. Heuser's 11th day embryo shows no yolk sac, but in the specimen of the 12th day it is just beginning, and in the specimen

of the 13th day it is seen clearly. In respect of the development of the yolk sac, then, our embryo corresponds with one of the 11th day in the macaque, the chief difference being in the thickness of the gut entoderm which, in the macaque, consists of a flattened layer of only one cell in thickness spread out on the inner surface of the inner cell mass.

Heuser states (p. 384) that 'Cells delaminating from the inner surface of the thickened trophoblast seem to be continuous with the primitive entoderm beneath the inner cell mass'. He finds that by the 11th day these cells become continuous with a layer that has split off from the ventral surface of the entoderm sheet so that a complete envelope, the exocoelomic membrane, is formed, having an origin partly trophoblastic and partly entodermal. In our ovum such a membrane is present, but its origin is not as clear as in the macaque; it appears (Figs. 3, 8, 10 and 11) to be continuous in the embryonic region not with a layer of cells split off from the entoderm but with the edges of the entoderm itself, nor is it certain (though it is probable) that the remainder has arisen by a splitting off from the inner surface of the trophoblast. It thus appears that, as far as the development of the exocoelomic membrane is concerned, our ovum is at a stage earlier than that of the macaque at the 11th day.

We have referred above to the primary mesoderm as forming a continuous lining for the inside of the blastocyst. Heuser finds that till the 13th day, 'except in a small zone around the embryo itself, there is little if any additional mesoblastic tissue', that is, additional to the tissue that has formed the exocoelomic membrane. Our ovum has a trilaminar blastocyst (Fig. 7) composed of an outer trophoblast, a middle primary mesoderm, and an inner exocoelomic membrane; it thus corresponds, as regards the development of the mesoderm, with a macaque of some days later than the 13th.

The primary mesoderm looks as if it might well have been derived from a splitting off of cells from the inner surface of the trophoblast, and in the embryonic region it is continuous with cells lying at the sides of the ectodermal plate and the amnion (Figs. 8, 10 and 11). These cells extend for some distance outward from the embryo and help to fill the space between the trophoblast and the exocoelomic membrane. This is seen particularly well in a glass-plate reconstruction in which the mesoderm cells are shown to be more numerous here than elsewhere.

With regard to the entodermal plate, we are unable to see more than one form of cell, though, in some sections, on the ventral surface of the plate there are a few cells which are less darkly stained than the majority, and we can see no film of flattened cells which might give rise to the basal portion of the exocoelomic membrane; nor can we see any splitting off of cells from its ventral surface to form the ventral wall of the yolk sac. We believe our specimen to be at a stage antecedent to the completion of the exocoelomic vesicle.

For some years it has been believed that the human yolk sac appears early in development and is already present in the youngest known specimens, that

the yolk sac develops by a process of cavity formation in the ventral part of the inner cell mass, and that all its walls are of entodermal origin. It has been believed that these conditions hold good for other primates also. For example, J. P. Hill (1932), in his Croonian Lecture, described the condition of the yolk sac in the earliest catarrhine embryo then known, the 'Keim S' of *Nasalis larvatus* (Selenka); he believed it was at 'the stage when an originally solid endodermal yolk-sac primordium is in course of becoming converted into a hollow vesicle by a process of vacuolization' (p. 108).

More recent work on primate material by Heuser, Stieve, and Streeter has cast some doubt on the truth of these older theories, and Streeter (1937), in discussing the origin of the yolk sac in primates, states that its earliest cells are differentiated 'as a thin membrane between which and the gut endoderm there arises a narrow cleft. This cleft becomes rapidly distended and so forms the conjoint yolk sac cavity and gut cavity. This cavity is therefore dual in origin and is bordered on its dorsal part by cells that are to form the gut endoderm, an induced product or migratory element from the embryonic ectoderm. It is bordered on its ventral part by the yolk sac endoderm which is a derivative of the primitive mesoblast and is essentially trophoblastic.'

Through Dr Streeter's kindness we have had the pleasure of examining photographs of the two new Hertig ova and of an ovum of the macaque at about the same stage of development. The Hertig ova are at much the same stage as our own and, like it, show ectodermal and entodermal plates and an exocoelomic membrane which appears to be continuous with the edges of the entodermal plate. The macaque ovum is at a rather later stage, and in it the exocoelomic membrane is separate from the entodermal plate and forms a closed exocoelomic vesicle on the ventral side of the entoderm. A yolk sac is present, and consists of a small vesicle with its dorsal wall formed by the entodermal plate and its ventral wall by cells which look different from those at the base; they are smaller, more flattened, and have more darkly stained nuclei, and they resemble the cells of the primary mesoderm and the dorsal wall of the amniotic cavity.

The study of our own specimen and of the photographs of the Hertig ova and the macaque lead us to believe that the older theories must be revised; for we find that the Hertig ova and our own, the youngest human specimens thus far known, have no yolk sac. The macaque ovum strongly suggests that the yolk sac does not arise by a process of cavity formation in the inner cell mass, and shows that the cells of the dorsal wall of the yolk sac are quite different in appearance from those of its other walls. Streeter's (1937) suggestion, quoted above, at first filled us with astonishment and confusion, for it seemed that, in his view, there was no such thing as entoderm *sui generis* if the gut entoderm is a migratory element from the embryonic ectoderm, and if the yolk sac entoderm is derived from the primitive mesoblast and is trophoblastic in origin. The difficulty, however, seems to be one of terminology

and of the distance back in their developmental history to which the different layers are traced.

After careful study, we agree with what we believe to be Streeter's views and the course of development seems to us to be as follows: The inner cell mass becomes differentiated into a thicker dorsal part, the embryonic ectodermal plate or embryonic disc, and a thinner ventral part, the embryonic entoderm. The exocoelomic membrane splits off from the inner surface of the trophoblast and becomes adherent to the edges of the embryonic entoderm, so that there is formed a temporary exocoelomic vesicle bounded dorsally by entoderm, and elsewhere by cells split off from the trophoblast. A layer of cells splits off from the ventral surface of the embryonic entoderm and joins with the cells of the exocoelomic membrane, or else the exocoelomic membrane grows round on the ventral surface of the entoderm and then becomes separated from it. Thus there is formed finally a complete exocoelomic vesicle, detached from the entoderm, occupying the interior of the blastocyst. The primary mesoderm, which has meanwhile been split off from the inner surface of the trophoblast outside the exocoelomic membrane, spreads as a thin layer over the ventral surface of the embryonic entoderm, between it and the exocoelomic vesicle. A cleft then appears between this film of primary mesoderm and the embryonic entoderm, so that there is formed a cavity bounded dorsally by the cells of the embryonic entoderm, and elsewhere by cells derived from the primary mesoderm. This cavity is the yolk sac, but, as Streeter pointed out, its dorsal wall will later be that of the gut, whilst its other walls will be those of the yolk sac proper. The alternative to this suggestion of the formation of the yolk sac is that the primary mesoderm does not spread over the ventral surface of the entoderm, and that the cleft is not between mesoderm and entoderm but within the entoderm itself. In opposition to this, however, it must not be overlooked that, at least in the macaque, the cells of the dorsal wall of the cleft are quite different from those of its other walls.

The amnion. As with the yolk sac, the cells of the ventral wall of the amnion are different from those of its other walls (Figs. 8, 10 and 11). Its ventral wall is formed by cells of the embryonic ectoderm; the cells of its other walls are smaller, more widely spaced and more mesodermal in character. Streeter & Heuser (1935) called attention to this sudden transition in the structure of the walls of the amniotic cavity, and suggested that whilst the floor was formed by the ectoderm of the germ-disc proper the remaining walls were trophoblastic in origin.

It has been thought that the human amniotic cavity develops, like that of the bat, by a process of cavity formation in the more dorsal part of the inner cell mass, that the dorsal wall of the cavity is closely adherent to the inner surface of the blastocyst, and that the cells of all its walls are of ectodermal origin. Our ovum, the Hertig ova, and the macaque ovum referred to above, all show the same characters of the amnion (Fig. 11). The cavity is rather

flattened in a ventro-dorsal plane, more so in the other specimens than in ours. The ventral wall is thick and formed by the embryonic ectoderm, the other walls are very much thinner and formed by cells that resemble those of the primary mesoderm. The dorsal wall is not continuous with the inner surface of the trophoblast, but is attached to it only indirectly through the intervention of a few scattered mesoderm-like cells. That the cavity has arisen by cleft formation seems clear, but it is not so certain whether the cleft has been formed within the dorsal part of the inner cell mass or between the inner cell mass and the trophoblast. If the cleft arose within the inner cell mass one would hardly expect to see such a difference between the cells of the ventral wall and the other walls of the cavity, and the amnion would be more closely attached to the trophoblast. If the cleft occurred between the inner cell mass and the trophoblast it would mean the separation of the inner cell mass from the inner surface of the trophoblast and the filling of the gap between the two with primary mesoderm, resulting in the formation of a cavity bounded everywhere, except ventrally, by cells of the primary mesoderm. The latter seems to be the more probable course and would explain the characters of the amnion described above, though it is more accurate to speak of a gradual separation of the dorsal part of the inner cell mass from the inner surface of the trophoblast accompanied by a filling in of the space with mesoderm rather than of any actual cleft formation.

It thus appears that the yolk sac and the amniotic cavity have a rather similar method of development and that, as Heuser (1938) pointed out, the original inner cell mass is responsible for the formation of a small part only of the actual embryo, that is, the germ disc or embryonic ectoderm and a thin film of entoderm on its ventral surface.

SUMMARY

A description is given of a human ovum at the previllous stage of development which was obtained at an autopsy.

The implantation cavity is unusually well defined and free from blood. It lies between and above greatly dilated glands which are almost filled with partly haemolysed blood, and of which one has burst into the uterine cavity. The closing coagulum appears to be derived partly from the contents of this ruptured gland, and partly from the contents of the implantation cavity. The operculum fills the aperture of entry into the uterine mucous membrane; it is an outgrowth from the wall of the blastocyst, and gives the impression of having almost outlived its usefulness.

The blastocyst shows, growing from its outer surface, cytotrophoblast and syncytium; the syncytium is at the stage intermediate between the formation of the 'Implantations-syncytium' and the 'Zotten-syncytium' of Grosser. The blastocyst is a trilaminar vesicle, its outer wall being the trophoblast, its middle the primary mesoderm, and its inner the exocoelomic membrane. The embryo is attached to the basal portion of the blastocyst, and is composed

of an ectodermal embryonic plate, an entodermal plate, and an amniotic cavity. There is no yolk sac.

The origin of the exocoelomic membrane, the yolk sac, and the amnion is discussed. It is suggested that the exocoelomic membrane is derived, like the primary mesoderm, by splitting off from the inner surface of the trophoblast, that, in agreement with Streeter's suggestions, the yolk sac has its dorsal wall derived from embryonic entoderm and its ventral wall from primary mesoderm, that the amnion has its ventral wall derived from embryonic ectoderm and its dorsal wall from primary mesoderm, and that the inner cell mass is responsible for only the embryonic ectoderm, or germ-disc, and a thin layer of entoderm on its ventral surface.

ACKNOWLEDGEMENTS

The authors are indebted to Mr W. Kiffin, of the Pathology Department, the University of Liverpool, for the preparation of the sections; to Mr C. Wilmott, of the British Postgraduate Medical School, University of London, and to Mr A. Welch, of the Anatomy Department, University College, Cardiff, for the photographs; and to Mr Douglas Kidd, of Liverpool, for the coloured drawing. They are also indebted to the Joint Academic Committee of University College, Cardiff, for a grant towards the expenses of the publication of this paper, and to Dr George L. Streeter for his personal interest in the specimen and for photographs of the Hertig ova and of a macaque ovum.

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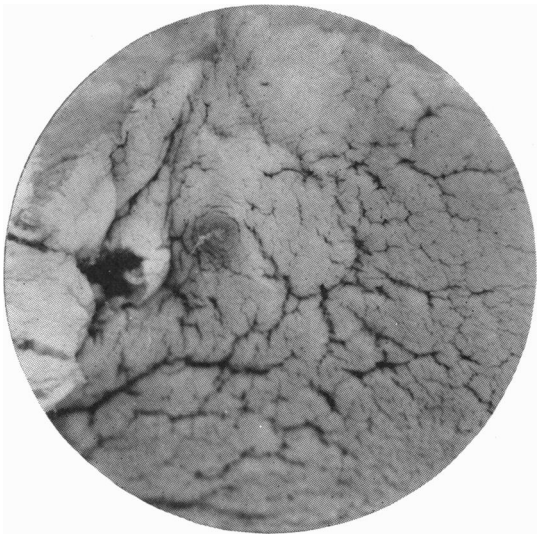
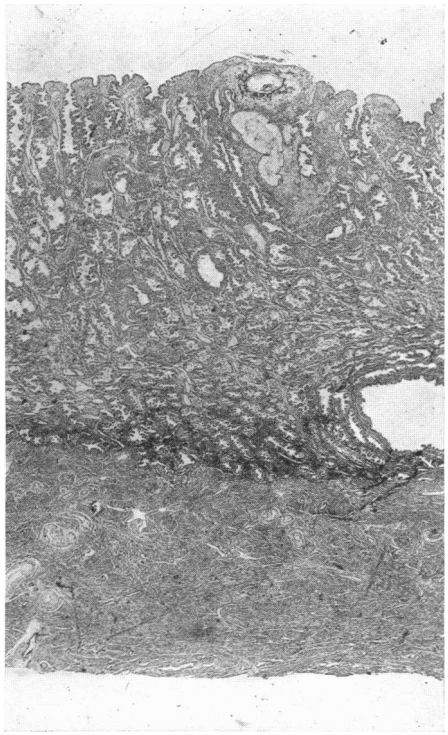


Fig. 1.



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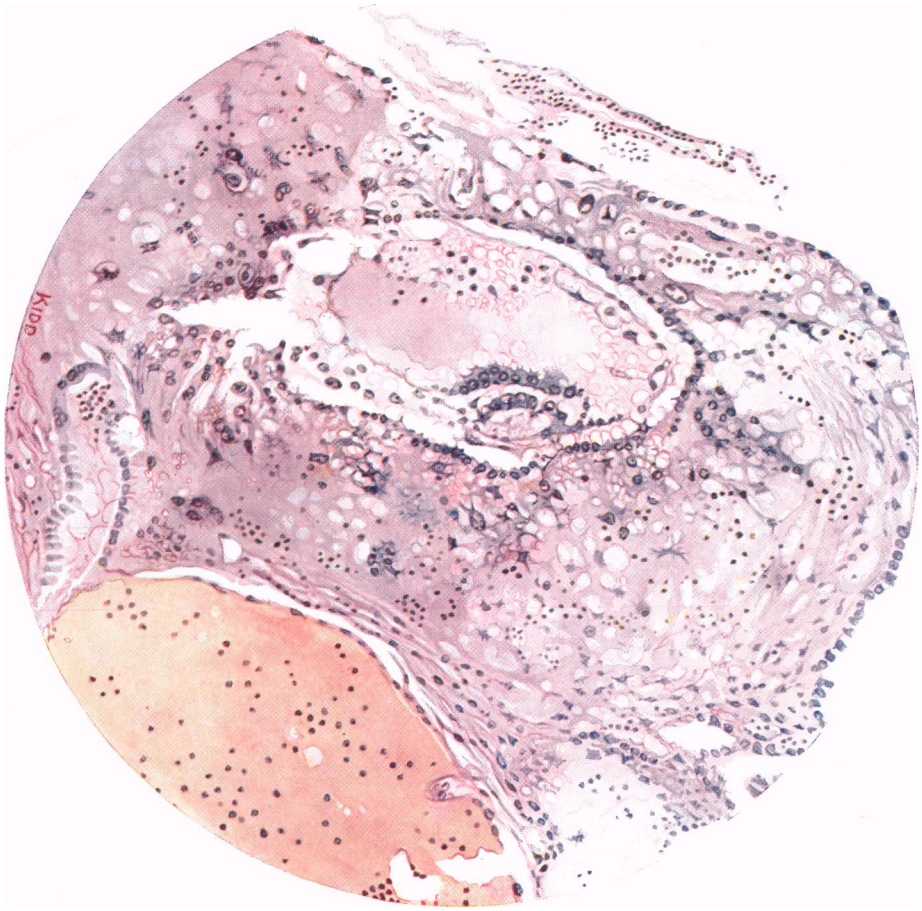
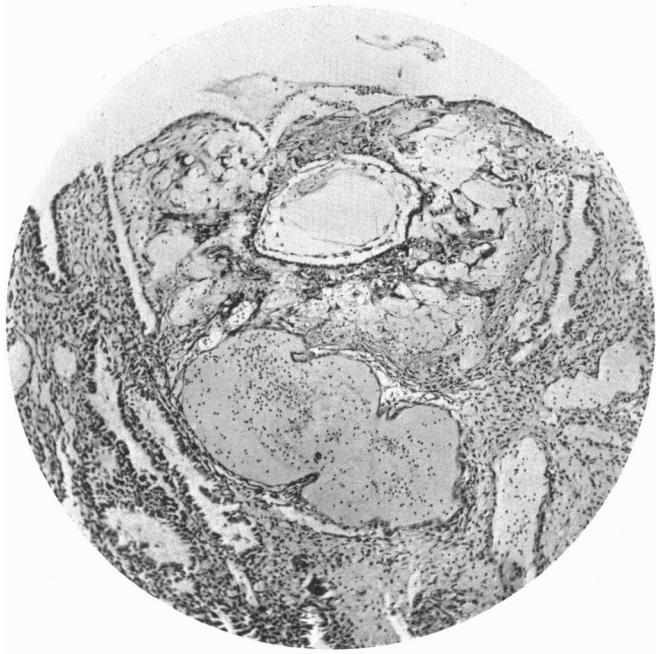


Fig. 3.

Fig. 4.



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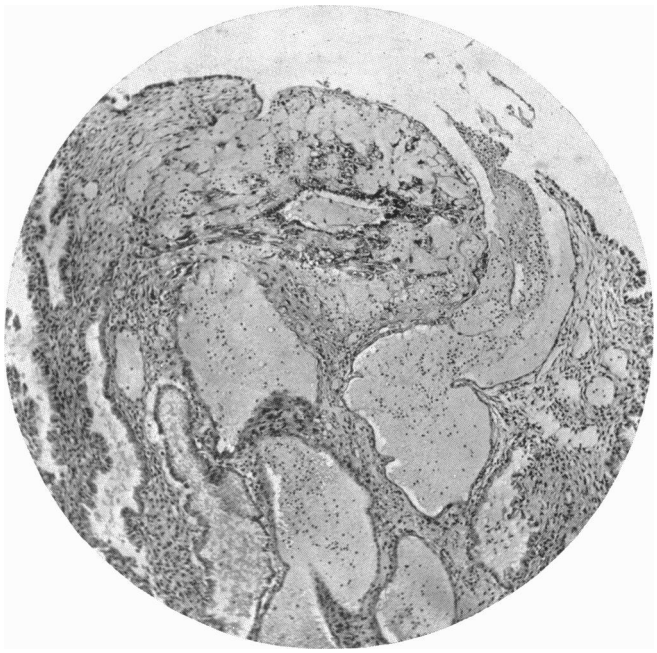

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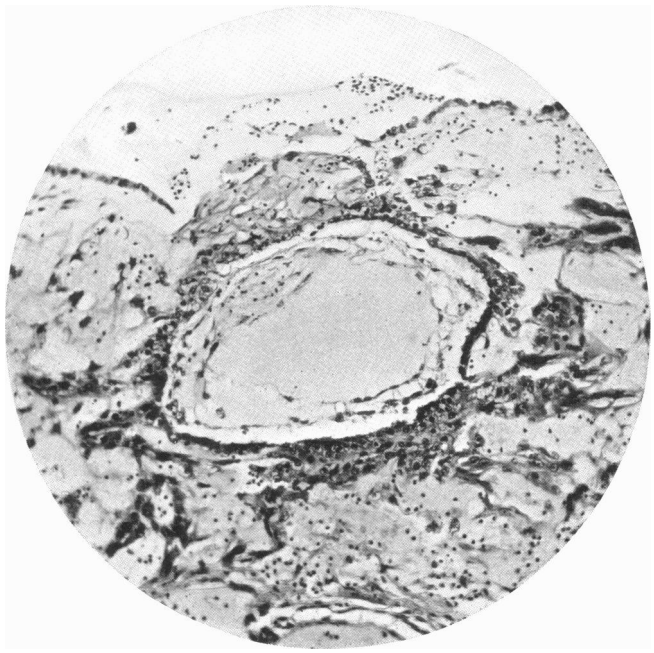

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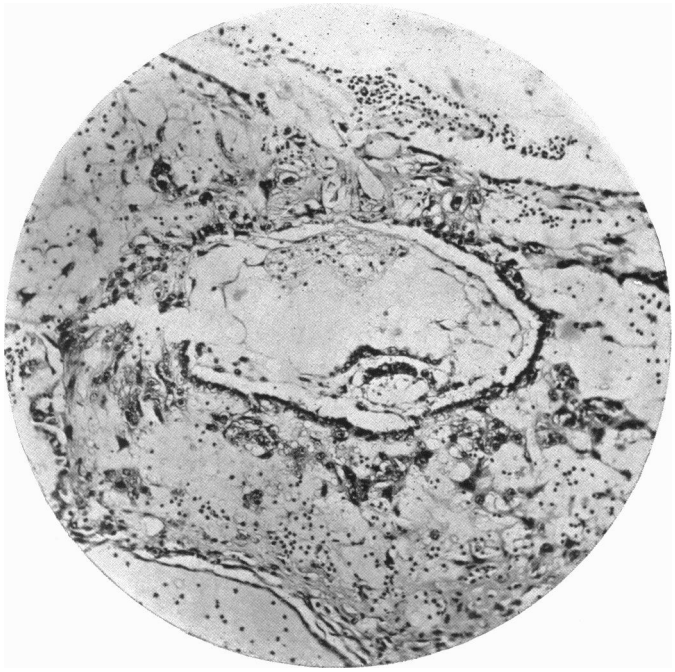

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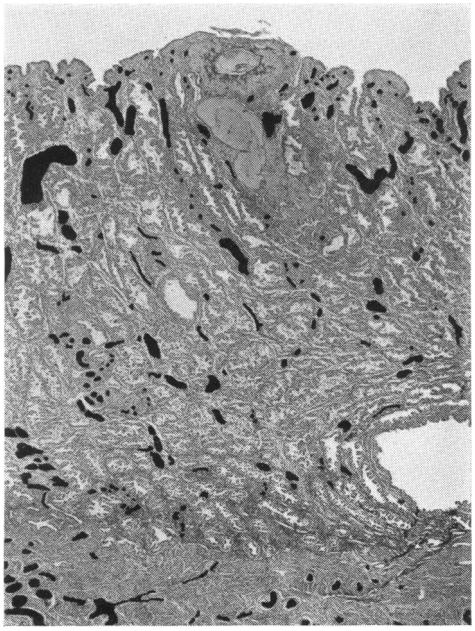

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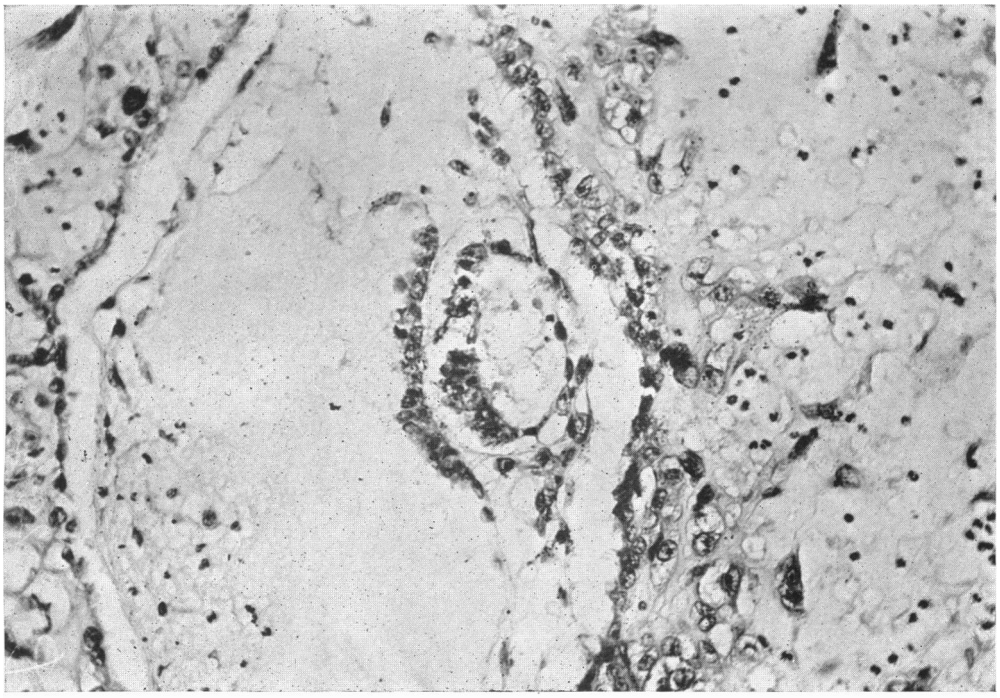

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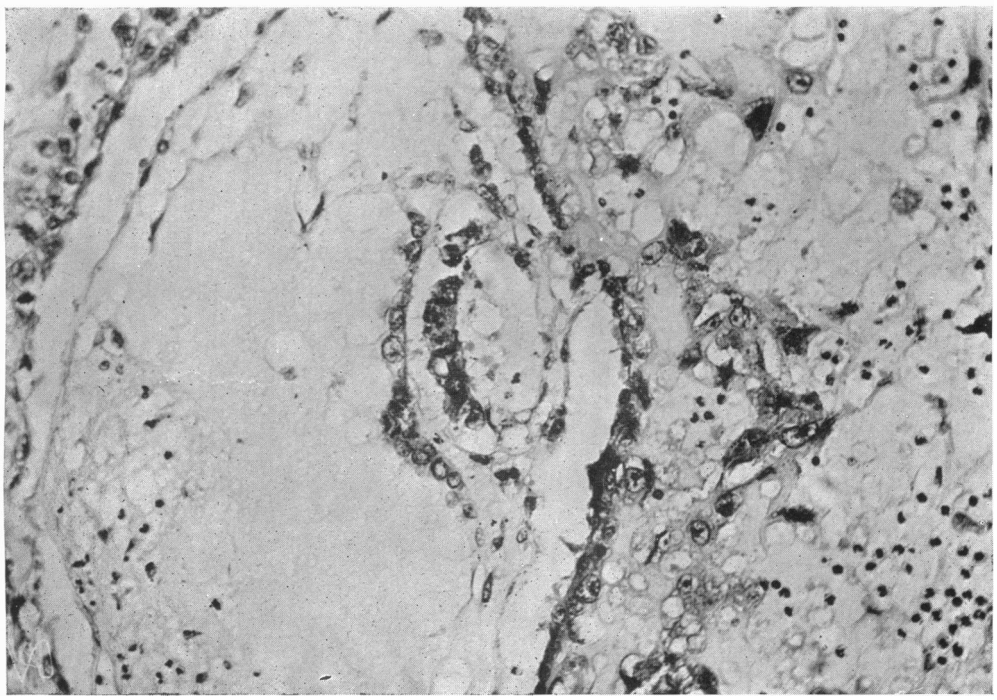

Fig. 10.

DIBLE AND WEST—A HUMAN OVUM AT THE PREVILLOUS STAGE

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EXPLANATION OF PLATES 1–6

PLATE 1

Fig. 1. The ovum, as seen when the uterus was opened. A wisp of fibrinous material on the summit of a small, dark, circular, congested and elevated area, just to the left of the centre of the photograph, marks the site of implantation. ×1·6 approx.

Fig. 2. A section (slide 25·4) through the uterine wall at the level of the middle of the ovum: this is seen at the top of the section. ×10. (There is an average of 5 sections on each slide.)

PLATE 2

Fig. 3. Coloured drawing of a section (slide 25·2) through the middle of the ovum. ×100.

PLATE 3

Figs. 4, 5. Sections (slides 21·2 and 23·4) through the blastocyst. ×33.

PLATE 4

Fig. 6. Section (slide 27·3) through the blastocyst. ×33.

Fig. 7. Section (slide 24·1) through the blastocyst. ×72.

PLATE 5

Fig. 8. Section (slide 25·2) through the blastocyst. ×90.

Fig. 9. Section through the uterine wall (slide 25·3) on which the blood vessels have been drawn with India ink. ×15·5.

PLATE 6

Figs. 10, 11. Sections (slides 25·2 and 25·4) through the embryo. The amnion is below and the entoderm above. ×200.