Observations

ON

TWO SPECIMENS OF EARLY HUMAN OVA

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(With Special Plate)

Specimens of young human ova are obtained only rarely, and the early development of the human embryo is not known with great accuracy. Such specimens are therefore of some value, and the two described below may help to call attention to the main features of the human ovum in the first few weeks of its development.

THE FIRST SPECIMEN: CLINICAL HISTORY

The ovum was obtained at St. Bartholomew's Hospital from a woman aged 32. She had had two previous pregnancies: a child had been born at term in 1922, and the patient had miscarried at the fourth month of her second pregnancy in 1926. Menorrhagia followed the birth of the first child, but the menstrual cycle was unaltered.

The patient came to the out-patient department on February 17th, 1930, complaining of an abdominal tumour and abdominal pain. She had last menstruated between January 12th and 17th, 1930. Her menstrual cycle was one of twenty-eight days, so the next period should have started on February 9th. The breasts showed no signs of activity. Rising from the pelvis there was an abdominal tumour 4 by 3 inches in diameter, which, on bimanual examination, was located to the right cornu of the uterus. The tumour was extremely tender, and it was impossible at the time to determine its consistence with any accuracy.

The patient was carefully questioned, and it was pointed out to her that she had missed a period. She denied that she could be pregnant, and even refused to admit that she was late with her period. Nevertheless, I thought she was gravid, and suspected that the tumour might be either an interstitial or an isthmus pregnancy. She was admitted to hospital at once. When I examined her again the next morning it was clear that the tumour was a cornual myoma. Again the patient stoutly denied the possibility of pregnancy. At the time the only evidence was the history of amenorrhoea, and even this was in some ways contradictory. I decided to operate, and obtained permission to remove the uterus if myomectomy was unsuitable.

A subtotal hysterectomy for the myomatous uterus was performed on February 19th. The left ovary contained a corpus luteum, and was removed. The convalescence was uneventful. The uterus was opened immediately after removal: it was lined by decidua, and there was a small prominence on the posterior wall about 1 cm. in diameter. This was carefully excised and fixed in Carnoy-sublimate solution for one hour, then passed through alcohol, xylol, benzene, and wax in the usual way. I succeeded in cutting a complete series of sections of the whole ovum at 10 μ , and the histological preparations are exceptionally good for this class of material. The value of the specimen depends upon its perfect preservation and upon its non-pathological nature, for a large number of the other early specimens are either from abortion material or from necropsy.

The patient and her husband were subsequently questioned, and it was amusing to observe their relief when they learned that not only had the pregnancy been removed, but that the woman could not become pregnant again. It was important to obtain the date of insemination, and both parties took the view that they could best show their gratitude for the favour I had done them by offering all the help they could to give the information we required. The woman now admitted that she was afraid that she was pregnant when she came to see me, and her policy had been to distract my attention from the amenorrhoea, and to concentrate my investigation upon the abdominal tumour, which she had noticed for some time previously. Coitus interruptus had been practised frequently during January and February, and I am not convinced that absolute reliance can be placed upon the credited date of

insemination as January 24th. However, the available data compare very favourably with the details of patients' sexual lives which one usually obtains.

The main discrepancy in the history was the patient's assertion that the February period was due on the 12th, whereas by calculation from the January period she should have menstruated on the 9th. The dating of the specimen is therefore as follows: (1) from the day of insemination, the twenty-sixth day; (2) from the day menstruation was expected by the patient, the seventh day; (3) from the calculated onset of menstruation, the tenth day; and (4) from the date of the last menstrual period, thirty-eight days from the onset of that period.

RELATION OF FERTILIZATION TO OVULATION

It is now generally believed that ovulation is limited to the intermenstrual phase of the cycle, and I myself have produced evidence that ovulation is restricted to between the thirteenth and sixteenth days of the menstrual cycle, the first day of the period of bleeding being taken as the first day of the cycle.¹ I am perhaps more dogmatic than some other workers on this subject, in that I maintain that ovulation is fixed in time with respect to the cycle, and that it is uninfluenced by such external factors as coitus. I have accumulated much additional evidence since the original contribution in 1925, and it all supports this contention.

Knowledge of the time of ovulation is essential for dating the time of fertilization, for it is obvious that fertilization cannot precede ovulation. In my view, therefore, the union of spermatozoon and ovum must be regarded as being restricted to the latter half of the menstrual cycle. This view does not imply that insemination before the date of ovulation must be sterile. Indeed, there is much statistical and clinical evidence that coitus may be fertile during the first half of the cycle. Siegel's well-known work, in which his evidence was based on the carefully recorded leave periods of German soldiers during the war, is a case in point.² The discrepancy is cleared up quite easily by the assumption that spermatozoa may survive in the female genital tract for some time after coitus. There is no direct evidence as to what this survival period may be in the human subject, but, on the other hand, there are no grounds for believing that spermatozoa quickly die in the environment of the female genital tract. If it is assumed that spermatozoa are capable of fairly long survival periods, the exceptional fertility of the human subject can be explained, and fertile insemination before the date of ovulation can be accounted for by the supposition that spermatozoa survive in the Fallopian tube and lie in wait for the ovum to be shed. The view also implies that the most fertile phase of the menstrual cycle is within a few days of the time of ovulation. Clinical evidence on this question is not convincing, but in my experience patients do not keep an accurate record of their sexual lives. On the other hand, in the cases that I have had reason to regard as reliable there has been evidence that the middle of the intermenstrual phase of the cycle is the most fertile time. The phase of fertility does not synchronize necessarily with the phase of desire. In many women desire is most marked in the post-menstrual and pre-menstrual phases of the cycle.

In the case under consideration insemination corresponded to the twelfth day of the menstrual cycle—two days before the development of ovulation—thus bearing out the views I have expressed above.

OTHER EARLY SPECIMENS OF HUMAN OVA

The most famous of the specimens of early human ova is that of Bryce and Teacher³; in recent years other examples have been added to the list. The Miller ovum,

described by Streeter⁴ in 1926, is certainly earlier; the Kleinhans ovum described by Grosser,⁵ and the von Möllendorff⁶ specimen are about the same date. The Miller and Kleinhans specimens are incomplete, the Möllendorff is badly preserved, and the Teacher-Bryce, although perfectly cut, has been regarded as pathological. It is surprising how small is the number of very early specimens on record, and one cannot help thinking that gynaecological material is not always carefully examined. Older ova are more numerous, and a fair number have now been recorded. They have been conveniently classified by Bryce⁷ into groups according to the degrees of development. Bryce's classification is as follows:

Groups A and B include the early specimens already mentioned.

Group C includes ova in which the primitive streak has not yet appeared. The amniotic and yolk-sac vesicles have been differentiated, and the magma reticulare is developed.

In Group D the primitive streak appears, the villi begin to branch, and the yolk sac becomes larger than the amnion.

In Group E the primitive streak and cloacal membrane are differentiated, and a complete chorda canal has been formed.

In Group F the neurenteric canal can be seen, together with the neural plate, neural folds, and notochordal plate.

Of the older specimens, Peters's falls into Group C, and Graf von Spee's ovum belongs to Group D. The specimen described below belongs to Group E, but it is earlier than the majority of other ova of this group. Altogether there are probably between fifteen and twenty earlier specimens than my own; but, as I pointed out above, a large number of these are either pathological or are imperfectly preserved. Even in the earliest specimens of Miller, Kleinhans, and Teacher and Bryce the ovum is surrounded by trophoblast, and amniotic and yolk-sac vesicles can already be seen. Later specimens sufficiently early to be included in Bryce's classification all retain this general form.

DESCRIPTION OF FIRST SPECIMEN

General Features

The ovum is embedded in the compact layer of the decidua, and is almost completely covered by a decidua capsularis. It is surrounded by chorionic villi, and the blastocyst contains an embryo consisting of two vesicles, an amnion, and a yolk sac. The dimensions of the embryo are 1.66 by 1.44 by 1 mm. Unfortunately the embryo has been cut obliquely (approximately at an angle of 45 degrees to the axis of the primitive streak), and although the material is well preserved, the obliquity of the sections makes the interpretation of the features of the embryo difficult, and it is very doubtful if a reconstruction of the ovum would serve any useful purpose.

Trophoblast

Chorionic villi surround the ovum and are more plentiful on the lateral poles than beneath the operculum, or adjacent to the decidua basalis. They show a minor degree of branching, but most of them are single, and are not vascularized. Characteristic syncytium is relatively scanty. The simple division of the chorionic epithelium into syncytium and Langhans's cells is impossible at this stage of development, for, although typical syncytium can be demonstrated and the basal layer of chorionic epithelium recognized, the bulk of the trophoblast consists of solid clumps of cells resembling Langhans's cells more than they do syncytium. It is convenient to adopt the nomenclature of Hubrecht and call the cells of the basal layer "cytotrophoblast," and to call these masses of cells

"plasmoditrophoblast." Plasmoditrophoblast is plentiful, and the volume occupied by this tissue is as great as that taken up by the whole of the chorionic villi. The cells of the plasmoditrophoblast are large and vacuolated; as is well known, they are found in specimens of hydatidiform mole.

The Decidua

The decidual glands are hypertrophied, crenated, and filled with a pink-staining coagulum. The gland cells are high columnar, and contain globules of secretion. The ovum lies embedded in the compact layer, and already the decidua capsularis is well defined. Most of the decidua which surrounds the ovum contains areas of necrotic tissue. Here the glands are disintegrated, decidual cells are degenerate, and there is much nuclear debris, interstitial haemorrhage, and leucocytic infiltration.

One of the most interesting features is the presence of trophoblastic cells immediately adjacent to the decidua. If the inner border of the decidua which surrounds the ovum is examined, it is remarkable how extensively trophoblast can be seen adherent to it. In some places—particularly in the depressions between projecting masses of decidua—there are large areas of adherent plasmoditrophoblast. This relation of trophoblast to decidua is not usually emphasized in descriptions of the development of the placenta. Again, the specimen throws doubt upon the classical descriptions of the development of the chorio-decidual space. There is little maternal blood in the space between the chorionic villi and the decidua; certainly there is no suggestion of a blood sinus. On the other hand, large maternal blood sinuses are found in the decidua in the immediate vicinity of the ovum; this suggests that the formation of the sinus of the chorio-decidual space is a later phenomenon of development than is usually believed. Furthermore, my own impression from studying the sections is that there is no true chorio-decidual space at this stage of embedding, but that there is a direct connexion between the chorionic villi and the decidua by means of masses of plasmoditrophoblast. It is quite possible that the plasmoditrophoblast is much more intimately connected with the decidua in the living state than the sections would lead one to believe, for however carefully one preserves such embryonic material the delicate tissues must be disturbed in the preparation of slides.

My specimen suggests that the trophoblast is loosely connected with the decidua over the greater part of its periphery, and that these attachments have been disturbed in the preparation of the sections.

The Ovum

Magma Reticulare.—The trophoblast is distributed around a roughly ovoid cavity, which contains the embryo and the magma reticulare (Fig. 1 on Plate). The embryo is attached to the peripheral chorionic epithelium by its connecting stalk. In earlier specimens the space around the embryo is filled by reticular embryonic tissue, but in my specimen it contains coagulated material which is completely acellular, except in the situation of the body-stalk and immediately beneath the chorionic epithelium. The formation of the magma reticulare is one of the peculiar features of the human ovum. Even in the Miller ovum the space is present, and the cells which it contains are described as belonging to extra-embryonic mesoderm. The embryonic mesoderm develops later in the orthodox way from the region of the primitive groove between ectoderm and entoderm. At the stage of development represented by the specimen the extra-embryonic mesoderm is collected to form a single layer of cells round the amnion and yolk sac of the embryo, and to form a thin, indefinite layer beneath the chorionic epithelium. Elsewhere the

primitive reticulated tissue has disappeared, and been replaced by coagulated material. It is of interest to observe that the extra-embryonic mesoderm is directly connected with the stroma of the chorionic villi. The cells are elongated and faintly stellate in type, some of them are vacuolated, and there is an intercellular matrix. No trace was found of a yolk-sac-duct connexion with the chorion, nor were there any remains of the extra-embryonic coelom which has been described in other specimens.

The Connecting Stalk.—This attaches the embryo to the chorionic epithelium, and is made up of round cells with spherical nuclei, which are quite different from those of the extra-embryonic mesoderm. Unlike the amnion and the yolk sac, the connecting stalk has no covering layer of extra-embryonic mesoderm, but its rounded cells merge with those of the extra-embryonic mesoderm at the periphery near the chorionic epithelium. The connecting stalk contains the amniotic duct, the allantois, and the allantoic vessels. The amniotic duct is well shown in the specimen; it does not reach as far as the chorion, and it is canalized for only a part of its length. It represents a narrow prolongation of the amnion into the connecting stalk.

The Allantois.—This can be demonstrated in thirty-three sections, and therefore measures 0.33 mm. in length. It is lined by high columnar epithelium, and is a prolongation from the caudal end of the yolk sac into the connecting stalk. It assumes the form of a narrow duct, and it is characterized by the regularity of its high columnar epithelium. It does not pass into the connecting stalk to the same extent as the amniotic duct. The allantois is surrounded by the allantoic vessels, which pass further into the body-stalk than does the allantois. They contain no blood cells, and are less conspicuous than the blood islands of the yolk sac. Vessels similar to those of the allantois are found in the extra-embryonic mesoderm beneath the chorionic epithelium in the region of the connecting stalk, but it was found impossible to trace a communication between the two systems. A large and well-defined blood island was identified in the wall of the yolk sac near the origin of the allantois. Already, therefore, the mechanism by which the foetal vessels form the umbilical vessels and pass to the chorion has been initiated.

The Vesicles.—The general structure of the embryo is that two vesicles, the amnion and the yolk sac, are joined by the connecting stalk to the chorionic epithelium. Both vesicles are small compared with the size of the magma reticulare. They are fused together along the embryonic plate, which gives rise on its amniotic side to the ectoderm, Hensen's knot, the opening of the blastopore, the primitive streak, and the cloacal membrane. From the under surface develops the entoderm, and between the ectoderm and entoderm the mesoderm proper and the notochordal plate develop.

The Amnion.—The dimensions of the amnion are 1.35 by 1.34 mm., and it is 0.32 mm. in height. It is therefore roughly circular in shape. It is longer than the yolk sac, because it extends caudally to form a primitive caudal fold. On the other hand, the yolk sac extends further forwards than the amnion by 0.09 mm. The lining cells of the amnion are flattened and elongated in type (Fig. 2); but caudally the amniotic cells are irregular. The covering extra-embryonic mesoderm varies with its position. Near the connecting stalk it is irregular, near the middle of the embryonic plate it is differentiated into a single layer of flattened cells, while cranially it is imperfectly developed.

The Yolk Sac.—This (Fig. 1) measures 1.21 mm. long, 1.35 mm. wide, and 0.4 mm. in height. It therefore differs from the amnion in shape because of its depth, for it is much more spherical than the amnion. The yolk sac

is lined by entodermal cells, which are flattened over the greater part of its length, but in the vicinity of the allantois the cells become columnar. Similar columnar cells are found in a small area of the yolk sac, which perhaps corresponds to the site of the connecting strand of the Bryce-MacIntyre ovum,⁷ but which is not represented in my specimen. In its caudal part the yolk sac is surrounded by a single layer of extra-embryonic mesoderm, so that two layers of cells, the entoderm and the extra-embryonic mesoderm, form the wall. Near the middle of the embryo blood islands are found between these two layers. They contain large polygonal cells, some of which possess deeply staining protoplasm. The nuclei are large, and show active mitoses. The endothelial lining of the blood islands is incomplete. The allantois passes backwards from the yolk sac as a small duct into the connecting stalk.

The Embryonic Plate.—This represents that part of the embryo which lies along the area of fusion of the amnion and yolk sac, and it is in the embryonic plate that the important structures are to be found. The plate is best described by tracing the individual structures from the caudal region of the connecting stalk to the cranial end of the embryo.

To prevent confusion in the description it should be remembered that the primitive streak, the cloacal membrane, and the blastopore are found on the amniotic side of the plate. The cloacal membrane lies at the caudal end of the primitive streak, and is seen best where the allantois arises from the yolk sac. It measures 0.09 mm. in length, and along the cloacal membrane the ectoderm and entoderm fuse. The primitive streak (Fig. 2) measures 0.43 mm. in length, and as the embryo has been cut obliquely it lies to one side of the mid-line. Cranially the streak ends at Hensen's knot. The knot measures 0.04 mm. in length; in front of it lies the blastopore opening and the chorda canal. The opening of the blastopore is luckily shown in one of the sections, and the chorda canal can be traced from the blastopore opening downwards and forwards towards the entoderm. It was not possible to trace a communication of the chorda canal with the entoderm, although the direction of the canal and the arrangement of cells around it were very suggestive that such communication existed. The blastopore is bounded cranially by a well-marked dorsal lip. Further cranially, there is no evidence of neural folds, but a neural plate is being formed. It will be seen that the embryo is too early for a neurenteric canal to be present.

Embryonic Mesoderm.—This is quite different from the extra-embryonic mesoderm, which, as has already been pointed out, is derived from the primitive cells of the magma reticulare. The embryonic mesoderm lies between the entoderm and ectoderm to form lateral sheets of cells, which arise mainly from the cells of the primitive streak (Fig. 2). There is no evidence in my specimen that the cells of Hensen's knot play any part in the formation of the mesoderm. The head process which surrounds the chorda canal is not well seen in the specimen, because of the obliquity of the sections.

The description which has been given above indicates the main features of the ovum, and a more detailed account belongs to the province of the pure anatomist. The general characters of the ovum allow the second specimen to be interpreted.

THE SECOND SPECIMEN

The second specimen is grossly abnormal, and represents an early stage of development of a human monster. The material was very kindly handed over to me by Dr. Malcolm Donaldson, who had removed it by abdominal hysterotomy. The patient was suffering from morbus cordis, and was found to have a fimbrial cyst

in the first few weeks of her pregnancy. The patient's last menstrual period began on December 30th, 1930, and the operation was performed on February 12th, 1931, forty-four days after the onset of the last menstrual period. The pregnancy had been perfectly normal, without symptoms of abortion, and there was no reason to suspect any abnormality of the ovum. The ovum was placed in spirit, and reached me within two hours of removal; it was then fixed in Carnoy's solution and passed through alcohol, xylol, benzene, and wax in the usual way. I did not detect any abnormality during its examination before fixation, and because of this a complete series of sections was not made. However, the majority of sections were kept, and, although no one regrets more than I that a complete series is not available, the sections that have been obtained allow the essential features of the ovum to be recognized without much difficulty. The embryo is seen in eighty-six sections, which were cut at 8μ . The maximum length of the larger embryo is 3.15 mm., the maximum breadth 1.46 mm.

The specimen is, I believe, unique, and I can trace no record of any ovum which is at all comparable. The nearest approach is the Mateer ovum, described by Streeter,⁸ in which there are two small accessory vesicles in the extra-embryonic mesoderm of an ovum of about the age of my first specimen, but there is no connexion between the two embryos, and the accessory vesicles are much smaller than those of the larger embryo.

My specimen consists of two embryos which are fused together in the umbilical region (Fig. 3). The larger of the two is normally developed, except along the line of fusion, and shows no gross abnormality. The smaller embryo is incomplete, for it consists only of a caudal part below the level of the umbilicus, and has no head, heart, or liver (Figs. 3 and 4). The monster has a single chorion and amnion, and there is only one umbilical cord (Fig. 3). The axes of the two embryos are parallel; there is little difference of corresponding parts in the two embryos, and the degrees of development are the same. The embryo is therefore an example of a double monster, and belongs to the very rare group of omphalopagus parasiticus. The most illustrious example of this type of double monster was the Hindu Laloo, whose umbilical hernia was reduced by Bland-Sutton.

Double monsters are uncommon, but the majority of interesting specimens are recorded in the literature, so a fairly comprehensive classification of the possible forms may be given. They are classified into (a) symmetrical forms, and (b) asymmetrical forms.

GROUP A

The majority of double monsters belong to this group. In most cases the embryos are fused along a vertical axis and are conjoined at the head, thorax, abdomen, or pelvis; theoretically the fusion may be dorsal, lateral, or ventral. In rare cases the fusion may be about a horizontal axis, either in the head region or in the situation of the breech. Group A may therefore be subdivided as follows:

Fused along a Vertical Axis

Upper Union.—Dorsal: craniopagus. Lateral: dipygus. Ventral: cephalo-thoracopagus.

Middle Union.—Dorsal and lateral conjoining are not recorded. Ventral, on the other hand, forms the commonest variety of conjoined twins; three types are recorded—namely, thoracopagus, sternopagus, and xiphopagus.

Lower Union.—Dorsal: pygopagus. Lateral: duplicatus superior. Ventral: ischiopagus.

Fused along a Horizontal Axis

Craniopagus and ischiopagus are the two common forms.

In addition to the types indicated above, modifications are known which depend upon more complete fusion—for example, dicephalus, diprosopus, and dipygus.

GROUP B

In this group are included such examples as acardiac foetus, foetus acardiacus amorphus, and teratomatous foetal inclusions.

Among monsters the parasitic tumours, such as epignathus, parasitic craniopagus, thoracopagus epigastricus, omphalopagus, and pygopagus belong to this group. The essential feature of monsters of this group is that they consist of a well-developed autosite with an incomplete parasitic foetus attached.

ETIOLOGY

A satisfactory explanation of the origin of double monsters cannot be given at the present time, for there is as yet insufficient knowledge of the segmentation of the mammalian ovum and of the method of production of the primitive vesicles. The specimen described below offers some help, because it indicates certain of the factors at work; but at the same time it shows that the problem of the origin of double monsters is more difficult than was previously supposed.

The origin of human double monsters cannot be explained by the assumption that the two embryos are derived from the two parts of the first blastomere division of the fertilized ovum. For example, in my specimen there is a common chorion, amnion, and umbilical cord. The blastomere hypothesis necessitates the assumption that each embryo possesses its own trophoblast, for both trophoblast and embryoblast (that is, inner cell mass) are developed from the fertilized ovum. This difficulty is overcome, in the case of uniovular twins, by supposing that the two trophoblastic systems fuse at an early stage of development, and in this way the common placenta with freely communicating vessels of uniovular twins is explained. In the specimen described there is no evidence of duplicity of the trophoblast, for there is no sign of fusion, and the trophoblast is single. Further, the presence of a common amnion is conclusive evidence against the blastomere hypothesis, for the ovum is at the stage of development when the amnion has only just encircled the embryo, and it is inconceivable that two amnions could have developed originally and fused by the time the stage of development of the specimen was reached.

The problem of the origin of double monsters must be attacked by considering the well-established facts of embryological morphology and experiment. The subject unfortunately lends itself to conjecture, and many of the explanations that have been put forward in the past are purely hypothetical. It is impossible to account for either uniovular twins or monsters with great precision, and the views expressed below indicate the limit to which scientific evidence will allow any explanation to go.

Since the blastomere hypothesis was first put forward much additional embryological evidence of the method of segmentation of the fertilized mammalian ovum has been found. It has been shown that segmentation becomes asymmetrical soon after the first few divisions of the fertilized ovum, and the daughter cells very soon differ in size and appearance. As long ago as 1909 Hubrecht suggested that the cells of the trophoblast and embryoblast were differentiated in this way, the smaller cells grouping themselves within the others to form the inner cell mass. This view is generally accepted, and it seems much more likely that the duplicity of conjoined twins is to be attributed to errors of development of these early cells of the embryoblast. In this way the common trophoblast of my specimen and the common placenta of uniovular twins can be explained, for the hypothesis limits the maldevelopment to the embryoblast, and does not postulate any abnormality of the trophoblast.

Experimental embryology has shown that monsters and maldeveloped embryos can be produced by environmental changes around the growing ovum. Diminution of oxygen

tension, lowering of temperature, and alteration of the concentration of inorganic salts (such as sodium chloride and magnesium chloride) have been proved to be factors capable of causing maldevelopments and monstrosities. It is possible that such factors influence abnormal growth of the fertilized human ovum.

In my specimen the embryos have a common amnion, and originally the yolk sac was probably single. The next step is to link up these morphological features with the known facts about the development of the normal ovum. Probably the extra-embryonic mesoderm becomes differentiated early in the growth of the ovum, even before the yolk sac and amniotic vesicles are developed from the inner cell mass. The two vesicles appear early in the development of the ovum, and are undoubtedly derived from the embryoblast (inner cell mass). In the early stage of development they are closely related, and there is little difference in the size of the two vesicles. It must be assumed that the early stage of my specimen was represented by a single amniotic vesicle. Whether two yolk sacs were present is uncertain, but there is no evidence of two yolk sacs in the specimen. Similarly, it must be postulated that only a single connecting stalk was present, for the umbilical cord is single and serves both embryos. The early stage of the ovum can therefore be assumed to be represented by a single trophoblast, extra-embryonic mesoderm, amnion, and connecting stalk.

The specimen strongly suggests, therefore, that duplication arose actually in the embryonic plate, for there is no reason to believe that the yolk sac was duplicated, and the amnion certainly was not. The important point to be grasped is that duplication must be attributed to a relatively late stage of development, much later than is postulated by the blastomere hypothesis, later, indeed, than the formation of the two vesicles. Unless this point of view is accepted it is impossible to account for the appearances of the specimen.

The most probable interpretation—though here one encroaches upon the field of conjecture—is that two embryonic axes arose in the embryonic plate. I think it extremely unlikely that a single embryonic axis underwent fission to produce two embryos, for the following reasons. The area of fusion between the two embryos is small, and the major organs, such as the neural tube and intestine, are separate, without any sign of communication. At the early stage of development illustrated by the specimen one would expect to find evidence of a communication between these structures if the two embryos had arisen by fission. Again, the two embryos are parallel, and there is no divergence between the two axes. These facts suggest that the embryos did not develop by fission of a single embryonic axis, and the evidence, though admittedly circumstantial, is in favour of the view that two embryonic axes developed originally (one being imperfect in its cranial end), and that fusion was a later phenomenon.

The specimen therefore supports the view that human uniovular twins and double monsters result from two embryonic axes developing on the embryonic disk. This conception has already been put forward by Stockard,⁹ and others, from embryological work on lower animals. It will be seen that the hypothesis is quite at variance with the blastomere theory, and that it attributes the formation of uniovular twins and monsters to a much later stage of development than has previously been supposed.

DESCRIPTION OF THE SECOND SPECIMEN

The two embryos (Figs. 3 and 4) are joined to the chorion by a common umbilical cord, and they have a single amnion. The axes of the embryos are parallel, but

the smaller embryo is distorted by the large vessels of the umbilical cord. The smaller embryo—embryo B—lies nearer to the chorion than embryo A, and the curvature of the umbilical cord has produced a rotation of embryo B around a vertical axis. Embryo B lies caudal to the cord, and no part of it cranial to the cord has developed.

The larger embryo A measures 3.15 mm. long, and is 1.46 mm. broad. Embryo B measures 1.45 mm. long and 1.15 mm. broad. The line of fusion between the two embryos is small, and is in the region of the mesonephric tubules and duct; it lies above the level of the lower limb bud of A, and below the umbilical cord. The two coelomic cavities communicate, but the two mesenteries and intestines are separate. It is not possible to calculate the number of segments which are fused, but it is unlikely that more than two take part in the fusion. The most difficult interpretation is the course of the vessels of the umbilical cord, for most of the vessels seem to favour embryo B rather than embryo A.

EMBRYO B

The embryo is imperfectly formed, and is represented only by its caudal part below the level of the umbilicus. The embryo has no head, heart, pharynx, or liver. Furthermore, there is no evidence of lower limb buds; in this respect the embryo differs from the parasite—*omphalopagus parasiticus*. The neural tube, notochord, mesonephros, mesentery, and intestine are normally developed for the part of the embryo which is represented in the specimen. The neural tube ends blindly in the cranial part of the embryo, and is closed. Six somites can be counted in the specimen, and they correspond in development with those of the larger embryo. The intestine also ends blindly when traced cranially, but there is a suggestion of division in its upper part which in some ways recalls the lung buds of the larger embryo. The vascular system is represented by a single dorsal aorta and cardinal veins.

EMBRYO A

The larger embryo is normally developed, except along the line of fusion with the parasite. Fortunately, the specimen is almost perfectly preserved, and shows optic cups, olfactory depressions, otic vesicles, and hypophyseal diverticulum. The primitive heart and liver are well shown, but there is as yet no sign of the suprarenal glands. The limb buds are well formed, and the vascular system is normally developed. It is difficult to trace the vascular connexions between the two embryos, and it is unlikely that the parasitic foetus would have been vascularized from the host during extrauterine life except by way of the umbilical vessels.

A detailed description of the larger embryo is beyond the scope of this contribution, as it is a subject for the pure embryologist. The essential features can easily be made out from the accompanying illustrations. The main object of this contribution is to indicate the method of formation of monsters rather than to describe the embryological features of an early human embryo of the stage represented by embryo A.

In conclusion, I have to record my thanks to Professors J. P. Hill and H. H. Woollard for the help they have given me in the interpretation of the specimens.

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WILFRED SHAW: TWO SPECIMENS OF EARLY HUMAN OVA

FIG. 1.—Section through region of primitive streak of specimen No. 1. The decidua (C) is necrotic, the villi (B) are simple, showing but a minor degree of branching. The magma reticular (A) intervenes between embryo and trophoblast. The upper of the two vesicles of the embryo is the amnion; the lower, the yolk sac. Blood islands (E) can be seen in wall of yolk sac. The primitive streak can be distinguished in the embryonic plate. The entoderm (D) has separated from the mesoderm in the preparation of the specimen.

FIG. 2.—Specimen No. 1. High power. Section through the region of primitive streak and groove. A, magma reticular; B, extra-embryonic mesoderm; C, cells of amnion; D, amniotic sac; E, entoderm; F, primitive groove; G, embryonic mesoderm; H, cavity of yolk sac.

FIGS. 3 AND 4.—A, cerebral vesicle; B, heart; C, coelom; D, intestine; E, primitive kidney; F, limb bud; G, dorsal aorta; H, neural canal; I, chorionic villi; K, amnion; L, umbilical vessel; M, mesonephric duct; N, neural canal of parasitic embryo, O, liver. The smaller embryo has no head, heart, or liver. The area of fusion is in the region of the primitive kidney and umbilicus. The amnion is single.